HARMONIZING REGULATORY FRAMEWORKS for Pharmaceutical Innovation

By Celeste Frankenfeld Lamm, PhD, Roger Nosal, and Ian Rees

To accelerate the adoption of innovation in the global administration of the pharmaceutical industry, regulatory authorities and industry trade organizations must expand their scope and pursue a collaborative approach to recognition and reliance to streamline processes, enhance product quality, and improve patient access to medicines.

The pharmaceutical industry faces significant barriers to innovation, primarily driven by regulatory divergence and the high costs associated with the development of new medicinal products and manufacturing processes. A collaborative approach between regulatory authorities and the industry is essential to streamline processes, enhance product quality, and improve patient access to medicines.

Implementing reliance pathways can facilitate the approval of innovative technologies by allowing regulatory bodies to leverage existing assessments from trusted authorities. Global alignment among regulatory authorities and transparency in presenting and addressing technical and regulatory challenges are essential to eliminating barriers to implementation of innovations globally.

BACKGROUND

Innovation has a multitude of definitions. It can refer to novel creations or ideas, new compositions, or inventions. The International Organization of Standardization (ISO) TC 279 Innovation Management technical committee defines innovation as "a new or changed entity, realizing or redistributing value" [1]. In the pharmaceutical industry, innovation most often refers to the development of more effective medicinal products, such as modalities, devices, and diagnostics. It also includes the practical implementation of new processes and technologies that improve manufacturing, enhance product quality assurance (e.g., ensuring product consistency and reducing product discards), and increase patient use, convenience, and access to medicines.

Leaders of several regulatory authorities have generally encouraged the development of technological innovations in pharmaceutical manufacturing. In fact, nearly all governmental regulations require that application authorization holders maintain accountability for technical and scientific integrity, quality, and modernization of manufacturing processes in accordance with evolving current and contemporary standards.

This prospective approach to continuous improvement is accomplished through the introduction of changes that enable medicinal products to be manufactured and verified by means of generally accepted contemporary scientific methods. For example, as the collective understanding of the potential mutagenic safety risks for the presence and/or formation of nitrosamines grew, the industry was forced to assess and, where appropriate, adopt optimized manufacturing to demonstrate requisite control. Similarly, emerging environmental concerns have driven the industry to adapt manufacturing processes, testing, and facility utility operations to demonstrate improved environmental safety and sustainability.

In principle, the scientific and technical justification for the approval and implementation of an innovative technology or modality should be the same for all pharmaceutical regulatory authorities. Global alignment among regulatory bodies enables and facilitates the preparation and submission of a single innovative product or variation application, prompts receipt and response to one list of questions, and can result in a globally harmonized approval. A globally aligned commitment among regulatory authorities that effectively expedites innovations will promote unprecedented process improvements and optimization. Further, it will significantly increase product quality assurance. In fact, many pharmaceutical manufacturers have signaled their intent to capitalize on established control strategies to adopt real-time process monitoring and automated and digital technologies where regulatory barriers are reduced [2].

Implementation of these technologies would increase opportunities to reinforce green chemistry and significantly reduce carbon footprints. By embracing these transformative practices, the pharmaceutical industry could enhance its responsiveness

to public health needs, reduce waste, and contribute to a more sustainable future. Increased quality assurance and the ability to respond quickly to health needs fosters a resilient supply chain. This resilient supply chain ultimately benefits patients and the environment.

Both regulators and industry agree that improving the health of patients through the development of medicinal products is fundamentally predicated on assuring appropriate product quality and increasing patient access. This patient-centric focus should be central in innovation efforts. In fact, it is incumbent on industry to convey transparency in the development of innovative technologies, including technical and regulatory challenges. Transparency is crucial for aligning expectations and facilitating the implementation of innovations to effectively ensure the reliability of high-quality medicinal products.

Intertwined industry and regulatory challenges limit the advancement of new technologies. Self-imposed industry barriers, such as the imprecision of gauging adequate and sustainable, short- and long-term return on investment (ROI), concern with the preservation of intellectual property, and the unpredictability of consistent and expeditious global regulatory approvals, has limited industry commitments to continuously improve manufacturing processes and adopt innovative technologies.

Although numerous industry and regulatory coalitions and working groups strive to promote global regulatory harmonization, divergent regulatory expectations, particularly with respect to novel technologies and modalities, remain a barrier to innovation. A striking example of the challenge associated with harmonization is the lengthy regulatory timelines, estimated to be greater than five years, required to approve and implement a single postapproval change globally.

