Impact, opportunities and challenges transitioning to CMC structured data submissions

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Global Impact of Digital Transformation in Regulatory

Our goal is to transform regulatory practice globally

Higher trust in medicines driven by global transparency of regulatory information, assessments and monitoring

Accelerated global approval of therapies:

- **Broaden collaboration and reliance** across health authorities, broaden impact by including other stakeholders (e.g. EC/IRBs, HTAs, payer).
- Decreased timelines with **dynamic review of structured data** supported by advanced analytics and AI

Enable innovation: Effective assessment and monitoring of **ATMPs**, implementation of innovative approaches in **clinical trials** and use of **RWD**; new areas in QA and PV signal management.

Reduce cost burden to society by saving and optimizing resources (human/ financial/timing): lessen administrative burden, increase real-time collaboration with potential of reducing research timelines and minimizing rejections, refocus R&D costs.

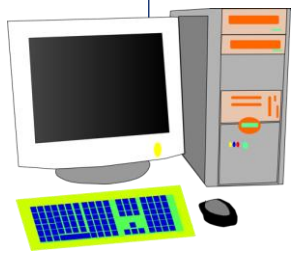
Increase availability of medicines downstream increase agility of supply chains from an optimized regulatory process. Ability to prevent and address shortages more effectively on a global basis

Evolution of ICH Initiatives Advancing Electronic Submission Standards

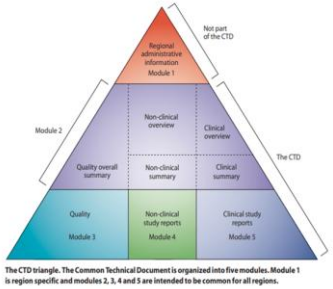
Focus on Chemical, Quality and Controls (CMC)

Pre-1989 Paper

1990's PDF

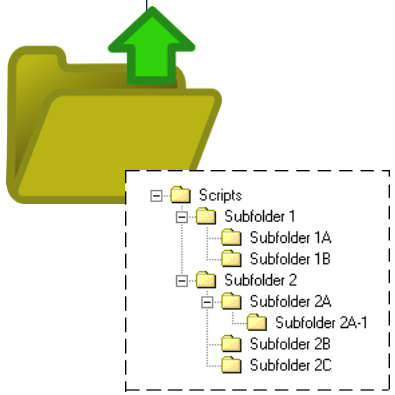


2000's CTD



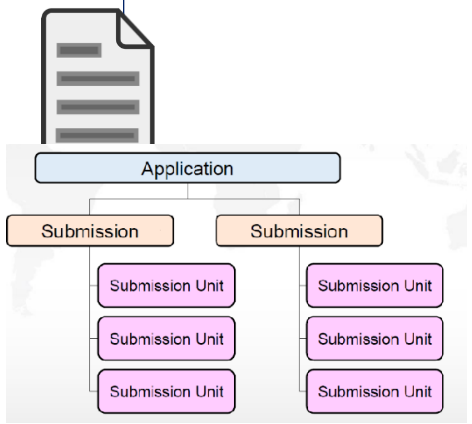
The CTD triangle. The Common Technical Document is organized into five modules. Module 1 is region specific and modules 2, 3, 4 and 5 are intended to be common for all regions.

2008 eCTD 3.2



2010's IDMP

2024 eCTD 4.0



2026 M4Q R2

TBD SPQS

TBC PQKM

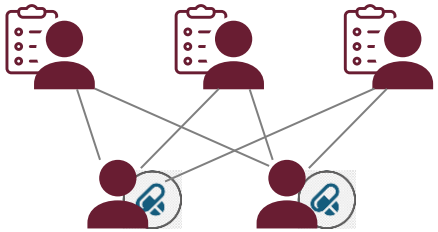
eCTD Evolution

Digital Transformation of CMC Regulatory Ecosystem

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

Health Authorities Sponsors

Current State

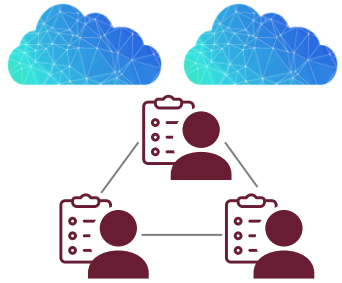


1 Point-to-point submissions

- 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)

