ICH M16 - Transitioning to Structured Product Quality submissions

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The Digital Imperative

Exchange of Unstructured Documents

Manual Review Burden
Regulators are overwhelmed by labor-intensive manual screening and verification.

Data Trapped in Paper
Information locked in static formats prevents computational analysis and decision support.

Data Volume Crisis
Data complexity in Biologics and cell therapies outpace human review capacity.

"Dark Data" Archives
Valuable regulatory information is archived and unavailable for further use.

Inefficient Comparisons
Manual side-by-side verification of historical vs current quality information.

Global Fragmentation
Duplication of effort across regions due to divergent requirements.

Lifecycle Friction
Static snapshots hinder agile post-approval manufacturing changes.

Scalability Barriers
Current paradigm fails to handle the exponential growth of submissions and treatments

The Future of Digital Regulatory Submissions:

From Electronic Paper to Structured Data

Strategic Transition

- Move from the current paradigm of "electronic paper" (PDFs) to a fully machine-readable data ecosystem supporting the entire product lifecycle,.

Harmonized Foundation

- Establish a uniform, global content standard for structured data that aligns with ICH M4Q(R2) and ISO IDMP,.

Digital Enabler

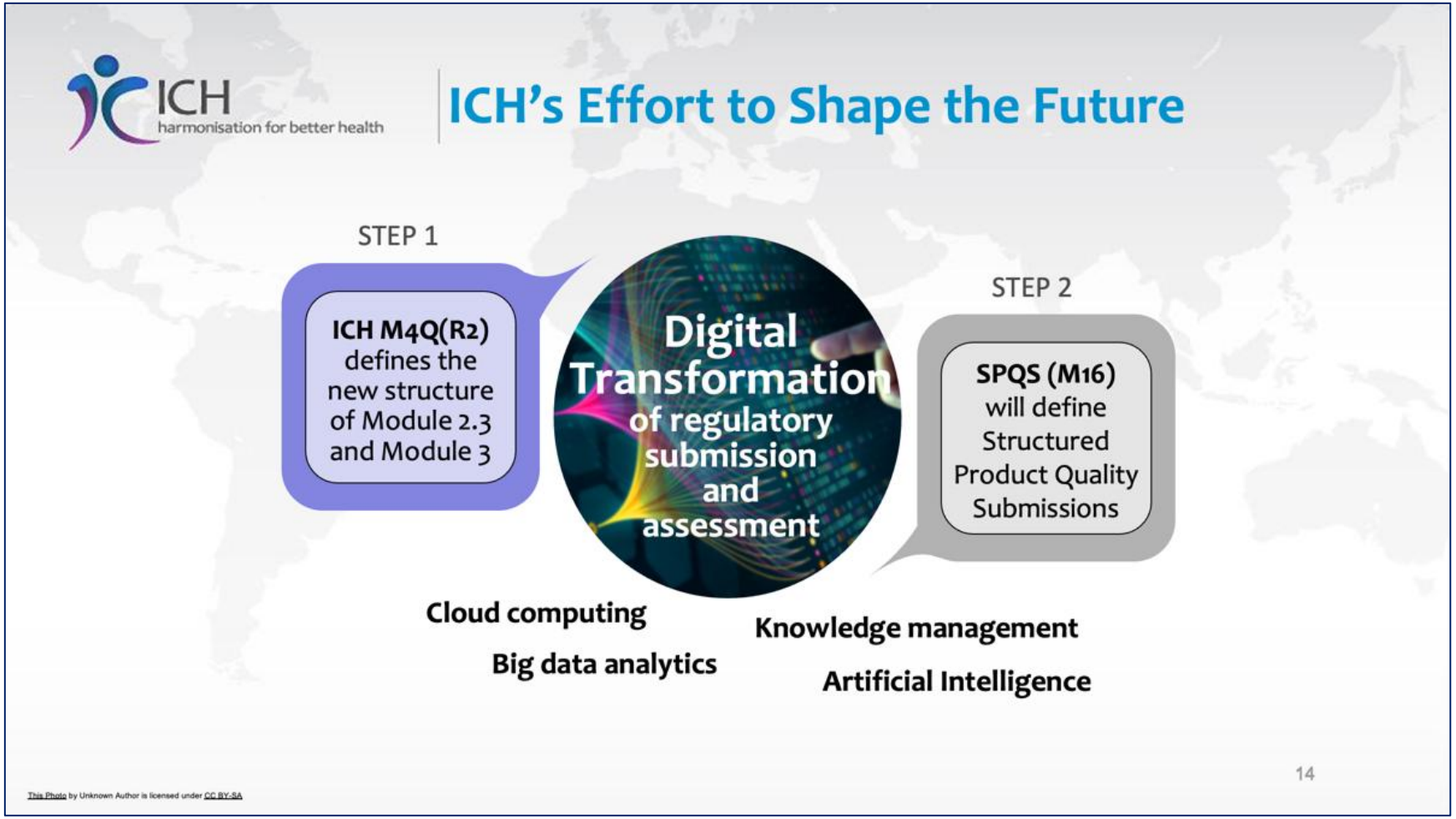
- Create a "digital layer" for the Common Technical Document (CTD) that facilitates automation, advanced analytics, and knowledge management,.

