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Life Sciences Regulatory Quality Framework

M4Q(R2): A catalyst for more structured regulatory quality operations[1]

OUR PERSPECTIVE

M4Q(R2) represents a strategic opportunity to build a more efficient, more resilient regulatory operation. Organisations that prepare now are positioned to manage submissions and variations more effectively as enforcement approaches. The shift from document-centric dossier maintenance toward more modular, governed and lifecycle-ready quality information is not just a compliance requirement, but a chance to transform how organisations manage quality knowledge. Deloitte can support organisations in planning and executing their M4Q(R2) readiness journey.

1 **Note:** *This article is based on the Step 2b draft of ICH M4Q(R2) released by the ICH Assembly on 14 May 2025. The guideline has not yet been finalised, and the content may evolve before final publication.*

Executive Summary

ICH M4Q(R2)—the International Council for Harmonisation's update to the scientific guideline on the Common Technical Document for the Registration of Pharmaceuticals for Human Use - Quality—may seem like a technical revision at first glance. But it is in fact the most significant overhaul of pharmaceutical quality submission content in more than two decades.

It is more than a formatting exercise: it reorganises how quality information is structured, governed and maintained across the product lifecycle. According to the current ICH work plan, final adoption of the guideline is expected in June 2027, after which each regional authority will define its own timeline for implementation and approach to the transition to the revised guideline. Though implementation is expected to begin soon after finalisation, regional implementation approaches, timelines and transition provisions have not yet been formally defined.

The revision does not eliminate the regulatory narrative. Rather, it changes how quality information is organised and maintained. Under M4Q(R1), quality dossiers are often structured as a series of interconnected documents that must be read sequentially to understand the complete quality story. M4Q(R2) retains the narrative approach but introduces a more granular and modular structure, allowing reviewers and applicants to navigate more directly to specific quality information. This creates a stronger foundation for content reuse, more systematic lifecycle management, and future structured product quality submissions.

Organisations that begin to prepare now can align quality information, governance and technology before regional enforcement timelines compress the implementation windows. Those that delay may face avoidable reworking and a more reactive transition.

Three factors make M4Q(R2) a strategic opportunity:

Data reuse supports efficiency gains:
Quality information managed in a structured, governed format can be reused internally and updated more selectively across submissions and lifecycle changes, subject to regional requirements and company implementation maturity.

Built for modern pipelines:
The framework is better suited to complex and novel modalities, advanced manufacturing technologies, and lifecycle management expectations that M4Q(R1) did not explicitly anticipate.

Existing investments provide a foundation:
Organisations that have invested in regulatory information management, master data management, ISO IDMP / EMA SPOR, structured authoring or related data-governance capabilities may already possess foundational elements that can support M4Q(R2) readiness.

1. Quality submissions: what M4Q(R2) changes

The original framework: a foundation, not a ceiling
Introduced in 2002, ICH M4Q(R1) established a globally harmonised structure for the quality section of the Common Technical Document (CTD), enabling companies to file a single dossier across ICH regions. Module 2.3 (Quality Overall Summary) and Module 3 (Quality Body of Data) became the universal language of quality submissions.
However, the pharmaceutical landscape of 2026 bears little resemblance to that of 2002. The pipeline now encompasses mRNA vaccines, antibody-drug conjugates, cell and gene therapies, complex biologics and continuous manufacturing processes. Regulatory philosophy has also shifted toward process understanding, quality by design (QbD), control strategy and lifecycle stewardship. Submissions are moving toward more structured, digitally enabled formats. M4Q(R1) provided the foundation, but it was not designed around this level of product, process and data complexity.

From Revision 1 to Revision 2
Revision 2 is a substantial revision, not an incremental update. It reshapes the CTD quality framework across four dimensions. Figure 1 summarises the key changes from M4Q(R1) to M4Q(R2).