This article proposes reinforcement of several strategic initiatives and approaches for mutual reliance among global regulatory authorities and the adoption of tactical and operational pathways to effectively expedite approval and implementation of innovative technologies. Leadership from consortia, like the International Coalition of Medicines Regulatory Authorities (ICMRA), has identified options and developed pilots to demonstrate the effectiveness of mutual reliance. In addition, the International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH) provides guidance on globally harmonized technical standards. However, the absence of meaningful pathways to operationalize these collaborative opportunities remains a rate-limiting obstacle. This is why we advocate for establishing an independent collaborative organization that includes representatives from regulatory authorities, pharmaceutical sponsors, manufacturers, equipment and material suppliers, patient advocacy foundations, and policymakers to develop streamlined pathways that eliminate barriers to innovation globally.

ADDRESSING REGULATORY HARMONIZATION

Regulatory authorities recognize the importance of creating incentives to foster modernization and innovation in pharmaceutical manufacturing. To this end, the ICMRA recently endorsed and sponsored exploratory pilot programs to improve alignment among regulatory authorities globally, with particular emphasis on innovation. Similarly, the US Food and Drug Administration (FDA) and European Medicines Agency (EMA) have taken prospective steps to facilitate the development and advancement of innovative technologies by forming dedicated teams to guide these technologies through the regulatory process.

Increased quality assurance and the ability to respond quickly to health needs fosters a resilient supply chain. This resilient supply chain ultimately benefits patients and the environment.

Industry experience indicates that these efforts and approaches have been largely positive and successful in improving communication, transparency, and engagement [2, 3]. An additional avenue to enable innovation is reliance and recognition, which promote opportunities for alignment in approvals and technical implementation among regulatory authorities. Under this framework, an assessment or inspection conducted by one authority can be accepted by others, expediting assessments, inspections, and streamlining the overall regulatory process. Several recent examples illustrate the viability and challenges of regulatory efforts to promote innovation.

ICMRA Pilot

The ICMRA collaborative assessment and inspection pilots bring regulatory authorities together to act as one team in assessing a postapproval change or hybrid inspection, with the goal of providing a single, simultaneous outcome. During the ongoing pilot, the ICMRA recognized the need to share information across a single platform to streamline the collaborative assessment of facilities and postapproval changes (PAC).

"Further reliance among regulators for CMC [chemistry, manufacturing, and controls] review requires that the data for the same product, same facility(ies) and same change(s) be submitted in the same format [e.g., following harmonized standards specified in ICH M4Q, M8, etc.]. It also requires convergence of regulators' specific data expectations for sponsor submissions, their standards for CMC related regulatory review, and their resulting assessments" [4].

Participation in collaborative processes such as ICMRA pilots can also engender the trust necessary to enact reliance or recognition between agencies as they have insight into the review or inspection processes.

ICMRA, ICH, IPRP, and PIC/S Work Plan

The ICMRA, ICH, International Pharmaceutical Regulators Programme (IPRP), and Pharmaceutical Inspection Convention and the Pharmaceutical Inspection Co-operation Scheme (PIC/S) have authored a joint work plan, with the intent to strengthen international collaboration [5]. Each organization has identified steps to promote greater harmonization, ranging from surveys across regulators on their use of quality assessment tools developed by the IPRP to assessing the need for internationally harmonized unique identifiers for key pharmaceutical quality information.

Pharmaceutical Company Collaboration

Several pharmaceutical companies have collaborated with national regulatory authorities in company-initiated reliance pilots. In the Sanofi reliance pilot, 21 national regulatory authorities agreed to participate, allowing Sanofi to submit a single dossier along with an assessment report from Health Canada for a postapproval change in vaccine filing and packaging activities.

Per the agreement, the participating authorities would approve the change within six months. The World Health Organization (WHO) recommended a review period for major postapproval changes [6]. The Roche-Accumulus Synergy reliance pilot, like the Sanofi reliance pilot, follows WHO reliance principles to enable cross-regulator visibility into the assessment of a postapproval change [7].

The participating agencies submit their review questions on the Accumulus platform, which provides a centralized location for all to view the questions and Roche's response. Amgen also conducted a reliance pilot using the Accumulus platform to enhance visibility for participating regulators [8]. During this pilot, the agencies involved accessed the information requests each agency submitted after reviewing the reference country's assessment of the major variation, along with Amgen's corresponding responses.

AstraZeneca also conducted two reliance pilots using predetermined reliance parameters. These included an agreement that the core package would not include market-specific requirements, no local testing would be conducted, and relying agencies would align to a predefined timeline [9]. The EMA established support for these company-initiated pilots, inviting pharmaceutical companies to contact the EMA to attend kickoff meetings with national authorities and provide clarification on assessment reports that are used as reference for the reliance procedure [10].

ISPE Survey

The ISPE Survey on Barriers to Innovation was completed at the end of 2023. The preliminary report confirmed that global regulatory divergence and industry reluctance to invest in innovative technologies without a positive ROI are the primary factors influencing the desire to innovate [11].

WHO Framework

In addition to being a transparent and evidence-based pathway for regulatory authorities operating at an advanced level of performance, the WHO's Listed Authorities (WLA) framework for designating and publicly listing regulatory authorities is intended to foster regulatory convergence, harmonization of approaches, and international cooperation [12].