The Ultimate Goal

- Enable a Single Global Dossier per product, allowing data submitted in one region to be interoperable and acceptable across all regions.

ICH is Working to Enable this Transition

ICH M4Q (R2) and M16 will set the foundations for digital transformation in CMC



Strategic Scope and Key Deliverables

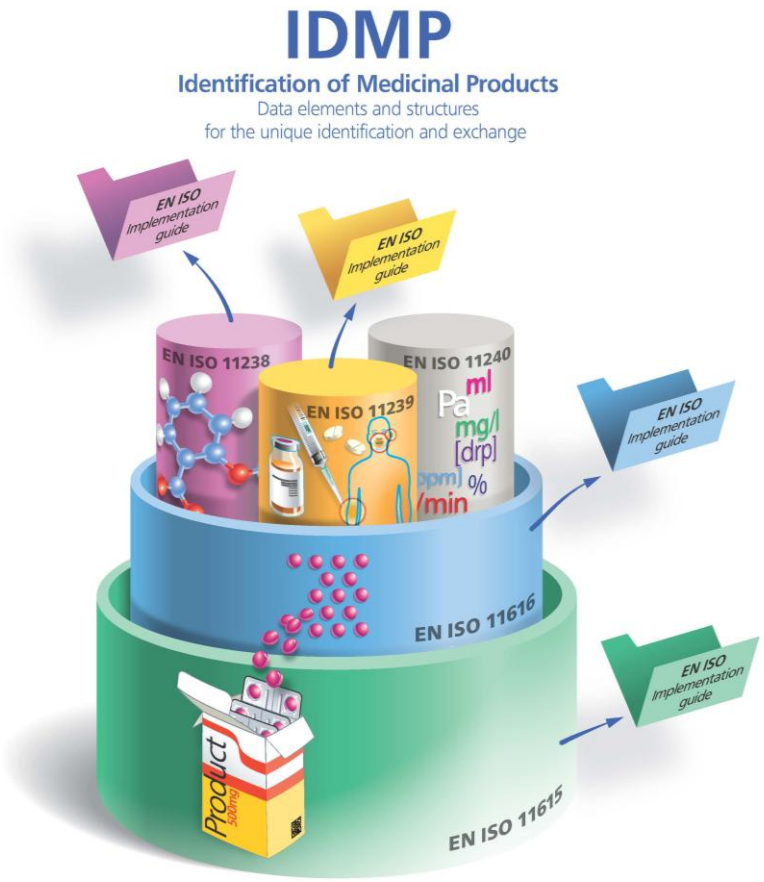
ICH M16 Framework

Scope:

- Establish global standards for data content and structure within the **ICH M4Q(R2)** framework (Modules 2 and 3) to enable efficient regulatory assessment and communication.
- **Data Content Standard:** Develop harmonized structured data models, including common elements, vocabularies, and ontologies, aligned with **ISO IDMP**.

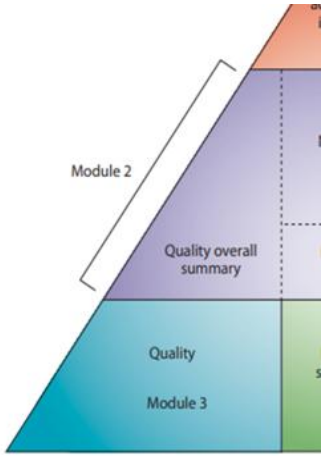
Specific Technical Deliverables:

- **Standardized Templates:** Define detailed expectations for required and optional content fields.
- **Technical Specifications (TS):** Establish conformance, cardinality, and technical attributes to ensure interoperable data exchange.
- **Data Exchange Standard:** Adopt or recommend a transport IT format (e.g., XML/JSON) for packaging and transmitting structured quality data to regulatory bodies.