	M4Q(R1) CURRENT	M4Q(R2)* FUTURE
Organisation of quality information	Quality information spread across dossier sections.	Quality information organised around the product and its constituent materials, with a consistent Description–Manufacture–Control–Storage (DMCS) framework applied across materials.
Role of Module 2.3	Module 2.3 or Quality Overall Summary (QOS) provides a high-level summary of Module 3 quality information.	Module 2.3, now termed the Quality Overview, introduces a Core Quality Overview (CQO) section that identifies the quality information most relevant to regulatory commitments, lifecycle management and post-approval changes.
Scope and Applicability	Framework developed primarily for traditional small molecules and biologics.	Provides a harmonised framework for organising quality information across both traditional and emerging modalities, creating a consistent location for quality data regardless of product type or manufacturing technology.
Lifecycle and Digital Readiness	Document-centric dossier maintenance and lifecycle management.	More modular and reusable quality content, supporting lifecycle management, eCTD 4.0 capabilities and future structured submissions under SPQS / M16.

Figure 1 - From M4Q(R1) to M4Q(R2): four key dimensions of the update.

*Based on draft M4Q(R2), 14 May 2025; not yet finalised.

Operational benefits: how M4Q(R2) improves quality management

Beyond structural compliance, M4Q(R2) can deliver operational benefits for organisations that view it as more than a dossier restructuring exercise. The revised framework improves how quality information is organised, maintained and reused across the product lifecycle, while creating a foundation for more efficient lifecycle management and future regulatory requirements:

Modular content reuse and reduced regulatory operations effort: Quality information managed in a modular, governed format can support internal reuse and more targeted updates across submissions and lifecycle changes, reducing unnecessary re-authoring, reconciliation and repeated rewriting.

Data-ready structure by design: The revised structure of Modules 2.3 and 3 enables quality information to be organised more consistently and reused more effectively across submissions and lifecycle changes. Combined with eCTD 4.0 lifecycle capabilities, it provides a foundation for future Structured Product Quality Submissions which are being developed under ICH M16 (SPQS / M16).

Designed for modern pharmaceutical complexity: The framework is intended to better accommodate biologics, advanced therapy products, complex or novel modalities, and advanced manufacturing technologies such as continuous manufacturing, which the original CTD quality structure did not explicitly anticipate.

Module 2.3 as a regulatory decision-making tool: Rather than serving primarily as a summary of Module 3, Module 2.3 introduces Core Quality Information (CQI), highlighting the quality information most relevant to regulatory commitments, lifecycle management and post-approval changes. This information is expected to form the foundation of the future SPQS / M16.

Structured change management framework:
The revised structure supports clearer documentation of Established Conditions, where applicable, and post-approval change management considerations, enabling more systematic and traceable change documentation and regulatory dialogue.

2. M4Q(R2) in the wider regulatory modernisation landscape

M4Q(R2) is one element of a broader regulatory modernisation effort aimed at improving how quality information is managed throughout the product lifecycle. As illustrated in Figure 2, it sits within a wider ecosystem of complementary initiatives that collectively support a more connected, consistent and digitally enabled regulatory environment.

While each initiative addresses a different aspect of the regulatory process, their value is greatest when viewed as part of an integrated ecosystem rather than as standalone programmes. Together, they represent a gradual shift from document-centric submissions towards more reusable, interoperable and lifecycle-managed regulatory information. Organisations that recognise these interdependencies can reduce duplication, accelerate readiness and establish stronger foundations for future regulatory requirements.