CURRENT STATE OF REGULATORY GUIDANCE

Pockets of reliance and recognition in regulatory guidance already exist. For example, the Medicines and Healthcare Products Regulatory Agency (MHRA) established an International Recognition Procedure (IRP). Under this procedure, applicants that have received an authorization from a recognized reference regulator (RR) can apply for IRP for marketing authorizations, line extensions, variations, and renewals. If the RR approval is within two years of application to IRP, then the submission may be eligible for approval within 60 days [13]. Other health authorities are also piloting or establishing reliance pathways [14, 15].

Furthermore, the Access Consortium composed of pharmaceutical regulatory authorities from Australia, Canada, Singapore, Switzerland, and the UK actively initiates work-sharing opportunities in the assessment of applications [16]. Work sharing offers an important means of building and maintaining regulatory expertise across the global regulatory network. For example, the PIC/S established inspection standards and advanced the harmonization of GMP inspections. These initiatives lay the groundwork for reliance and recognition.

During the COVID-19 pandemic, the pharmaceutical industry, along with regulatory authorities, faced an unprecedented challenge to expedite approval of vaccines and to provide distribution and access to people globally. In response, a shift in the development and commercialization paradigm was deployed to accommodate these objectives in three significant ways.

- Industry adopted a parallel rather than sequential approach to product development, simultaneously developing drug substance, drug product, and administration devices.
- Industry representatives consistently engaged regulatory authorities. The increased communication and transparency enabled rapid development and improved decision-making.
- Regulatory authorities communicated directly among themselves and mutually recognized application approvals, inspections, and testing.

The rapid development, approval, and distribution of vaccines globally would not have been possible without these adaptations [17–26]. Perhaps most important, these approaches demonstrate that industry and regulators are able to effectively collaborate to advance technological development with appropriate incentives. The concept of reliance and recognition in conjunction with increased transparency and communication are, perhaps, the most ostensibly enduring and applicable approaches to improve the advancement of innovative technologies and modalities.

The initiatives mentioned, along with the unprecedented response to the COVID-19 pandemic, reflect incremental progress toward establishing streamlined pathways for innovation

implementation. Although the measures taken by regulatory bodies have effectively motivated the industry to develop and adopt certain technological advancements—such as process analytical technology and continuous manufacturing—the degree and pace of technological innovation adoption across the industry have remained limited and slow.

BENEFITS OF INVESTING IN INNOVATIVE TECHNOLOGIES

The pharmaceutical industry undertakes development of innovations only after rigorously evaluating the cost, impact, and results. There must be legitimate and tangible incentives for industry to invest in innovations, and a positive ROI is the primary justification for developing and implementing an innovative technology. The value for industry is measured by increased productivity, improved product quality assurance, and expanded patient access to medicines globally. These incentives are not mutually exclusive but serve as key factors in balance against anticipated investment costs that are largely influenced by regulatory acceptability.

The financial implications of innovation are seldom addressed by regulatory authorities because they fall outside the scope of pharmaceutical regulation. Nevertheless, understanding the significance of costs is essential for fostering innovation. Decisions to innovate are largely driven by economic factors that are frequently determined in response to several key questions:

- When will the innovative technology result in a positive ROI and how will this gain be translated into cost savings?
- Is this new technology or modality a legitimate platform for multiple products?
- Does the increased level of assurance of quality justify the cost of investing and maintaining innovative technologies or modalities?
- Will this innovation be acceptable with the same expectations from regulatory authorities globally or will there be significant divergence that could complicate or delay implementation?

The responses to these questions largely govern decisions to proceed with technological innovations and manufacturing optimizations. Consequently, the impact of regulatory acceptability and harmonization cannot be underestimated.

The tangible benefits of innovative technologies are frequently less straightforward than the concrete and measurable cost of investment in new infrastructure, equipment, or facilities. Quantifying improvements in quality assurance and productivity prior to implementation can be particularly challenging, and the initiation of new technologies may require substantial lead times to resolve initial operational issues. The adoption and full implementation of innovative technologies coincide with the strong desire to expedite medicines to patients. As a result, economic benefits of innovation are most effectively assessed over the life cycle of a product, which is not precisely predictable.

Additionally, continuous improvement of manufacturing processes, controls, and analytical methods are hampered by various barriers. Delays encountered when installing and implementing nonstandard technology and the high cost of investment in new infrastructure to establish and support innovations frequently determine whether the ROI is justified. Divergent and inconsistent global regulatory acceptability contributes to additional delays and costs, particularly when different technologies (e.g., batch and continuous manufacturing) must be maintained while awaiting approval from a large number of regulatory authorities.

