Ahluwalia *et al. AAPS Open* (2025) 11:9
https://doi.org/10.1186/s41120-025-00113-7

AAPS Open

REVIEW

Open Access

The future of regulatory filings: digitalization

Kabir Ahluwalia[1*], Michael J. Abernathy[1], Marquerita Algorri[1], Nina S. Cauchon[1], Natalie M. Perico-Norred[1] and Rita Y. Albert Youssef[2]

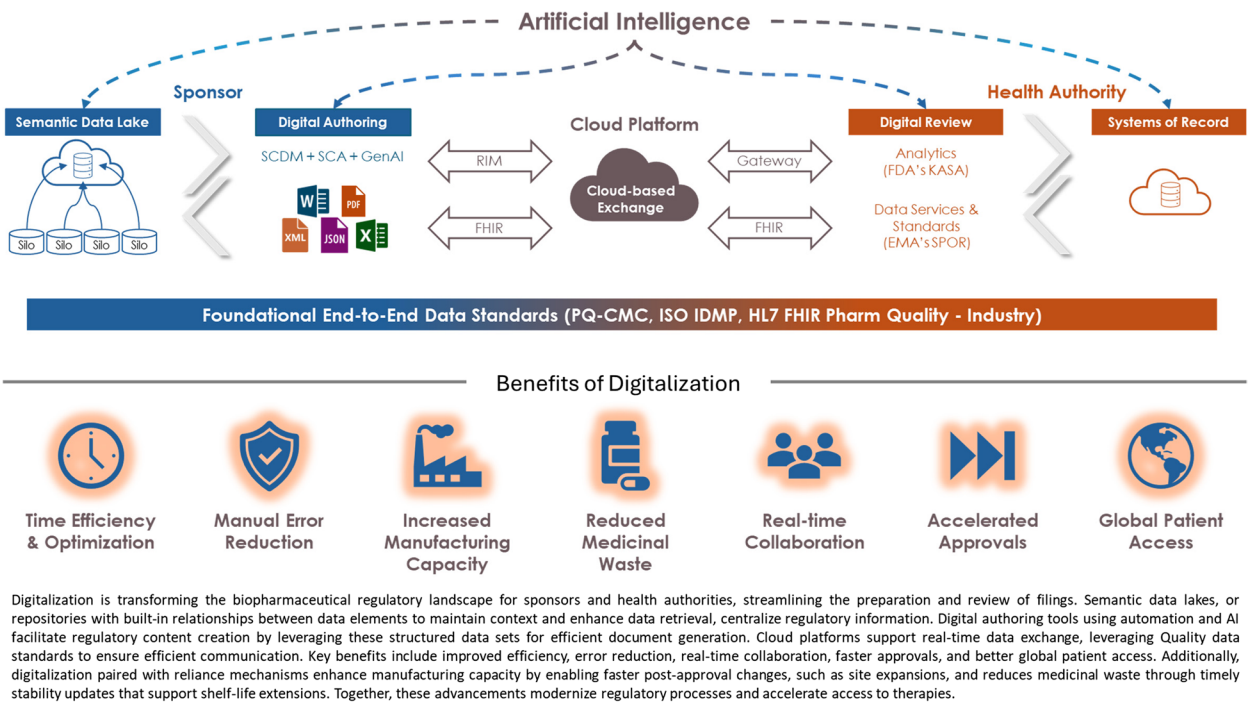
Abstract

The biopharmaceutical industry, while advancing rapidly in drug development, has lagged in the digitalization of regulatory submissions, leading to inefficiencies, delays, and increased administrative burdens. Current processes rely heavily on manual input, increasing labor burdens and the risk of errors, which in turn prolongs the preparation and submission of regulatory documents and delays global market access for patients. This review explores the transformative potential of emerging digital solutions such as Structured Content and Data Management (SCDM), Artificial Intelligence (AI), and cloud-based platforms. These technologies offer significant advantages, including automation of document preparation, real-time data integration, and enhanced collaboration between sponsors and global health authorities. Additionally, efforts to standardize data formats, such as PQ/CMC, ISO IDMP, and HL7 FHIR, are foundational to creating a harmonized framework for seamless information exchange. By integrating these tools and adopting standardized practices, the industry can reduce errors, improve compliance, and accelerate timelines for global regulatory approvals. Ultimately, this digital transformation can deliver more efficient pathways to market, increasing manufacturing capacity while reducing medicinal waste and ensuring faster patient access to new therapies. Implementation of digitalization practices will position the biopharmaceutical industry at the forefront of innovation in a rapidly evolving regulatory environment.

Keywords Artificial intelligence, Cloud platforms, Digitalization, Regulatory affairs, Structured content, Data standards, Automation

*Correspondence:
Kabir Ahluwalia
kahluwal@amgen.com
Full list of author information is available at the end of the article

Graphical Abstract



Digitalization is transforming the biopharmaceutical regulatory landscape for sponsors and health authorities, streamlining the preparation and review of filings. Semantic data lakes, or repositories with built-in relationships between data elements to maintain context and enhance data retrieval, centralize regulatory information. Digital authoring tools using automation and AI facilitate regulatory content creation by leveraging these structured data sets for efficient document generation. Cloud platforms support real-time data exchange, leveraging Quality data standards to ensure efficient communication. Key benefits include improved efficiency, error reduction, real-time collaboration, faster approvals, and better global patient access. Additionally, digitalization paired with reliance mechanisms enhance manufacturing capacity by enabling faster post-approval changes, such as site expansions, and reduces medicinal waste through timely stability updates that support shelf-life extensions. Together, these advancements modernize regulatory processes and accelerate access to therapies.

Introduction

The rapid expansion of digital technologies has revolutionized business processes across various industries, driving efficiency and innovation in sectors such as automotive, electronics, and chemicals through Artificial Intelligence (AI)-powered manufacturing and optimized logistics (Rathore et al. 2023). Despite these advancements, the biopharmaceutical industry has been slower to embrace digital innovation, particularly in the realm of regulatory submissions (Beierle et al. 2023). This hesitancy is partly due to the complexities of drug development and regulatory processes, as well as perceived regulatory risks, which is particularly relevant to major markets supported by mature regulatory agencies. Resource constraints further complicate digitalization efforts in low- and middle-income countries (LMIC), and further work is required to understand how digital tools can be effectively implemented in these regions. Delaying modernization may hinder timely and efficient regulatory submissions, prolonging drug approvals and delaying patient access to therapies, especially as regulatory requirements continue to evolve, and often diverge. Simply put, digitalization enables industry-wide internet-based collaboration, making regulatory information exchange more efficient. By improving submission efficiency and expediting reviews, it ultimately accelerates patient access to medicines.