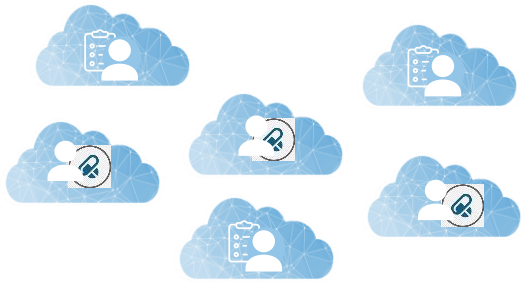


2 Limited data submission in cloud

- 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

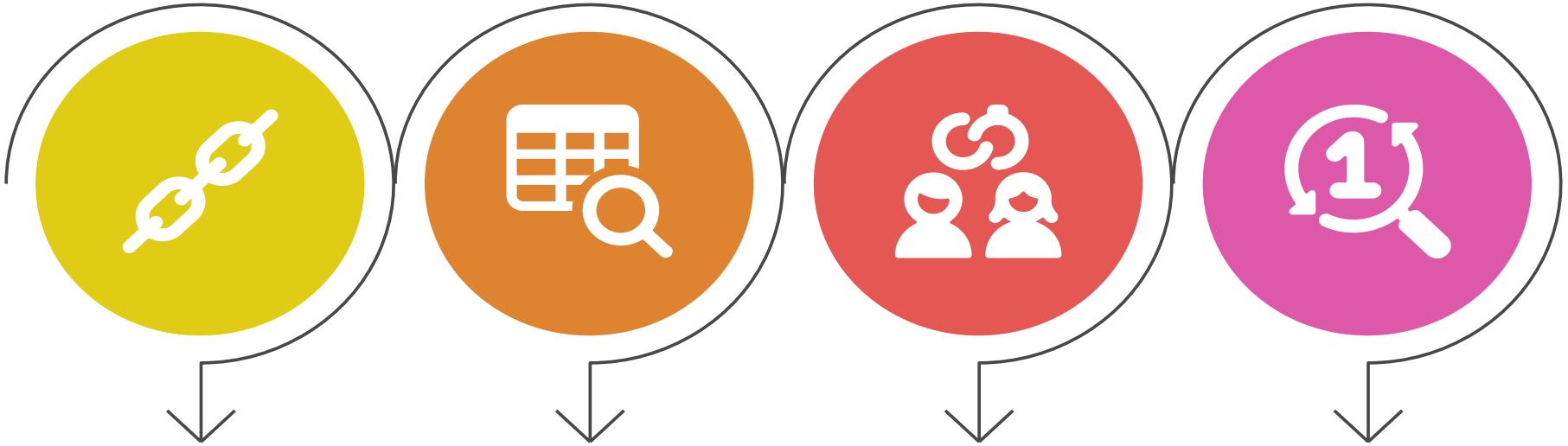
Very Long Term (never?)

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

Enablers of Digital Transformation in Regulatory



Structured Data and Content

Foundation for automation and interoperability across functions and with regulators.

A.I. and Analytics

Increase efficiency of regulatory authoring, submission and assessment as well as compliance monitoring

Cloud-based Collaboration

Enable collaboration across regulators and sponsors.and scale up reliance pathways

Dynamic Review

Accelerate regulatory process by exchanging and assessing data throughout development.

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

Regulators and Industry are aware and actively working to address these challenges

DIA 2024 GLOBAL ANNUAL MEETING SAN DIEGO, CA | JUNE 16-20 — 60TH ANNIVERSARY — CHARTING NEW HORIZONS

Supporting Regulatory Convergence and Reliance Through a Pharmaceutical Quality Knowledge Management (PQKM) Capability

Theresa Mullin, PhD
Associate Center Director
FDA CDER

DIA Session Chair
ICMRA PQKM WG Co-Chair

Concerted International Effort by Regulators:

International Coalition of Medicines Regulatory Authorities (ICMRA)

Pharmaceutical Quality Knowledge Management (PQKM) Capability

ICMRA working with ICH, PIC/S and IPRP to coordinate work to address these key enablers