GLOBAL REGULATORY DIVERGENCE

In the current landscape of pharmaceutical regulation, the goal of establishing a single regulatory application that satisfies all global regulatory authorities remains aspirational, underscoring the complexities and challenges faced by the industry. Despite significant advancements made by the ICH, different regional requirements persist, not only in accommodations articulated in formal guidelines but also in country-specific expectations that exceed the criteria established in those guidelines.

These differences are further complicated by varying interpretations and applications of the same guidelines across jurisdictions, reflecting diverse regulatory cultures, risk tolerances, statutory sovereignty, and local priorities. The lack of uniformity means that the content of a regulatory application for an innovative technology deemed acceptable in one region may face additional scrutiny or require increased information and data or modifications in another. This level of divergence creates inefficiencies and delays in approval and implementation. It also increases costs and complicates supply chain integrity.

Moreover, the regulatory landscape is fragmented by the involvement of numerous local and national agencies. Each of these agencies is responsible for distinct areas, such as environmental assessments (i.e., emissions, water, and soil pollutants); health and safety standards; fire protection and evacuation protocols; supply chain ethics; cyber safety; and data management. These agencies operate under different legislative frameworks worldwide, further amplifying the complexity. Together, these factors contribute to prolonged timelines and increased uncertainty in the approval process, posing significant challenges to pharmaceutical innovation and the global implementation of new technologies.

The impact of global regulatory divergence on innovation is a long-standing issue. Currently there is a chronic and significant regulatory lag for global approval of postapproval changes associated with continuous improvement [27]. A recent review article from the One-Voice-of-Quality initiative, which compiled data from 18 global pharmaceutical companies on gathered postapproval changes, revealed a stark reality: within the three-year span the data was collected, only one country out of 156 approved all changes within six months [28]. Although the survey period from 2019–2021 overlapped with the global pandemic, which conceivably impacted timelines, the data nevertheless illustrates the broader implications that time to approval for postapproval changes has been growing since before the pandemic and continues to present a challenge for global products [29–31].

This situation is exacerbated by the variation in information that is approved, even when the product and process are the same.

In particular, one recent source highlights that the concept of a drug product control strategy—which is a globally aligned, innovative regulatory approach adopted under ICH Q8 and reinforced in ICH Q9, Q10, Q11, and Q12—has not been effectively harmonized. In fact, the global acceptability of a regulatory starting material strategy by four or more regulatory authorities was less than 5% [32]. In addition, the same survey from the IQ Consortium indicates that global acceptability of the common technical document for a given product manufactured one way at one site for global distribution is relatively low, at less than 30%. This regulatory fragmentation forces companies to adhere to several different sets of requirements to manage compliance separately for multiple countries where the product is approved.

The probability of global regulatory inconsistency and duplication, which significantly increases costs and liabilities, reduces the value of incentives to innovate. Global projections that establish and maintain timely reliability of product supply are severely challenged when multiple equipment lines, facilities, product specifications, and divergent regulatory requirements must be adopted to accommodate divergent regulatory expectations or approval timelines. Consequently, technological innovations and optimizations can be rendered out of economic reach, especially for manufacturers of generic products where the economic margins are slim and manufacturing facility turnover is tight. Incorporating innovations within this manufacturing paradigm is generally limited to products manufactured for single markets or for platform technologies used for the manufacture of multiple products.

It is not surprising that the industry is challenged to advance innovative technologies, even those that improve product quality, without assurance that the cost to manage regulatory divergence is not prohibitive. This is because well-established ICH guidelines are not globally accepted; there is disharmony even when ICH approaches are followed, and process and analytical improvements require lengthy approval times. The impediment to the adoption of innovation is even more disconcerting when considering the global issue of drug shortages. A large proportion of drug shortages are the direct result of quality failures or supply chain disruptions. The implementation of innovative technologies that currently exist could theoretically mitigate many of these failures and disruptions.

For instance, machine learning algorithms that monitor manufacturing processes and assist in decision-making could reduce product discards. Similarly, continuous processing and distributed or decentralized manufacturing could provide greater flexibility to scale production volumes in response to changing demand. However, the costs associated with investing in these technologies are compounded by the differences in global regulatory environments. Even if all WHO Listed Authorities were to harmonize their expectations for these innovations, many other agencies have yet to do so, which discourages investment. One clear incentive for improving global harmonization is the potential to reduce the prevalence of drug shortages. Additionally, reducing regulatory divergence would help address other challenges, such as the following:

- Redundant application assessments and facilities inspections create a significant burden for both regulatory authorities and industry.
- Regulatory authorities do not have sufficient capacity to separately engage in the requisite dialog necessary to enable innovative technologies to effectively and efficiently proceed through the regulatory approval process.
- Currently, many regulatory authorities do not have the capacity to assess applications that include innovative technology and/or inspect innovative manufacturing facilities independently.
- Global delays in approvals for continuous improvement supplements increases inventory and supply chain complexity and costs, which has resulted in drug shortages.