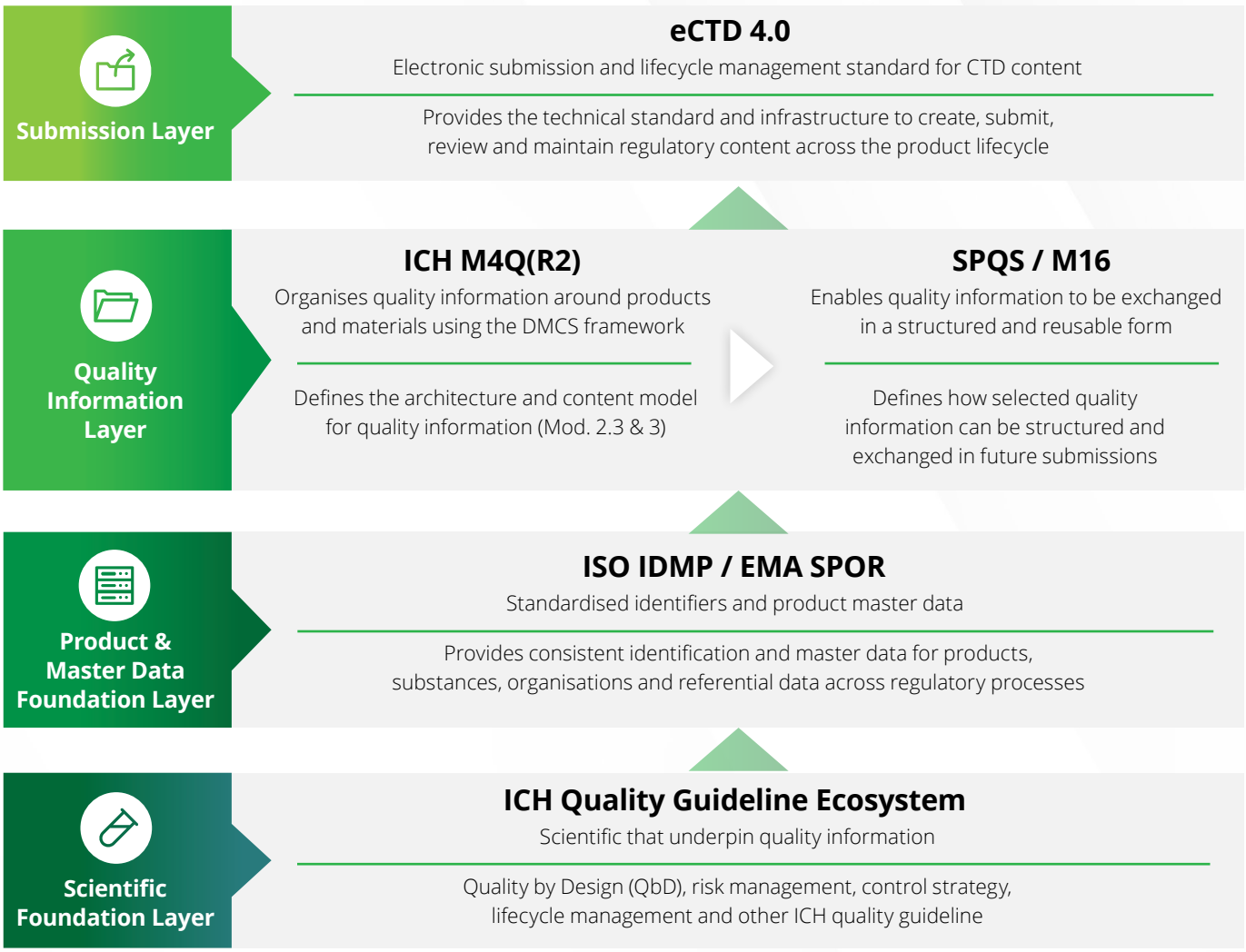


Figure 2 - M4Q(R2) within the regulatory modernisation ecosystem – Each layer builds on the one below, creating a digital foundation for future regulatory innovation and structured quality submissions.

3. Leveraging existing investments and capabilities

For many organisations, M4Q(R2) readiness does not start from zero. Existing investments in regulatory information, data and content management can provide valuable foundations for implementation, reducing the effort required to establish the governance, consistency and lifecycle capabilities needed under the revised framework.

Capabilities developed through Regulatory Information Management (RIM), master data management, structured authoring and data-governance initiatives can support different aspects of M4Q(R2) implementation. They can help organisations manage information consistently across submissions, maintain trusted product and organisational data, reuse content more effectively and establish clear ownership of quality information throughout the product lifecycle. Figure 3 illustrates how these existing capabilities can help close specific M4Q(R2) readiness gaps.