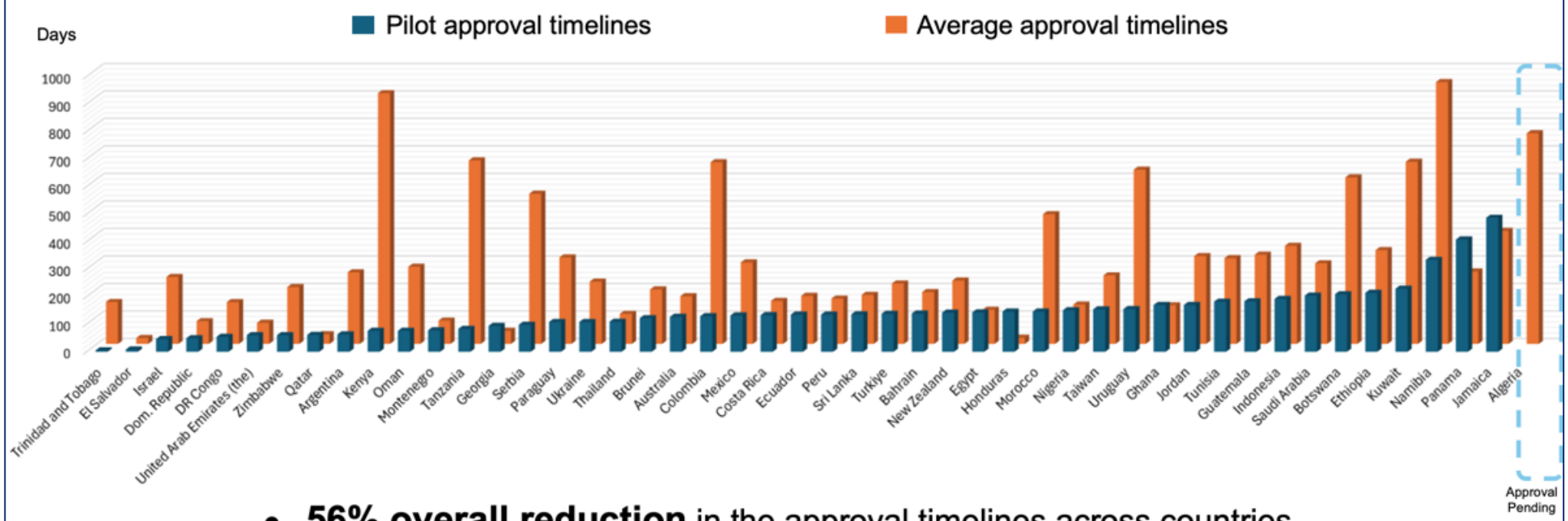
Enabler	Efforts under way
Harmonized regulatory requirements across regions	**ICH** Q GLs; Q12, M4Q(R2), SPQS (*expected start 11/24*)
Comparable/convergent basis for making regulatory **assessments**; reports	**ICMRA** PQKM--PACMP and CHIP collaboration pilots **IPRP** QWG & surveys
Readily accessible and usable **"reports"** for reference by other regulators	ICH PQKM Task Force **PIC/S** – more structured data in inspection reports
Assure **non-disclosure** of confidential trade secret info	**ICMRA** PQKM pilot design ICH PQKM Task Force
Regulators reviewing **same product, quality dossier, PAC-related submissions, etc.**	**ICMRA** PQKM WG on Identifiers to enable greater reliance

EMA/WHO Reliance Pilots

- Reliance can streamline both initial authorizations and post-authorization activities, which require significant regulatory resources throughout product lifecycle management.
- EMA processes over 8,000 post-authorization variations and renewals annually, while 70% of industry regulatory efforts focus on post-approval changes.
- Post-authorization changes are complex and time-intensive, and unpredictable timelines heighten the risk of shortages.
- EMA, with WHO, is supporting a pilot to submit EMA-approved variations to multiple non-EU national authorities.

Example #1 – Roche PAC Reliance Pilot

Pilot Approval Timelines vs Historical* Approval Timelines



- **56% overall reduction** in the approval timelines across countries
- Roche will be able to **implement** the change **2 YEARS AHEAD** of PROJECTED TIMELINES