In addition to the challenges faced by the pharmaceutical industry when pursuing innovation, it is important to consider the resource constraints faced by both large and small regulatory agencies. These agencies often operate with limited budgets and staffing. This means they may struggle to establish regulatory frameworks or the expertise needed for increasingly complex medicines. Moreover, as processes are continuously optimized, these agencies may also find it difficult to have the requisite expertise and capacity to expeditiously review and process the increased volume of regulatory submissions.

For these reasons, it is incumbent on industry and regulatory authorities to collaborate on solutions to reduce barriers to innovation adoption. Although industry and regulators have attempted to mitigate the barriers to implementation of innovative technology, the impact has been modest at best. While the success of mutual recognition agreements has been encouraging, the benefits have been limited and narrowly focused. Streamlining regulatory expectations, review processes, and approval of post-approval optimizations/innovative technologies across multiple regulatory authorities will provide a significant incentive for the pharmaceutical industry. Regulatory authorities and patients will also benefit as regulatory capacity constraints diminish, thereby expediting patient access to medicines. Improving global alignment and acceptability emphasizes a concerted focus on sustainably increasing patient compliance as well. Given the challenges and the considerable resources required for existing pathways, it is imperative to identify a long-term, sustainable solution.

PROPOSED SOLUTIONS

The ICMRA plays a vital role as a thought leader in advancing regulatory innovation. However, a gap remains in translating its strategically collaborative initiatives into concrete, coordinated operational action. In the collaborative assessment and hybrid inspection pilots, the significant resources required to bring multiple regulatory agencies together and into alignment is a constraint that limits its expansion. The ICH has established harmonized scientific and technical standards but does not govern how individual regulatory authorities interpret those standards, nor does it extend to promoting harmonized national statutory

requirements or implementation frameworks that enable mutual reliance and recognition.

In exploring potential solutions, it is beneficial to draw upon established instances of reliance and recognition rather than relying solely on pilot programs. Noteworthy examples include the cooperation between member states of the European Union through the EMA, as well as the collaborative practices observed within the civil aviation industry.

In the civil aviation industry, bilateral agreements ensure mutual recognition between aviation authorities [33, 34]. These agreements guarantee the recognition of safety standards and certifications to enable flight operations and associated services, such as maintenance, across the globe and ensure stringent safety standards while minimizing administrative burden. Similar to the model of the EMA, these agreements are built on agreed-upon standards and shared work, promoting recognition. The pharmaceutical sector could draw valuable lessons from the aviation industry: a single aircraft design is compliant with the regulations of multiple countries, allowing it to operate internationally with a standardized set of performance and safety requirements. The standardization of aircraft compliance along with harmonized air travel criteria are governed by collaborative regulatory alignment.

The successful collaborative approaches in aviation can be mirrored in the pharmaceutical industry through the expansion of existing regulatory programs that ensure comprehensive global coverage and a unified regulatory framework and pathways. The EMA relies upon specific elements of cooperation: convergence, which aligns national regulatory frameworks; collaboration, which involves sharing data, expertise, and participation in EMA committees; and recognition, where regulatory decisions, including GMP authorizations, are mutually acknowledged. The success of these elements relies upon an accepted set of standards, trust in maintaining those standards, and cooperative efforts among stakeholders. Although the system is not without its limitations, it is noteworthy that European regulators operate within a framework characterized by collaboration and mutual recognition.

During the COVID-19 pandemic, the importance of open, clear, and regular communication between regulatory authorities and industry was a hallmark of regulatory agility and adaptation that led to unimpeded innovative development and implementation. Although the occurrence of future pandemics is uncertain, a surge in the development of innovative and complex new therapies and technologies poses regulatory and operational challenges that warrant effective communication, transparency, and collaboration between and among industry and regulatory authorities globally. It is therefore imperative to establish a sustainable framework of flexible pathways that enable and expedite innovative technologies and improve approval efficiency that reduces the burden on resource capacity. Regulatory authorities already face resource capacity constraints and are frequently forced to adapt to the advent of diverse and nonstandardized technologies in applications and inspections.

Effective application of regulatory reliance, mutual recognition, and harmonization requires a collaborative and inclusive forum that brings together industry, regulatory authority, and legislative stakeholders.

CALL TO ACTION

Effective application of regulatory reliance, mutual recognition, and harmonization requires a collaborative and inclusive forum that brings together industry, regulatory authority, and legislative stakeholders. Such a forum can convene leadership from diverse jurisdictions to share expertise and align priorities, leveraging the WHO's global mandate to ensure broad representation. In addition, the active involvement of policymakers is crucial to facilitate necessary legislative revisions that go beyond current national legislation, enabling flexible regulatory pathways for innovative technologies.