Among these investments, ISO IDMP / EMA SPOR provides a particularly relevant foundation by standardising key product, substance and organisational information, supported by controlled terminology and identifiers. While it does not capture the detailed quality information required under M4Q(R2), it strengthens the consistency and interoperability of the data referenced throughout the dossier. Emerging ISO work such as ISO / AWI 26060 may further extend this landscape into manufacturing process and controls information.

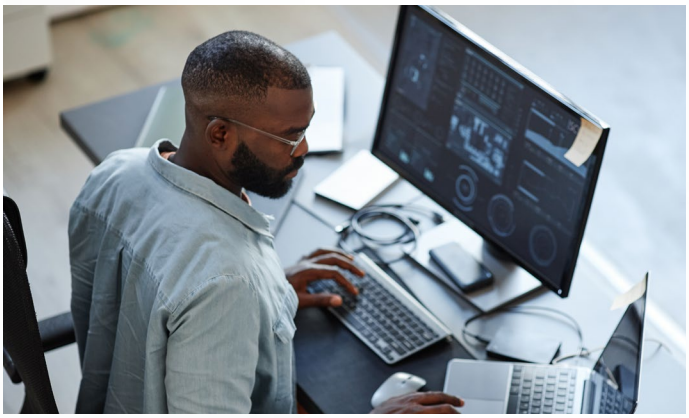
However, these capabilities are not a substitute for implementing M4Q(R2). Rather, they can help organisations establish the foundations needed to implement the revised framework more efficiently. The challenge is therefore less about building entirely new capabilities and more about understanding how existing investments can be leveraged, connected and extended to support the future management of quality information.

What you may already have	How it helps	Close the M4Q(R2) gap
Regulatory Information Management (RIM) & Lifecycle Processes	Provide visibility over submissions, registrations, commitments and post-approval changes.	Connect quality information to regulatory commitments and lifecycle events.
Master Data Foundation, incl. ISO IDMP / EMA SPOR	Provides trusted product, substance, organisation, and referential data.	Link master data to quality information such as materials, specifications, methods and manufacturing sites.
Structured authoring and content reuse	Supports modular content creation and controlled reuse.	Reorganise quality content around the M4Q(R2) material-based structure and DMCS framework.
Data and content governance	Provides ownership, standards and change control.	Define ownership of Core Quality Information, reusable quality content and lifecycle maintenance.

Figure 3 - Leveraging existing capabilities to close the M4Q(R2) readiness gap.

4. The path ahead: portfolio-based readiness and implementation enablers

M4Q(R2) will not affect every product in the same way. The urgency, scope and timing of readiness activities will depend on where a product sits in its lifecycle, the regions in which it is submitted, and the frequency of post-approval change. Organisations should therefore take a portfolio-based approach rather than applying a single implementation strategy across all products.



Products in active development heading toward a first submission

A product entering Phase 3 today with a realistic Marketing Authorisation Application (MAA) timeline of three to five years may reach submission around or after the expected finalisation of M4Q(R2) in 2027. Depending on the region, it may therefore reach submission in an environment where M4Q(R2) expectations are emerging or beginning to be applied. As quality documentation is being built now, considering the proposed M4Q(R2) structure can help reduce the risk of rework before submission.

Practical readiness step: Map current or planned quality content, including Module 3 and Module 2.3, against the proposed M4Q(R2) structure to identify areas of potential rework, duplication or reuse. For high-change or high-reuse content, explore how quality information could be managed as a single source and published in the format required by each region, depending on timing and organisational capabilities.

New marketing authorisation applications post-enforcement
For products submitting their first MAA after regional authorities establish M4Q(R2) enforcement, M4Q(R2)-aligned submissions may be required from the outset, subject to regional transition guidance. Quality data infrastructure, authoring processes and regulatory operations capabilities should therefore be prepared well before formal enforcement dates.

Practical readiness step: Assess whether quality governance, content models and authoring processes can support the DMCS structure, Module 2.3 cross-referencing and lifecycle-oriented content management. Evaluate technology enablers such as structured authoring, master data management and data governance capabilities needed for implementation.