To obtain global approval of their biopharmaceutical products, companies must submit and maintain regulatory documentation for clinical investigation and marketing authorizations to global health authorities. Following the initial submission, post-approval requirements must be met through regulatory submissions and/or inspections throughout a product's lifecycle to maintain compliance. Given the variation amongst these requirements in the global landscape, the process of gaining approval and maintaining global files is cumbersome and time consuming. Further, the current state of preparing regulatory files requires substantial manual input and administrative burden, such as consolidating regulatory requirements, tracking and monitoring previously submitted information, and making manual updates to multiple documents across many regions. As illustrated in Fig. 1, the process of generating, authoring, and exchanging regulatory information is time-consuming and labor-intensive, typically requiring several hundred hours to author and data-verify a single clinical trial application, and tens of thousands of hours annually to submit and maintain regulatory information for a moderately sized product portfolio. This process impacts all aspects of

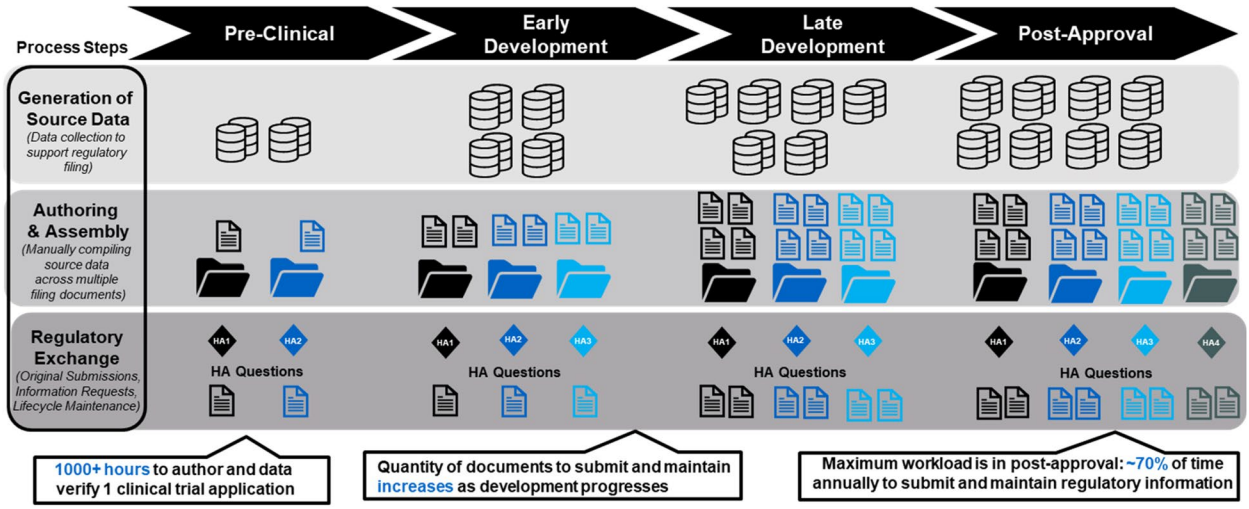


Fig. 1 Current Regulatory Filing Paradigm. Approximately 70% of time spent on regulatory filings is spent on post-approval submissions and maintenance for a moderately sized product portfolio. This extensive process affects all aspects of regulatory authoring, from pre-clinical all the way to post-approval, including the data collection to support filing, manually compiling source data across multiple filing documents, and regulatory exchange

regulatory authoring and associated filing types, clinical trial and marketing applications, responses to questions, life-cycle variations, facility filings, and others (Ahluwalia et al. 2022).

The technologies discussed in this article offer substantial advantages to simplify data management procedures, improve oversight of business processes, reduce the risk of human error, and can improve adaptability towards dynamic regulatory requirements. The current process of preparing, reviewing, and data verifying regulatory filings is a prime candidate for digitalization, which is the conversion of human-based processes to computer-operated processes. This review will discuss emerging data standardization efforts to establish a universal, harmonized language for information exchange between sponsors and health authorities, as well as technologies like Structured Content and Data Management (SCDM) and AI that streamline data assembly and management. Additionally, we will discuss cloud-based solutions that facilitate real-time, collaborative reviews. The integration of these advanced technologies provides a comprehensive approach to modernizing regulatory submissions. With these capabilities, the biopharmaceutical industry can achieve greater efficiency, enabling real-time responsiveness and broadening remote accessibility. Setting up automation systems may speed up adoption of data standards and implementation of cloud-based exchanges of regulatory information. Ultimately, these technologies have the potential to streamline and accelerate the development, manufacturing, and registration of novel therapies. By digitizing regulatory processes, companies can rapidly implement manufacturing changes, such as new production sites, increasing capacity to meet demand. Likewise, faster stability data updates can lead to timely approvals for shelf-life extensions, reducing medicinal waste. Together, these advancements facilitate faster global market access for patients.

Data standards

Data standardization is a cornerstone in the ongoing digital transformation of the biopharmaceutical industry, supporting the enhancement of data integrity, facilitating seamless data exchange, and improving regulatory compliance. These efforts not only streamline product approvals but also support simpler maintenance and consistent quality across global markets. As the industry moves towards a real-time, cloud-based data exchange ecosystem, interoperability and standardization across data systems are becoming increasingly critical.