Equally important is the engagement of industry groups to provide practical perspectives on regulatory bottlenecks, including appropriate estimates for ROI and to identify where harmonization efforts will have the greatest impact. Beyond addressing these challenges, the forum must also serve as a critical bridge to translate initiatives and thought leadership into concrete, coordinated action. By integrating these stakeholders within a single, coordinated platform, the forum can drive actionable solutions that bridge the gap between thought leadership and implementation, ultimately accelerating patient access to innovative medicines worldwide.

Uniting strategic leadership offers incentives for all stakeholders by:

- Improving aligned expectations for global acceptability of innovative technologies
- Expediting application approvals, especially for those that include innovative technologies that increase product quality assurance
- Reducing compliance and supply chain complexity associated with different regulatory commitments
- Reducing the capacity required for redundant review and assessment of regulatory applications, including postapproval continuous improvement supplements as well as redundant inspections
- Introducing opportunities to establish appropriate criteria for platform technologies

In addition to establishing a collaborative forum that translates concepts to action, industry should take steps to understand the costs of not innovating. In particular, industry should give attention to tangible metrics such as product discards resulting from less-robust processes and raw material consumption of less-efficient processes.

It is also essential to evaluate the long-term and immediate financial impact of global regulatory divergence. The cost of delays in market entry and the concomitant and incremental increase in resources required to manage manufacturing variations, adjustments to control strategies, and duplicative regulatory applications have an unequivocal impact for regulatory authorities, pharmaceutical companies, and patients globally.

CONCLUSION

Improving global administration of postapproval changes has been an industry focus. However, the need for reliance and recognition to enable adoption of innovation demands an expanded and concerted approach from a consortium of regulatory authorities in collaboration with industry trade organizations. The limited efforts, to date, to adopt regulatory reliance and recognition have been encouraging [2]. An expansion of these reliance programs to address barriers to innovation adoption that provides broad, harmonized acceptance will undoubtedly promote the appropriate financial incentives for industry to adopt innovation. The reduction in duplicative application reviews will similarly improve resource capacity among regulatory authorities.

The discovery, development, and delivery of a new medicine is complicated. The probability that a therapeutic compound identified during discovery will lead to a commercial product is extremely low, and only about 10% of all candidates that enter clinical trials result in products [35–37]. Most advancements in medicine are dependent on incremental, progressive, and concerted research, and development with multiple contributors from a wide range of disciplines. Development of those assets into a ready-to-use medicine that is manufactured reliably with consistent assurance of quality is a major undertaking, even without innovative technologies. The introduction of innovative modalities and technologies demands a transparent and concerted alignment between regulatory authorities to continue to improve patient access globally to state-of-the-art medicines.