Why Move to M4Q(R2) + M16

M4Q(R2) defines the 'What' and 'Where', while M16 delivers the 'How' via concrete data structures



Module 2

2.3.1 General Information

2.3.2 Overall Development and Overall Control Strategy

2.3.3 Core Quality Information (CQI)

2.3.4 Development Summary and Justification (DSJ)

2.3.5 Product Lifecycle Management

2.3.6 Product Quality Benefit Risk (Optional)

Module 3

3.2 Body of Data

- **Optimize Reviews** with dynamic navigation of control strategy linking to key information and data analysis tools
- Deterministic comparison of key attributes to **support lifecycle management, regulatory collaboration and reliance pathways**
- Leverage supportive data linked to structured content to verify claims, **facilitating assessments**
- Enable the automated tracking of regulatory commitments and significantly **streamlining post-approval changes** to prevent supply disruptions
- Convert subjective narrative arguments into trackable, scientific justifications that support **accelerated decision-making for innovative therapies**
- Structured supportive data is the basis for verification of claims, **enabling automation, advance analytics and AI in** support of all use cases

ICH M16: Transforming Quality Data into Global Public Health Outcomes

The Foundation: Machine-Readable Quality Data

Transitioning from Narratives to Data

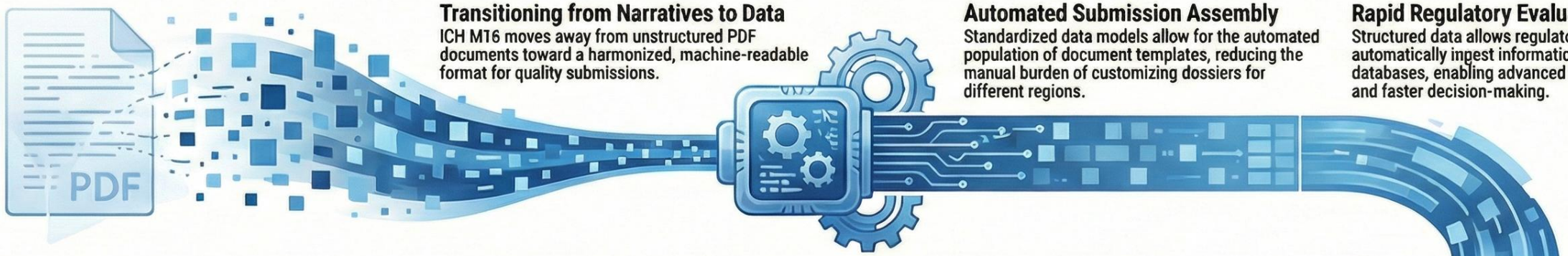
ICH M16 moves away from unstructured PDF documents toward a harmonized, machine-readable format for quality submissions.

Automated Submission Assembly

Standardized data models allow for the automated population of document templates, reducing the manual burden of customizing dossiers for different regions.

Rapid Regulatory Evaluation

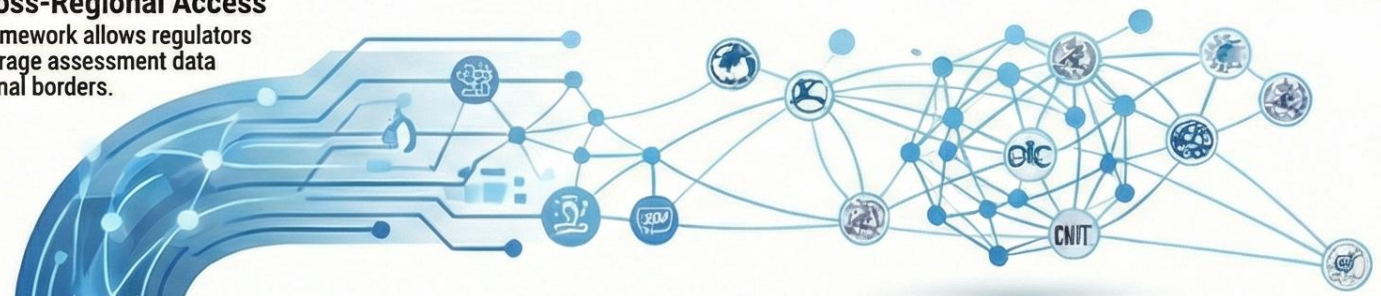
Structured data allows regulators to automatically ingest information into local databases, enabling advanced analytics and faster decision-making.