In 2022, the U.S. Food and Drug Administration (FDA) introduced an enhanced version of the Pharmaceutical Quality/Chemistry, Manufacturing, and Controls (PQ/CMC) data elements, mapped to Health Level 7 (HL7) Fast Healthcare Interoperability Resources (FHIR) (Beierle et al. 2023). Similarly, the European Medicines Agency's (EMA) has developed the Substance, Product, Organization, and Referentials (SPOR) program for the implementation of International Organization for Standardization (ISO) Identification of Medicinal Products (IDMP) standards. Both the FDA's PQ/CMC and the EMA's SPOR standards utilize FHIR as the exchange

specification for transferring information between sponsors and health authorities. FHIR is an open-source data format with an Application Programming Interface (API) that provides flexibility and standardization in healthcare information exchange (Beierle et al. 2023). Through FHIR, sponsors and health authorities can securely exchange electronic correspondence using FHIR messages, which are downloadable in formats like XML and JSON. Its ability to accommodate regional terminology variations makes FHIR a versatile, global standard. Building on this foundation, the HL7 FHIR project known as "Pharmaceutical Quality—Industry" was initiated in late 2022 and published in 2024 (HL7 International 2024). This project aims to develop global internal quality data standards for the biopharmaceutical industry, covering scenarios such as technology transfers, manufacturing process changes, and stability data updates. This initiative, conducted in collaboration with industry stakeholders, aligns with PQ/CMC and ISO IDMP, representing a significant step towards global standardization (Beierle et al. 2023).

While the establishment of harmonized data standards is a significant advancement, their effectiveness hinges on the ability of both sponsors and health authorities to produce, analyze, and exchange data using tools that are fully interoperable with these standards. Data standards alone are not sufficient; they must be integrated into practical, operational tools that enable efficient data handling throughout the drug development and regulatory process. From the sponsors' perspective, these standards can be directly utilized by SCDM tools, which streamline the creation, management, and submission of regulatory documentation. The ability to seamlessly exchange data between sponsors and health authorities, facilitated by these standardized tools, is essential for realizing the full potential of a harmonized global regulatory environment. The Pharmaceutical Quality-Industry HL7 FHIR standard mentioned above can deliver submissions in any format required by a regulator (as either data or documents). The following section will explore how SCDM tools can leverage these data standards to enhance regulatory processes.

Structured Content and Data Management (SCDM)

SCDM is an approach that can be used to enhance the efficiency and automation of regulatory processes in the pharmaceutical industry. By organizing data into reusable, modular components, SCDM reduces redundancy, facilitates seamless updates, and ensures compliance with regulatory requirements. This methodology systematically organizes and manages data and information, thereby improving accessibility, reusability, and integrity.

At the core of SCDM is a centralized data repository composed of modular content blocks and data elements. These blocks may contain product-specific records or general information applicable across multiple products. Each content block acts as a container for related data elements, which can be reused to build or update filing documents for various regulatory applications. Data elements can then be efficiently distributed and updated across multiple electronic common technical document (eCTD) sections, simplifying the maintenance of regulatory dossiers. This significantly reduces the need for repetitive authoring, reviewing, and approval cycles by allowing content to be authored, reviewed, and verified once, independent of any specific document. SCDM facilitates real-time updates and auto-population of content, thereby minimizing manual data transcription, verification, and reducing the potential for human error. This structured approach not only streamlines the authoring process but also enhances automation, allowing for simultaneous updates across multiple sections and regions. SCDM digitalization can deliver regulatory information in multi-modal formats to accommodate the needs of individual health authorities where technological infrastructure is at different stages of maturity. Additionally, digital solutions like FHIR, which leverage internet-based platforms, support parallel submission and review activities across different regulatory agencies, further streamlining the regulatory process. FHIR also simplifies the integration of data during acquisitions and enables efficient retrieval and use of archived data for new submissions throughout the product lifecycle. Previous publications have described the use of SCDM in regulatory processes (Beierle et al. 2023; Ahluwalia et al. 2022; Algorri et al. 2020).

As SCDM establishes a solid foundation for structured data management, the role of AI becomes increasingly critical. AI can extend the capabilities of SCDM by automating complex data analysis, identifying patterns within regulatory submissions, and even forecasting regulatory outcomes with appropriate oversight and safeguards in place. In regard to regulatory compliance, leveraging SCDM and AI allows manufacturing facilities to identify and adhere to global registered details more efficiently. By combining SCDM with AI, organizations can significantly enhance the efficiency and strategic decision-making capabilities of their regulatory affairs teams. The following section will delve deeper into how AI can be harnessed to further revolutionize regulatory processes, ultimately driving greater efficiency, accuracy, and innovation in the pharmaceutical industry.

Leveraging Artificial Intelligence (AI)

AI encompasses a broad range of computer systems designed to mimic human cognitive functions, including reasoning, learning, and decision-making. Machine Learning (ML) is a subset of AI that uses statistical methods to enable machines to improve tasks with sufficient historical examples, allowing them to identify patterns and rules without explicit programming (European Medicines Agency 2023). ML algorithms produce models that can be used to organize data, identify patterns, and create predictions for similar datasets. This technology is a key tool in AI, helping to gain understanding, make predictions, and assist in decision-making potentially for both sponsors and health authorities (Patil et al. 2023).

Since AI technology is already in use, it is important for international bodies to make their assessments and establish the policies as efficiently as possible to recognize the advantages of the technology along with the concerns, and to facilitate effective implementation rather than to restrict it. Several international bodies have commented on the implementation of AI tools within the biopharmaceutical industry. In one example, the World Health Organization (WHO) acknowledges the significant potential of AI in revolutionizing pharmaceutical development and distribution. AI is already being integrated into many phases of pharmaceutical development, and it is anticipated that many pharmaceutical products entering the market will be influenced by AI at some point in their product journey. While AI's incorporation may offer commercial advantages, it is crucial that its usage also prioritizes public health benefits and adheres to appropriate governance standards. WHO plans to monitor the impact of AI on pharmaceutical and vaccine development and explore avenues for collaboration among Member States, pharmaceutical firms, civil society, and global health-oriented partnerships and researchers to leverage AI for enhancing pharmaceutical development and accessibility to address health disparities. Additionally, WHO may formulate new ethical guidelines and tackle governance issues related to data management, regulatory considerations, and legislation to effectively navigate the myriad benefits and challenges associated with AI's role in pharmaceutical and vaccine development and distribution (World Health Organization 2024).

Similarly, the EMA advises thorough regulatory impact and risk analysis for AI/ML in medicine. Early regulatory engagement is crucial, especially when AI significantly influences product lifecycle or documentation. The EMA offers early engagement through the Innovation Task Force (ITF) and scientific advice from the Scientific Advice Working Party (SAWP). Sponsors should seek guidance when specific rules are unclear, ensuring detailed documentation and addressing potential risks like bias. AI/ML holds great promise but requires careful management to maintain patient safety and ethical standards (European Medicines Agency 2023).