References

1. ISO Standard 56000:2025. "Innovation Management — Fundamentals and Vocabulary." January 2025. www.iso.org/standard/84436.html
2. Potter, C. "ISPE Global Pharmaceutical Innovation Survey Findings: A Review." *Pharmaceutical Engineering* 44, no. 5 (2024):50–56.
3. Nosal, R., and C. Potter. "Harmonization of Manufacturing Innovation, Results from the ISPE Survey." Presented at the Global Pharmaceutical Manufacturing Leadership Forum, Orlando, Florida. 14 October 2024.
4. International Coalition of Medicines Regulatory Authorities. "Pharmaceutical Quality – Regulatory Collaboration PIlots: Call for Industry Applications." www.icmra.info/drupal/en/strategicinitatives/pqkms/pq_pilots_call_for_industry_applications
5. International Coalition of Medicines Regulatory Authorities. "ICMRA - ICH-IPRP-PICS Joint Work Plan for Harmonisation and Convergence Work to Advance Development of a Reuglatory Pharmaceutical Quality Knowledge Management Capability." icmra.info/drupal/strategicinitatives/pqkms/joint_work_plan_24sept2024
6. Gastineau, T., C. Ban, A. Basso, F. Brehme, A. Silva, O. Faure, et al. "Worldwide Regulatory Reliance: Launcing a Pilot on a Chemistry, Manufacturing and Control Post Approval Change for a Vaccine." *PDA Journal of Pharmaceutical Science and Technology* (November 2023). doi:10.5731/pdajpst.2023.012850
7. Accumulus Synergy. "Accumulus Synergy Launches Highly Anticipated Cloud Based Platform." 4 August 2025. www.accumulus.org/accumulus-synergy-launches-highly-anticipated-cloud-based-platform/
8. Singh Deo, S. "Amgen and Accumulus Revolutionize Regulatory Submissions with First Digital CMC Dossier." 6 February 2025. www.pharmanow.live/latest-news/amgen-accumulus-submits-first-ever-digital-cmc
9. Pellett, M. "Regulatory Reliance in LCM: A Reality, Not Just a Dream?" Presented at the CASSS CMC Strategy Forum Europe, 2024. www.casss.org/docs/default-source/cmc-strategy-forum-europe/2024-speaker-presentations/pellett-mark-astrazeneca-2024.pdf?sfvrsn=dc0abf5f_6
10. European Medicines Agency. "Reliance for Post-Authorisation Changes: Pilots for the Pharmaceutical Industry." 15 July 2025. www.ema.europa.eu/en/partners-networks/international-activities/multilateral-coalitions-initiatives/reliance-applied-post-autorisation-changes-pilots-pharmaceutical-industry#ema-role-73987
11. International Society for Pharmaceutical Engineering. "Enabling Global Pharmaceutical Innovation: Delivering for Patients." 18 November 2025.ispe.org/initiatives/regulatory/enabling-global-pharmaceutical-innovation-delivering-patients
12. World Health Organization. "WHO-Listed Authority (WLA)." 18 November 2025. www.who.int/initiatives/who-listed-authority-reg-authorities
13. Medicines and Healthcare Products Regulatory Agency. "International Recognition Procedure." Updated 17 September 2025. 18 November 2025. www.gov.uk/government/publications/international-recognition-procedure/international-recognition-procedure
14. Jiuang, W. W. "HSA's Regulatory Journey and Regulatory Reliance, IMDRF." 2024. www.imdrf.org/sites/default/files/2024-03/05%20-%20WJ%20Wong%20%28HSA%29.pdf
15. Government of Brazil. "ANVISA Published Normative Instruction (IN 289/2024) and Guidelines on Regulatory Reliance." 10 January 2024. www.gov.br/anvisa/pt-br/english/updates/anvisa-published-normative-instruction-in-289-2024-and-guidelines-on-regulatory-reliance
16. Medicines and Healthcare Products Regulatory Agency. "Access Consortium." 10 December 2020. Updated 26 February 2024. www.gov.uk/guidance/access-consortium
17. Nosal, R., A. Stokes, F. Montgomery, T. Watson, and A. Redmond. "Panel Discussion on COVID-19 and the Vaccine." ISPE Expert Xchange Series. 18 November 2021.
18. Nosal, R. "Developmen tof the COVID-19 mRNA Vaccine. Is the Paradigm Shift Sustainable?" ISPE Expert Xchange Series. 18 November 2021.
19. Nosal, R., N. Baylor, B. Allen, and C. Schnedar. "DIA Advanced Therapies: Lessons Learned from Development of Vaccines and Therapeutics in Response to COVID-19 Panel Discussion." Presented at the DIA Advanced Therapies: Innovations in CMC Conference. 10 November 2021.
20. Nosal, R. "A Summary of COVID-19 Vaccine Development: Is the Paradigm Shift Sustainable?" Presented at the DIA Advanced Therapies: Innovations in CMC Conference. 10 November 2021.
21. Nosal, R. "Keynote Address: A Summary of COVID-19 Vaccine Development; Is the Paradigm Shift Sustainable?" Presented at the Innovation and Quality Consortium Annual Summit. 13 October 2021.
22. Nosal, R. "mRNA Vaccines: A Paradigm Shift for Product Development and Manufacturing Capacity - COVID-19 Vaccine Experience." Presented at the PDA/FDA Joint Regulatory Conference. 29 September 2021.
23. Barrett, A., and R. Nosal. "Panel Discussion on SARS CoV-2 Vaccine Development." Presented at the Gulf Coast Consortium: Innovative Drug Discovery and Developmnet. 3 June 2021.
24. Nosal, R. "COVID-19 Vaccine Development and Commercialization: Industry Collaboration with Global Regulatory Authorities to Establish Quality Criteria to Expedite Access." Presented at the Gulf Coast Consortium: Innovative Drug Discovery and Development. 3 June 2021.
25. Barrett, A., and R. Nosal. "Panel Discussion on SARS CoV-2 Vaccine Development." Presented at the Gulf Coast Consortium: Innovative Drug Discovery and Development. 2 July 2020.
26. Nosal, R. "COVID-19 Vaccine Development: Industry Collaboration with Global Regulatory Authorities to Establish Quality Criteria to Expedite Access." Presented at the Gulf Coast Consortium: Innovative Drug Discovery and Development. 2 July 2020.
27. Harris, R., M. Vanhooren, K. Follman, B. Kendsersky, T. Watson, M. Imperati, et al. "An Evaluation of Postapproval CMC Change Timelines." *Pharmaceutical Engineering* 43, no. 5 (September/October 2023):26–33.

28. Vinther, A., E. Ramnarine, T. Gastineau, L. O'Brien, O. Brehm, and D. Fryrear. "Approaches to Design and Efficient, Predictable Global Post Aproval Change Managment System that Facilitates Continual Improvement and Drug Product Availability." *Therapeutic Innovation and Regulatory Science* 58 (2024):433–42. doi:10.1007/s43441-024-00614-9

29. Nosal, R. "Regulatory Harmonization Depends on Global Industry Connectivity." *Pharmaceutical Engineering* 36, no. 4 (July/August 2016):58.