The Catalyst: Global Collaboration & Reliance

Seamless Cross-Regional Access

A harmonized framework allows regulators to share and leverage assessment data across international borders.



The Single Global Dossier

M16 advances the goal of a single global dossier per product, where data submitted in one region is interoperable and accepted in others.

Collaborative Review Pathways

Machine-readable formats enable multiple agencies to assess the same data simultaneously, accelerating global access to new therapies.

The Outcome: Public Health, Availability, and Safety

Coordinated Crisis Response

In the event of manufacturing disorspancies, harmonized standards allow regulators to trace and manage safety events across borders more efficiently.

Proactive Supply Chain Monitoring

Rapid access to structured quality data is critical for monitoring supply chains and preventing drug shortages before they occur.

Enhanced Safety Tracing

Structured data facilitates the ability to trace safety events directly to specific product quality attributes on a global scale.

Maintaining Continuity of Care

Standardized mechanisms for post-approval changes ensure that lifecycle updates do not cause unnecessary interruptions in drug availability.

Obstacles To Achieve This Vision

Legislation, capabilities and mindset need to evolve

Regulatory Environmental Challenges

National policies for data governance: stemming from differing values regarding privacy, security, ethics

Lagging data capability: sponsors and regulators lack a generalized skillset on good data and AI practices (mindset)

Regional Variations: variance between countries' technical requirements for drug regulation remain despite ICH Harmonization

Lack of trust in cloud: general perception that cloud is less secure drives protectionist legislation (e.g. blocks for cross-border data sharing)

Differing interests across stakeholders: technology providers, local manufacturers, HTA, payers, patients – strong collaboration and transparency is needed

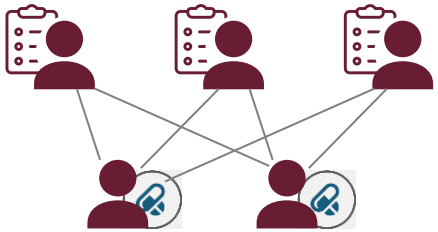
Risks emanating from major transformations impacting broad sectors

Implementing M4Q(R2), M16 and Cloud Submissions

Best case scenarios if regulations, mindset and skill sets can meet pace of change

Health Authorities Sponsors

Current State

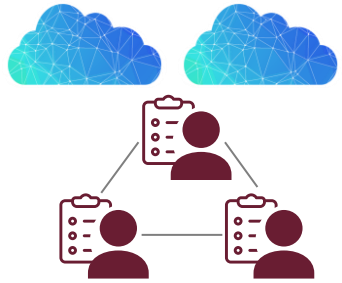


1 Point-to-point submissions

- MoW willing to "try" cloud
- Top regulators piloting collaboration
- Digitalization high priority MoW
- Broad alignment on vision for 1 world 1 submission 1 assessment

Global PAC 5 years

Mid Term (5 years)

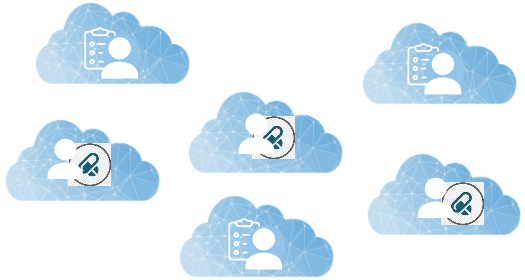


2 Limited data submission in cloud

- Core ICH countries accept M4Q R2 IMAs
- Broad eCTD 4.0 implementation
- Starting to submit CMC structured data (IDMP) for FDA/EMA
- PQKM in place, scaled PAC reliance and expanded collaborative review by top regulators

Global PAC 1.5 years

Long Term (10 years)



3 Broad adoption

- All regulators supported by cloud platforms and able to share information with each other
- M4Q R2 + structured CMC data is global standard
- Work sharing, reliance and recognition become default pathways

Global PAC 3 Months

Very Long Term (never?)