Established and legacy products
No ICH region has yet formally published whether existing approved dossiers must be converted, on what timeline, or to what extent. Industry groups have called for transition periods and exemptions from mandatory full conversion. Until regional guidance is published after finalisation, a monitor-and-plan approach is appropriate.

However, not all legacy products carry equal risk. Products with frequent variations, renewals, global filings or submissions in regions that move earlier on implementation may encounter M4Q(R2)-aligned expectations sooner than stable products in limited markets.

Practical readiness step: Segment the portfolio by variation frequency, submission geography, dossier complexity and business criticality. High-change or high-value products may benefit from earlier mapping and selective restructuring, while stable products may follow a gradual approach, aligned to regional guidance.

Cross-cutting governance and technology enablers
Across all portfolio segments, successful M4Q(R2) readiness will also depend on common governance, process and technology capabilities. Successful M4Q(R2) implementation requires alignment across Regulatory, CMC, Quality, Manufacturing, and IT functions. Key enablers include:

Data governance: Clear ownership, stewardship, controlled terminology and change control for quality information, aligned to product lifecycle management principles.

Technology infrastructure: Regulatory Information Management (RIM), structured authoring, document management and master data capabilities that can manage governed quality content, support cross-referencing and enable efficient lifecycle management. System and vendor capabilities will be a practical implementation dependency. Organisations should monitor how RIM, structured authoring, document management and master data platforms evolve to support M4Q(R2), eCTD 4.0 and future SPQS / M16 requirements, including the ability to manage quality information once and publish it into different submission formats.

Process and organisational alignment: Quality workflows and cross-functional collaboration models that support modular, component-based content management and lifecycle-ready governance.

Organisations should begin evaluating these capabilities now, independent of regional enforcement timelines.

5. Conclusion: how can you best prepare for M4Q(R2)?

M4Q(R2) will not affect every product in the same way. The urgency, scope and timing of readiness activities will depend on where a product sits in its lifecycle, the regions in which it is submitted, and the frequency of post-approval change. Organisations should therefore take a portfolio-based approach rather than applying a single implementation strategy across all products.

To advance your M4Q(R2) readiness, consider the following key steps:

Assess the current state: Evaluate quality content, data foundations, governance and technology capabilities against the proposed M4Q(R2) structure.

Design a portfolio-based roadmap: Prioritise readiness activities based on product lifecycle stage, submission geography, dossier complexity and variation frequency.

Establish governance and process alignment: Define data ownership, mapping and enrichment approaches, and cross-functional processes needed to sustain modular, lifecycle ready quality content.

These actions are not only about preparing for one guideline update. They are part of a broader shift from document-centric regulatory operations toward more structured, reusable and lifecycle-managed information.

The path forward will depend on each organisation's maturity, portfolio profile and submission timelines. Determining where you stand today and defining the right sequence of actions will enable a more efficient and systematic approach to M4Q(R2) implementation.

KEY TAKEAWAYS

- **M4Q(R2) is a structural shift** in how quality information is organised, governed, authored and maintained across the product lifecycle.
- **Early preparation creates a strategic advantage,** even while regional implementation timelines and transition provisions are still to be confirmed.
- **The proposed structure supports more modular and reusable quality content,** helping organisations move away from document-centric dossier maintenance toward more systematic lifecycle management.
- **Products in active development with anticipated MAAs after 2027 should be assessed early** against the proposed M4Q(R2) structure to reduce avoidable rework later.
- **Established products will require a differentiated approach,** with portfolio segmentation based on variation frequency, submission geography, dossier complexity and business criticality.
- **ISO IDMP / EMA SPOR can provide useful foundations,** but M4Q(R2) readiness still requires DMCS mapping, quality-specific enrichment, validation and governance.
- **M4Q(R2) sits within a broader regulatory modernisation ecosystem,** including eCTD 4.0, SPQS, which is being developed under ICH M16, ISO IDMP / EMA SPOR and the ICH Quality guideline ecosystem. Understanding these connections will help organisations prepare more efficiently for future structured submission expectations.

Contributors: We thank Juliette Odorico and Zinnia Truan for their contributions to the article.

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