30. Nosal, R. "Regulatory Harmonization, Leveraging Inspection Reliance." Presented at the Global Pharmaceutical Manufacturing Leadership Forum, Dublin. March 2019.

31. Nosal, R. "Keynote Address: At the Crossroads of New Quality Paradigm: Innovation, Acceleration and Regulatory Harmonization." Presented at the 5th Annual ISPE/FDA/PQRI Quality Manufacturing Conference, Arlington, Virginia. June 2017.

32. Beierle, J., N. S. Cauchon, T. Graul, Y. Hedberg, M. B. Holm, J. Lepore, et al. "Toward a Single Global Control Strategy: Industry Study." *Pharmaceutical Engineering* 42, no. 1 (January/February 2022):20–31.

33. European Commission. "Bilateral Agreements on Civil Aviation Safety." Accessed 18 November 2025. transport.ec.europa.eu/transport-modes/air/aviation-safety/aviation-safety-and-international-cooperation/bilateral-agreements-civil-aviation-safety_en

34. US Federal Aviation Administration. "Aviation Safety – International Agreements." Accessed 18 November 2025. www.faa.gov/aircraft/air_cert/international/bilateral_agreements/baa_basa_listing

35. Schuhmacher, A., M. Hinder, E. Brief, O. Gassmann, and D. Hartl. "Benchmarking R&D Success Rates of Leading Pharmaceutical Companies: An Empirical Analysis of FDA Approvals (2006–2022)." *Drug Discovery* Today 30, no. 2 (2025):104291. doi:10.1016/j.drudis.2025.104291

36. Yamaguchi, S., M. Kaneko, and M. Narukawa. "Approval Success Rates of Drug Candidates Based on Target, Action, Modality, Application, and Their Combinations." Clinical and Translational Science 14, no. 3 (2021):1113–22. doi:10.1111/cts.12980

37. Georgetown University. "Drug Discovery and Development." Georgetown Univeristy Office of the Senior Vice President for Research. 18 November 2025. https://osvpr.georgetown.edu/research-domain/health/drugdiscoveryanddevelopment/

About the authors

Celeste Frankenfeld Lamm, PhD, is Senior Director at Merck & Co., Inc., where she leads the CMC & Quality External Advocacy team. She serves as co-chair of ISPE's Product Quality Lifecycle Implementation (PQLI®) initiative and is an active contributor to several ISPE working groups, in addition to developing and delivering ISPE regulatory training workshops. She holds a bachelor's degree in biology and chemistry from Greenville University and a PhD in pharmaceutical chemistry from the University of Kansas. She joined ISPE in 2020.

Roger Nosal is the Senior Vice President and Head of Regulatory Affairs and Quality Assurance for Vaxcyte, Inc. He is also the Principal Consultant for Roger Nosal PharmaCMC Regulatory Consultants, LLC, supporting The Blackstone Group. For 12 years prior to September 2022, he was Vice President and Head of Global Chemistry, Manufacturing, and Controls at Pfizer, where he was accountable for all global regulatory CMC strategies and applications for innovative products and medical devices. He joined ISPE in 2007.

Ian Rees is a GMP Inspector for the MHRA since 2001. Previously, he was an Inspector with the Veterinary Medicines Directorate, and prior to that he helped create a startup biopharmaceutical firm, the MCA. In 2014, Ian was part of the team that created the UK cross-regulatory "one-stop shop" to provide regulatory advice on ATMPs. Ian led the MHRA's work in developing the new regulatory framework for decentralized manufacture. He joined ISPE in 2009.

2026 FOYA PROGRAM
SCHEDULE OF EVENTS

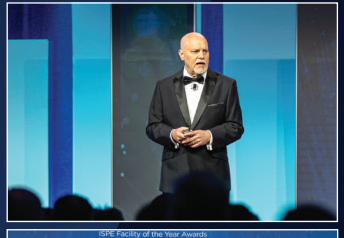
JANUARY
FOYA Judging Panel selects the 2026 FOYA Finalists and 2026 FOYA Category Winners

2 FEBRUARY
2026 FOYA Submission Finalists announcement
2026 ISPE Facilities of the Future Conference | San Diego, California, USA

20 APRIL
2026 FOYA Category Winners announcement
2026 ISPE Europe Annual Conference | Copenhagen, Denmark

18 OCTOBER
Celebrate with us as we formally recognize and honor the 2026 FOYA Category Winners on their achievements plus announce the 2026 FOYA Overall Winner!
2026 ISPE FOYA Banquet and Awards Celebration | Washington D.C., USA

18-21 OCTOBER
Engage with FOYA Category Winners and Judges through educational panels and networking opportunities
2026 ISPE Annual Meeting & Expo | Washington D.C., USA







Visit ISPE.org/FOYA for more information