The FDA also recognizes the transformative potential of AI in this industry and is focused on managing its integration through the medicinal product lifecycle. Through collaboration across its centers, the FDA is addressing AI challenges by engaging stakeholders, promoting transparency, and advocating for international standards. The agency is developing adaptable regulatory policies and refining safety and ethical guidelines. The FDA supports research to address AI biases, ensure data representativeness, and maintain oversight of AI tools. Balancing innovation with safety, the FDA's strategies will evolve as AI continues to advance (U.S. Food & Drug Administration 2024). Both the EMA and FDA are actively engaged with stakeholders and sponsors and have established task forces and working groups to provide guidance and feedback.

For sponsors, implementing AI in various aspects of regulatory filing processes has the potential to minimize delays as well as enhance decision making. Currently, there is significant room for improvement in electronic filings and submissions via eCTDs. In the future, industry will likely transition from eCTD filing to structured data submissions. As the biopharmaceutical and pharmaceutical industry continues to transition towards digitalization including the utilization of AI, regulatory submission and review processes will significantly accelerate. Once structured, CMC data exchanged rapidly through APIs will significantly increase in volume and speed. Manual-based, traditional paper/electronic workflows will struggle to keep up with this rapid exchange. Hence, developing AI tools to efficiently handle tasks such as creating, receiving, processing, submitting, and managing the data flow is essential (Anderson et al. 2023). Implementing AI in these applications has the potential to enhance efficiency by automating labor-intensive tasks, reducing errors, and enabling real-time data management and decision-making.

In addition, these advanced technologies would be able to curate and analyze both publicly available information and company-specific data in various domains. Automation and AI-driven systems could automatically distill and provide concise summaries of pertinent information while delivering timely alerts regarding legislative changes and health authority regulations. Also, these technologies can assist subject matter experts by extracting valuable insights from approved products and existing data collected during routine operations, thereby aiding in decision-making (Liu et al. 2023). For example, "prior knowledge", which refers to the pre-existing

information and insights gained from previous research, development, and regulatory activities, can be applied to current and future projects. This concept is critical in pharmaceutical development and lifecycle management, as outlined in the International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH) guidelines Q8, Q10, and Q11 (European Medicines Agency 2017). Managing prior knowledge involves systemically capturing, documenting, and utilizing this information to inform decision-making processes, optimize development strategies, and ensure compliance with regulatory requirement. In addition, the EMA's 2017 Prior Knowledge Workshop emphasized the importance of integrating structured content and advanced data analytics to effectively harness prior knowledge (European Medicines Agency 2017). Creation of robust databases that compile historical data, regulatory feedback, and scientific literature is needed in order to employ AI-driven tools to analyze and extract actionable insights. These practices enable organizations to predict potential challenges, streamline regulatory submissions, and enhance the overall quality of pharmaceutical products. Lastly, these tools are poised to play a pivotal role in aggregating and analyzing insights derived from competitor experiences, market analysis, and real-world evidence to inform strategic regulatory decisions (Liu et al. 2023). Table 1 demonstrates just a few other examples of how AI/ML can provide solutions to current regulatory challenges.

The application of AI within regulatory processes not only addresses these challenges but also sets the stage for a significant transformation in how regulatory affairs are managed. By automating repetitive tasks, reducing manual data accuracy checks, and providing predictive insights, AI has the potential to revolutionize the speed and effectiveness of regulatory submissions and reviews. As the industry moves towards a future where digitalization plays a central role in regulatory processes, the integration of AI will be key in navigating the complexities of modern pharmaceutical regulation. This transition will ultimately lead to faster, more efficient regulatory pathways, benefiting both the industry and patients worldwide. The following sections will further discuss examples of AI implementation including 1) an Amgen developed AI tool for authoring Common Technical Document (CTD) Module 2.3, Quality Overall Summary (QOS) and 2) the use of AI in regulatory intelligence.

Quality overall summary (CTD Module 2.3)

At Amgen, AI is being leveraged to accelerate regulatory submissions by automating the time-consuming tasks of assembling regulatory submission documentation and authoring of the QOS. Quality content within Module 3 of regulatory filings yield over thousands of pages of data and narrative which are summarized into the QOS. As shown in Fig. 2, a large language model (LLM)-powered drafting tool was used which maps the appropriate Module 3 content to a given section of the QOS and then generates a summary for that content based on predefined section-specific prompts. In addition to summarizing narrative content, this tool eliminates the manual transcription of tables and figures and produces its own audit trail to accelerate the data verification process. A key strength of this AI tool is its flexibility including the ability to follow regulatory guidelines, and adhere to template style and formatting, resulting in the ability to use the tool across various product modalities and submission types. By minimizing the tasks the users will need to perform, this tool aims to dramatically reduce drafting time of the QOS from approximately 2 weeks to under an hour to produce the initial draft. The estimated time reduction to prepare full QOS drafts with this tool is >60%, and it can be expanded to work synergistically with other tools for accelerating the end-to-end regulatory process.

Regulatory intelligence

Ensuring that country-specific requirements for global regulatory submissions are accurate is critical to obtaining global approvals for biopharmaceuticals. As discussed above, varying country-specific requirements related to data content become cumbersome for companies to manage and maintain. Regulatory requirements vary based on country, submission type, and product modality and are constantly evolving. Additionally, requirements can be misconstrued through the translation process, causing delays to submission approval. Companies have developed creative, but highly manual methods to handle country-specific requirements. For instance, CMC regulatory submission requirements are gathered from health authority websites, competitive intelligence, news releases, industry events, regulatory platforms, or published papers (Penkrat et al. 2022). These requirements can be compiled into spreadsheets listing active country-specific requirements. Reviewing these for each submission can delay timelines and maintaining the spreadsheets becomes challenging due to the expanding global presence and changing requirements. Furthermore, this manual process is not only resource-intensive but may still fall short of current health authority expectations, leading to questions and approval delays.