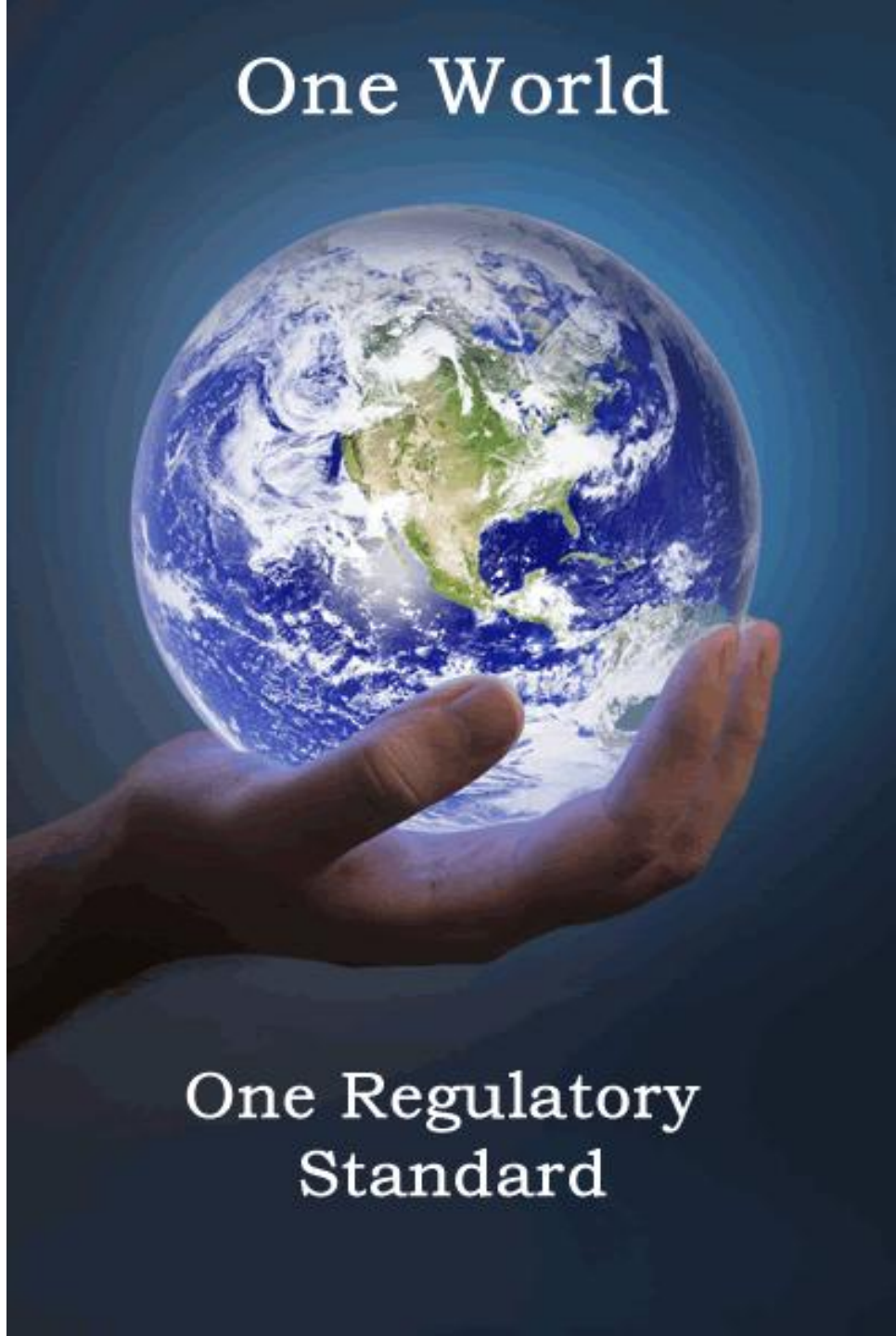
4 Global Cloud Network

- 1 dossier, 1 submission, 1 assessment
- Central agency makes decisions accepted globally
- PAC approved as fast as fastest AI + human check

Global PAC 7 Days

Key Takeaways

- Our vision is achievable in the next decade
- The benefits are clear and directly impact patients
- ICH is key to advance and scale digital transformation in regulatory
- Companies should define their implementation strategy now
- Follow ICH, ICMRA PQKM, ISO/TC 215 (IDMP)
  - Get involved through trade associations in your region/sector



Doing now what patients need next