AI applications have been developed in the field of regulatory intelligence, facilitating strategic data management using natural language processing models. These models aggregate insights from public data sources, evaluate the confidence and knowledge gathered to

Table 1 Current regulatory challenges and AI solutions

Category	Current Challenge	AI-Driven Solution
Regulatory Monitoring and Updates	Manual monitoring of health authority websites for regulation changes	Transforms unstructured text into structured data, enabling automated and real-time updates (Reed 2023)
	Managing regulatory project management tasks, such as scheduling, audits, and data organization	AI automates low-risk administrative tasks, including categorization, processing, and resource management, through chatbots and information routing tools, enhancing overall project management efficiency (Patil et al. 2023; Anderson et al. 2023)
Data Integration and Management	Labor-intensive and error-prone manual data integration and quality assessments	ML algorithms perform data curation, including masking, de-identification, and identifying data inconsistencies (U.S. Food & Drug Administration 2024)
	Managing large volumes of regulatory data across multiple regions and products	AI integrates with SCDM to ensure consistent data application, reducing redundancy and enhancing compliance
Regulatory Documentation	Compiling and analyzing inquiries from health authorities manually in spreadsheets to improve drug dossiers. Additionally, the analysis is complicated by human bias depending on the interpretation of the question	AI analyzes patterns in inquiries, identifies potential deficiencies in new documentation, and proposes pertinent content based on historical data, creating a quick first draft and enhancing overall dossier quality (Billev Pharma East 2023)
	Time consuming document creation and review cycles	AI autonomously generates documents using predefined templates and suggests improvements based on historical data
Data Exchange and Submission	Time consuming management of rapid data exchanges and submission requirements	AI streamlines the processing and submission of regulatory data, improving the efficiency of real-time data management
Analytics, Predictions, and Planning	Analyzing visual data, such as diagrams or structural images, during regulatory reviews	AI-powered visual analysis tools assist with examining diagrams, structural images, and 3D models, identifying relevant features or anomalies for regulatory compliance
	Predicting regulatory challenges and planning submissions	AI analyzes historical regulatory feedback, health authority guidelines, and market data to predict potential regulatory hurdles and optimize submission strategies
Stakeholder Communication	Consistent and efficient communication across the business enterprise. Including distribution to and consumption by patients	Virtual assistants and AI-augmented call centers can streamline communication between regulatory teams and stakeholders
Automation of Routine Tasks	Repetitive administrative tasks	AI automates routine tasks like meeting minutes and schedules, freeing up resources for more strategic activities

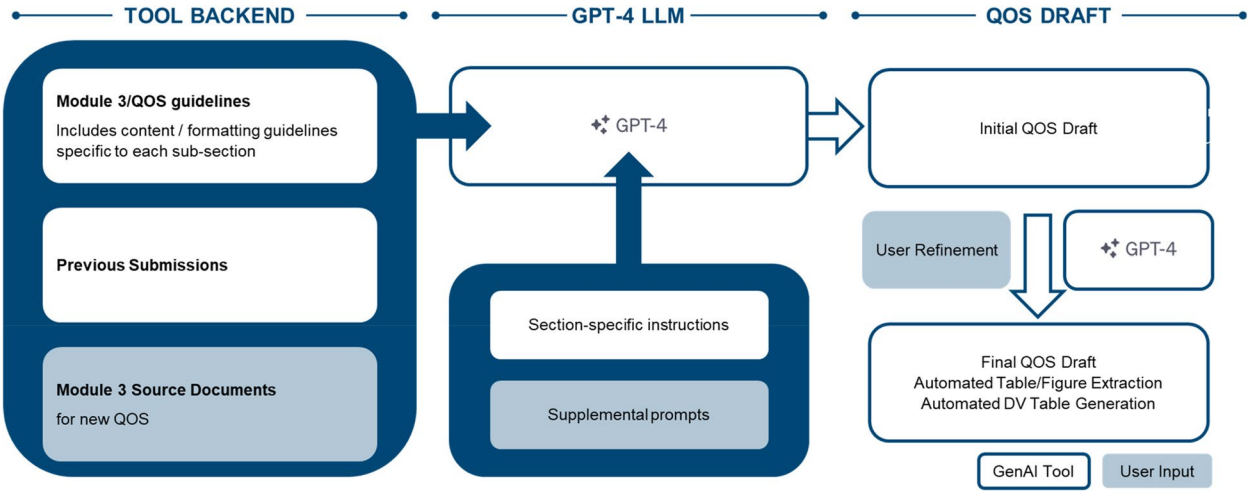


Fig. 2 Utilizing an LLM-Powered Drafting Tool to Create a QOS Draft. This is an LLM-powered drafting tool that maps out the relevant Module 3 content and formatting guidelines specific to each sub-section of the QOS. Furthermore, it generates a summary for that content based on predefined section-specific prompts. Beyond summarizing narrative content, the tool also automates the transcription of tables and figures. It further streamlines the process by creating its own audit trail, speeding up data verification

assess submission risks, and apply predictive analytics to determine optimal filing strategies (Penkrat et al. 2022). Additionally, AI enables the collection and utilization of precision intelligence, translation services, and the creation of alerts, thereby improving capabilities and increasing efficiency. The use of AI technologies to monitor and report data related to regulatory requirements would ensure that companies maintain up-to-date information in a centralized repository for relevant data and real-time updates on evolving regulations, thereby expediting global submissions and approvals of lifesaving medicines.

As an early example, in 2019, Eli Lilly and Company published findings from a study exploring the potential application of AI and related technologies in the field of regulatory intelligence, identifying key challenges and the potential value that AI could bring. The study included 25 pharmaceutical companies and highlighted several major challenges to the management of regulatory intelligence in its current state, such as the volume of information, accessibility and accuracy of the data, resource management, and the complexities of the regulatory environment. Upon interviewing 22 companies in the study, results indicated that 20 companies saw significant opportunities in using AI for regulatory intelligence. Specifically, 32% of the companies envisioned using AI for data synthesis, 36% for data analysis, and 22% for decision-making (Mayer et al. 2019). This utilization of AI in regulatory intelligence is now widespread, both within companies and for vendors that provide regulatory research.

Examples of AI-driven solutions that can be used to facilitate management of regulatory intelligence include:

- Automated Data and Compliance Monitoring: AI technologies can be used to monitor and sift through large amounts of data stored on health authority websites, industry publications, and internal databases at much faster speeds than humanly possible. In doing so, these technologies can help identify new requirements or modifications to existing requirements across jurisdictions. Furthermore, AI translation technology can be used to ensure proper interpretation of the requirements. AI can also be programmed to provide real-time alerts when changes to regulatory requirements occur.
- Data Analysis: AI technology can process the collected data to identify trends across countries and/or submission types. These data can support decision making and support simplification of country specific requirements to enable cross-country use. Furthermore, AI can be used to provide suggestions on regulatory strategies, helping companies navigate complex regulatory landscapes.
- Generative Artificial Intelligence (GenAI): GenAI technology can be used to convert the external regulatory intelligence and data from the internal quality systems to generate country specific documents to meet the health authority expectations.

Overall, AI technology can streamline the manual processes currently used to monitor, update, and create country-specific documents required to meet individual health authority requirements for regulatory submissions. Sponsors can integrate AI-driven solutions with standardization and SCDM principles to save time and

resources, while ensuring compliance to changing regulatory requirements around the world. However, to achieve the full future vision, implementation of cloud platforms to facilitate real-time data exchange is necessary to accelerate information sharing, decision-making, and patient access while being more cost-effective.

Cloud platforms

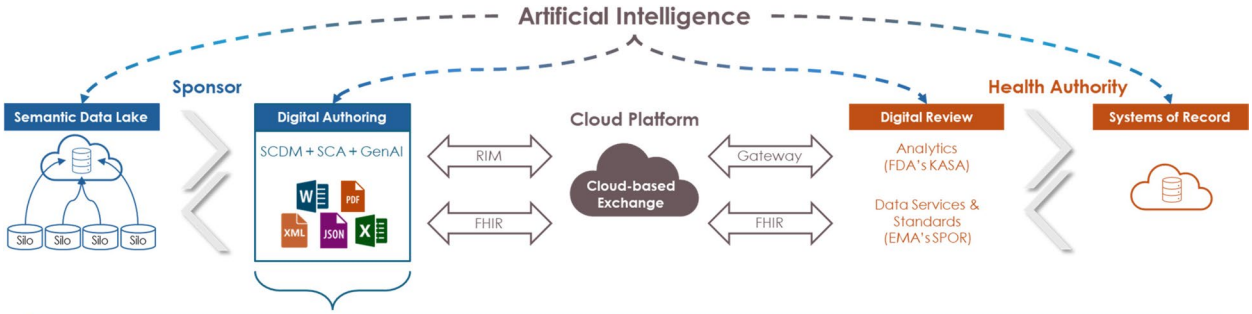
Over the past two decades, the use of cloud computing systems has become widespread across multiple industries, as large service providers such as Google and Amazon have made these services increasingly available and affordable. These systems enable remote accessibility of computing resources on an as-needed basis, allowing companies to scale up or scale down resources based on current needs. Additionally, cloud data storage capabilities allow users to access data from anywhere at any time. Cloud platforms offer notable cost efficiencies over typical "on-premises" software paradigms, which requires users to have their own locally accessible servers in-house.

While many biopharmaceutical organizations have successfully leveraged cloud-based technologies for some of their internal operations, the industry has generally been slower to adopt cloud platforms in comparison to other industries due to perceived regulatory risks and cybersecurity concerns (Goulder 2024; De Miglio, et al. 2021). However, perception is changing over time, particularly as health authorities are also increasing investment in cloud technology adoption, with EMA setting a goal to be cloud based by 2025, with a similar cloud platform strategy shared by the FDA. Similarly, there is increasing interest across industry and health authorities towards adopting cloud-based platforms to enable global regulatory collaboration. Accumulus Synergy, a nonprofit organization founded in 2020, launched a cloud-based platform in early 2024 to help enable use of regulatory reliance mechanisms for post-approval CMC changes, with other capabilities expected in future releases. The focus for Accumulus Synergy is to improve the existing method of information and data exchange through a multi-tenant platform. Their platform enhances insight generation and supports regulatory convergence, facilitating bilateral exchange between industry and health authorities, that is, via real-time data exchange. The objective here is to encourage collaboration among regulators for the ultimate benefit of patients worldwide, while simultaneously enabling the exchange of structured data, and aligning with evolving regulatory requirements (Accumulus synergy 2024). Leveraging cloud-based platforms for reliance brings the additional benefit of facilitating the verification of identical submission content to both reference and relying health authorities as well as the verification of approval by a reference authority. This is particularly impactful for LMIC health authorities in which there are technological and capacity constraints, and the use of reliance mechanisms is more prominent (Deavin et al. 2024).

To achieve these objectives, pilot programs using cloud-based platforms are underway. For example, Roche's Post-Approval Change (PAC) Reliance Pilot represents a significant advancement in regulatory affairs by streamlining the global implementation of PACs for pharmaceutical products. This pilot utilizes a reference agency to assess submissions, which other health authorities can then rely on, promoting the submission and approval of a single global dossier. This approach simplifies document management and accelerates the submission and approval processes, ultimately facilitating earlier patient access (Mangia et al. 2024). The Roche pilot is a particularly important milestone for CMC submissions, where differences in registered details across regions typically create significant challenges for managing post-approval filings globally. Often, these differences appear to be purely bureaucratic in nature, as products are typically developed, characterized, manufactured, tested, released, and distributed in the same manner regardless of region, despite the required variances in regulatory submission content. The Roche pilot demonstrates that by combining PAC Reliance pathways with digital innovation, it is possible to eliminate most, if not all, CMC differences that arise from diverging regulatory filing content and requirements, which result in lengthy registration timelines.

Conclusion

Figure 3 illustrates the digitalization of regulatory submissions in which the integration of data standards, structured content, AI, and information exchange platforms has the potential to fundamentally reshape the biopharmaceutical regulatory landscape. Data standards (e.g. PQ-CMC, ISO IDMP, HL7 FHIR Pharmaceutical Quality-Industry) build the foundation for efficient information exchange by providing a common language between sponsors and health authorities. Sponsors can use these data standards to initiate building data models to bring in siloed data into a semantic data lake which retains the relationship between sparse information. This data lake can then be leveraged by digital authoring tools such as structured content authoring (SCA) and GenAI to accelerate submission timelines and allow for both electronic paper-based (PDFs) and data-based (structured) submissions. This information can then be shared with health authorities using cloud platforms which facilitate data exchange, reviews, and health authority questions. Health authorities can also leverage similar



Digital Authoring				
Technology	**Planning**	**Authoring**	**Review and Approval**	**Publishing and HA Interactions**
Structured Content Authoring (SCA)	• Instantiates templates for all applicable countries at once.	• Can populate templates based on structured data model. • Excels with semi-structured narrative, tables, figures, and reuseable content.	• Drives review and approval workflows, maintains version control.	• Assembles documents and structured submissions (PDF, XML, JSON). • Re-uses content across related filings.
GenAI	• Intelligent content planning • Predict HA questions from internal and external sources	• Can generate variable content to be managed by SCA platform. • Excels with unstructured narrative and summaries.	• Performs Quality Control checks.	• Performs language translation. • Populate HA forms • Supports analysis of, categorization of, and response to HA questions.

Foundational End-to-End Data Standards (PQ-CMC, ISO IDMP, HL7 FHIR Pharm Quality - Industry)

Fig. 3 The Future of Regulatory Filings. The future of regulatory filings relies on the digitalization of many end-to-end processes for both sponsors and health authorities (HAs). Data standards (e.g. PQ-CMC, ISO IDMP, and HL7 FHIR Pharmaceutical Quality-Industry) will facilitate the efficient exchange of regulatory information and structured submissions (e.g. FDA's Knowledge Aided Assessment and Structured Application (KASA)). Sponsors can leverage data standards to build data models to capture structured data and enable digital authoring tools like SCA and GenAI. Sponsors and health authorities can integrate with cloud platforms to exchange data and communications using both traditional submission formats as well as structure data submissions through FHIR. Similarly, health authorities can leverage the data standards and digital tools to ingest submissions and perform analytics

technologies to ingest submissions and perform analytics for their review. By transitioning from a heavily manual and error-prone paradigm to a digitized, reliable, and efficient system, these technologies offer a transformative opportunity. While detailed analysis of regulatory submissions has traditionally relied on the expertise of experienced subject matter experts, there is immense potential for these professionals to benefit from advanced technological support, particularly through data-driven insights and predictive analytics (Liu et al. 2023).

However, the adoption of these technologies is not without challenges. The development of multiple data standards and cloud-based systems, while necessary, may initially hinder global harmonization and delay widespread implementation. In addition, the adoption of digitalization tools varies across regulatory landscapes, with implementation largely dependent on infrastructure, funding, and policy alignment. While digital tools on the sponsor side can support the multi-modal needs of diverse health authorities, their feasibility for LMIC regulatory agencies remains uncertain. In these settings, cloud-based reliance models and collaborative regulatory frameworks may offer more immediate benefits by reducing duplicative reviews and enabling faster approvals, even in the absence of full-scale digital transformation. Continued efforts to harmonize global regulatory processes and provide technical support to under-resourced agencies will be essential in ensuring that modernization efforts translate into tangible regulatory improvements worldwide. To overcome these challenges, continuous dialogue between industry stakeholders and regulators is essential. Pilot programs will play a critical role in testing and refining emerging systems, helping to identify the most effective solutions for broader adoption. The alignment of modern regulatory guidelines, such as ICH M4 Quality Revision 2 (M4Q(R2)), with cloud-based systems, structured content, and robust data standards will establish the foundation for future reliance-based collaborative submissions and reviews (Eglovitch 2022).

Effective change management will be crucial as organizations navigate the shifts in workflows and culture required by these technologies. The challenge of consistently structuring data across diverse systems underscores the need for harmonization of data standards. Additionally, while automation and AI offers powerful capabilities, concerns regarding transparency, accuracy, and ethical use remain significant. Overcoming these challenges require clear strategies for standardizing and structuring content elements across functional areas including regulatory affairs. By ensuring that internal technical reports are structured or standardized, companies can

more reliably utilize AI to generate submission documents, mitigate risks, and enhance the overall efficiency of the submission process. A strategic approach that leverages the strengths of each technology while addressing their individual challenges will be key to successful implementation.

The biopharmaceutical industry has a unique opportunity to lead a transformation in regulatory processes, much like other highly regulated industries have done with advanced technologies. Industries such as automotive, electronics, and banking have already shown the profound impact that AI and digital platforms can have on efficiency, decision-making, and overall performance (Rathore et al. 2023; Beierle et al. 2023). As digital industrialization continues to demonstrate the benefits of rapid information sharing, the initial resistance to leveraging twenty-first-century technologies is likely to diminish (Beierle et al. 2023).

For the biopharmaceutical sector, embracing these technologies is not just about improving company efficiencies; it's about the broader, global impact. By leveraging, empowering, and integrating these advanced tools, the industry can make lifesaving, chronic, and everyday medicines more accessible to populations worldwide at unprecedented speeds. Furthermore, these technologies have the potential to optimize manufacturing processes, minimize the risk of drug shortages, make processes to ensure product quality and compliance more efficient, and ultimately accelerate patient access to new treatments. The time to embrace this transformation is now, as the potential benefits for both industry and global health authorities are too significant to ignore.

Abbreviations

AI	Artificial Intelligence
SCDM	Structured Content and Data Management
FDA	Food and Drug Administration
PQ/CMC	Pharmaceutical Quality/Chemistry, Manufacturing, and Controls
HL7	Health Level 7
FHIR	Fast Healthcare Interoperability Resources
EMA	European Medicines Agency
SPOR	Substance, Product, Organization, and Referentials
ISO	International Organization for Standardization
IDMP	Identification of Medicinal Products
API	Application Programming Interface
eCTD	Electronic Common Technical Document
ML	Machine Learning
WHO	World Health Organization
ITF	Innovation Task Force
SAWP	Scientific Advice Working Party
ICH	International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use
CMC	Chemistry, Manufacturing, and Controls
CTD	Common Technical Document
GenAI	Generative Artificial Intelligence
QOS	Quality Overall Summary
LLM	Large Language Model
LMIC	Low- and Middle-Income Countries
PAC	Post-Approval Change
SCA	Structured Content Authoring
HAs	Health Authorities
KASA	Knowledge Aided Assessment and Structured Application
M4Q(R2)	M4 Quality Revision 2

Authors' contributions

KA helped with writing the original draft, reviewing and editing the manuscript, and visualization. MJA helped with conceptualization, writing the original draft, reviewing and editing the manuscript, visualization, and supervision. MA helped with conceptualization, writing the original draft, reviewing and editing the manuscript, and visualization. NSC helped with conceptualization, reviewing and editing the manuscript, and supervision. NMPN helped with conceptualization, writing the original draft, and reviewing and editing the manuscript. RYAY helped with conceptualization, writing the original draft, reviewing and editing the manuscript, and visualization. All authors read and approved the final manuscript.

Declarations

Data availability

Not applicable.

Competing interests

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: [Kabir Ahluwalia reports a relationship with Amgen Inc that includes: employment. Michael J. Abernathy reports a relationship with Amgen Inc that includes: employment. Marquerita Algorri reports a relationship with Amgen Inc that includes: employment. Nina S. Cauchon reports a relationship with Amgen Inc that includes: employment. Natalie M. Perico-Norred reports a relationship with Amgen Inc that includes: employment. Rita Y. Albert Youssef reports a relationship with Rutgers University that includes: employment].

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Acknowledgements

The authors would like to thank Paul J. Kirwan, Connie Wang, Simon Hotchin, Randy Mohr, and Drew Hickerson for their helpful suggestions and review throughout development of this manuscript.

Author details

[1]Department of Global Regulatory Affairs and Strategy – CMC, Amgen Inc, Thousand Oaks, CA 91320, USA. [2]Department of Global Regulatory Affairs, Regulatory Promotions and Material Compliance – Amgen Inc, Thousand Oaks, CA 91320, USA.

Received: 28 November 2024 Accepted: 13 March 2025
Published online: 18 April 2025

References

Ahluwalia K, Abernathy M, Beierle J, Cauchon N, Cronin D, Gaiki S et al (2022) The future of CMC regulatory submissions: streamlining activities using structured content and data management. J Pharm Sci 111(5):1232–1244

Algorri M, Cauchon NS, Abernathy MJ (2020) Transitioning chemistry, manufacturing, and controls content with a structured data management solution: streamlining regulatory submissions. J Pharm Sci 109(4):1427–1438

Anderson C, Algorri M, Abernathy MJ (2023) Real-time algorithmic exchange and processing of pharmaceutical quality data and information. Int J Pharm 645:123342

Accumulus synergy (2024) What we do. Available from: https://www.accumulus.org/what-we-do/. Accessed 13 Feb 2025

Billev Pharma East (2023) Artificial Intelligence in Regulatory Affairs? Available from: https://billeveast.com/artificial-intelligence-in-regulatory-affairs/. Accessed 13 Feb 2025

Beierle J, Algorri M, Cortés M, Cauchon NS, Lennard A, Kirwan JP et al (2023) Structured content and data management—enhancing acceleration

in drug development through efficiency in data exchange. AAPS Open 9(1):11
Deavin A, Hossain A, Colmagne-Poulard I, Wong KC, Perea-Vélez M, Cappellini S et al (2024) A global industry survey on post-approval change management and use of reliance. Ther Innov Regul Sci 58(6):1094–1107
Del Miglio A, Hlavka T, Lewis J, Möller M, Prieto-Munoz P (2021) The case for cloud in life sciences
Eglovitch JS (2022) FDA official pushes for cloud-based regulatory assessments. Regulatory Affairs Professionals Society, Regulatory Focus
European Medicines Agency (2017) Meeting report: joint BWP/QWP workshop with stakeholders in relation to prior knowledge and its use in regulatory applications.
European Medicines Agency (2023) Reflection paper on the use of Artificial Intelligence (AI) in the medicinal product lifecycle. Available from: https://www.ema.europa.eu/en/documents/scientific-guideline/draft-reflection-paper-use-artificial-intelligence-ai-medicinal-product-lifecycle_en.pdf. Accessed 13 Feb 2025
Goulder A (2024) Why are pharmaceutical companies reluctant to adopt cloud technologies? Pharmaceutical Technology, Online Exclusive Article
HL7 International (2024) Pharmaceutical quality - industry. Available from: https://build.fhir.org/ig/HL7/uv-dx-pq/. Accessed 13 Feb 2025
Liu L, Fazal K, Pandya V, Thiagarajan S (2023) How technology enabled regulatory intelligence can accelerate drug development. Available from: https://www.zs.com/insights/technology-regulatory-intelligence-accelerate-drug-development. Accessed 13 Feb 2025
Mangia F, Lin YM, Armando J, Dominguez K, Rozhnova V, Ausborn S (2024) Unleashing the Power of Reliance for Post-Approval Changes with 48 NRAs. 2024: DIA Global Forum.
Mayer M, Canedo A, Dinh T, Low M, Ortiz A, Garay C (2019) Potential use of artificial intelligence for regulatory intelligence: biopharmaceutical industry's views. Ther Innov Regul Sci 53(6):759–766
Patil RS, Kulkarni SB, Gaikwad VL (2023) Artificial intelligence in pharmaceutical regulatory affairs. Drug Discovery Today 28(9):103700
Penkrat V, Batra SS, Edward AE, Priyanka K, Thomas T, Medikonda P (2022) Regulatory Intelligence- A Key to Successful Submissions
Rathore AS, Nikita S, Thakur G, Mishra S (2023) Artificial intelligence and machine learning applications in biopharmaceutical manufacturing. Trends Biotechnol 41(4):497–510
Reed J (2023) How pharma can improve regulatory compliance with AI-based technology. Available from: https://pharmaphorum.com/digital/how-pharma-can-improve-regulatory-compliance-ai-based-technology. Accessed 13 Feb 2025
U.S. Food & Drug Administration (2024) Artificial Intelligence & Medicinal Products: How CBER, CDER, CDRH, and OCP are Working Together. Available from: https://www.fda.gov/media/177030/download?utm_medium=email&utm_source=govdelivery. Accessed 13 Feb 2025
U.S. Food & Drug Administration (2024) Using artificial intelligence & machine learning in the development of drug & biological products. Available from: https://www.fda.gov/media/167973/download?attachment. Accessed 13 Feb 2025
World Health Organization (2024) Benefits and risks of using artificial intelligence for pharmaceutical development and delivery. Available from: https://iris.who.int/bitstream/handle/10665/375871/9789240088108-eng.pdf?sequence=1. Accessed 13 Feb 2025

Publisher's Note