* Based on similar major DS process changes

Example #2 – AMGEN PAC Reliance Pilot

Amgen's PAC Reliance – Cloud Collaboration Pilot

Target

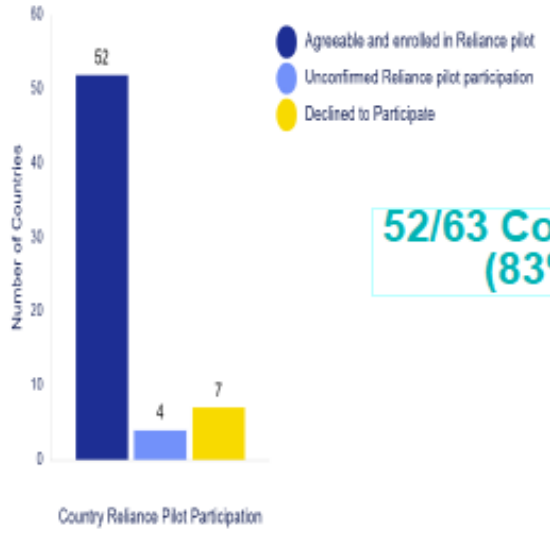
63 countries

where Vectibix is licensed

Target Countries

Algeria, Argentina, Australia, Bahrain, Bosnia and Herzegovina, Brazil, Canada, Chile, Colombia, Costa Rica, Ecuador, Egypt, Guatemala, Israel, Jordan, Kuwait, Lebanon, Malaysia, Mexico, Montenegro, Morocco, Oman, Panama, Peru, Philippines, Qatar, Saudia Arabia, Serbia, Singapore, South Africa, Taiwan, Thailand, Turkey, UAE, UK, Ukraine and EU (27 countries: Austria, Belgium, Bulgaria, Croatia, Republic of Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Netherlands, Poland, Portugal, Romania, Slovakia, Slovenia, Spain and Sweden.)

Country Reliance Pilot Participation

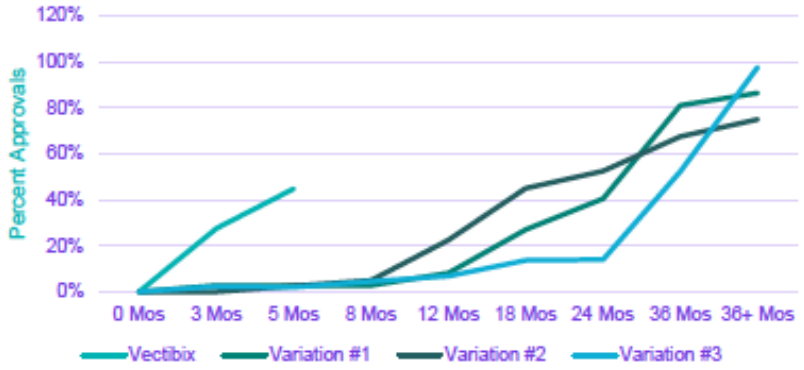


52/63 Countries (83%)

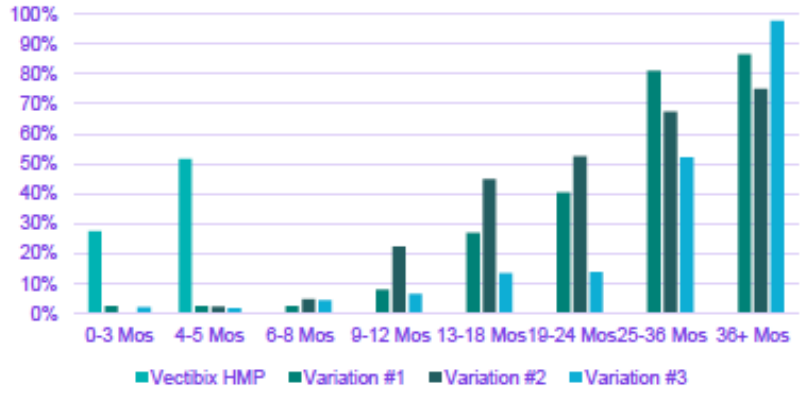
Country Reliance Pilot Participation Detail

Number of Countries Participating in Reliance Pilot	52
Countries Agreeable and enrolled in Reliance Pilot	Argentina, Australia, Brazil, Canada, Colombia, Ecuador, Egypt, Austria, Belgium, Bulgaria, Croatia, Republic of Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Netherlands, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, Guatemala, Israel, Jordan, Malaysia, Mexico, Montenegro, Oman, Panama, Peru, Saudi Arabia, Serbia, Singapore, South Africa, Taiwan, Thailand, Turkey, UK, Ukraine
Countries Unconfirmed Reliance Pilot participation	Algeria, Chile, Costa Rica, Philippines
Countries Declined to Participate in Reliance Pilot	Bahrain, Bosnia and Herzegovina, Kuwait, Lebanon, Morocco, Qatar, UAE

Approvals over Time

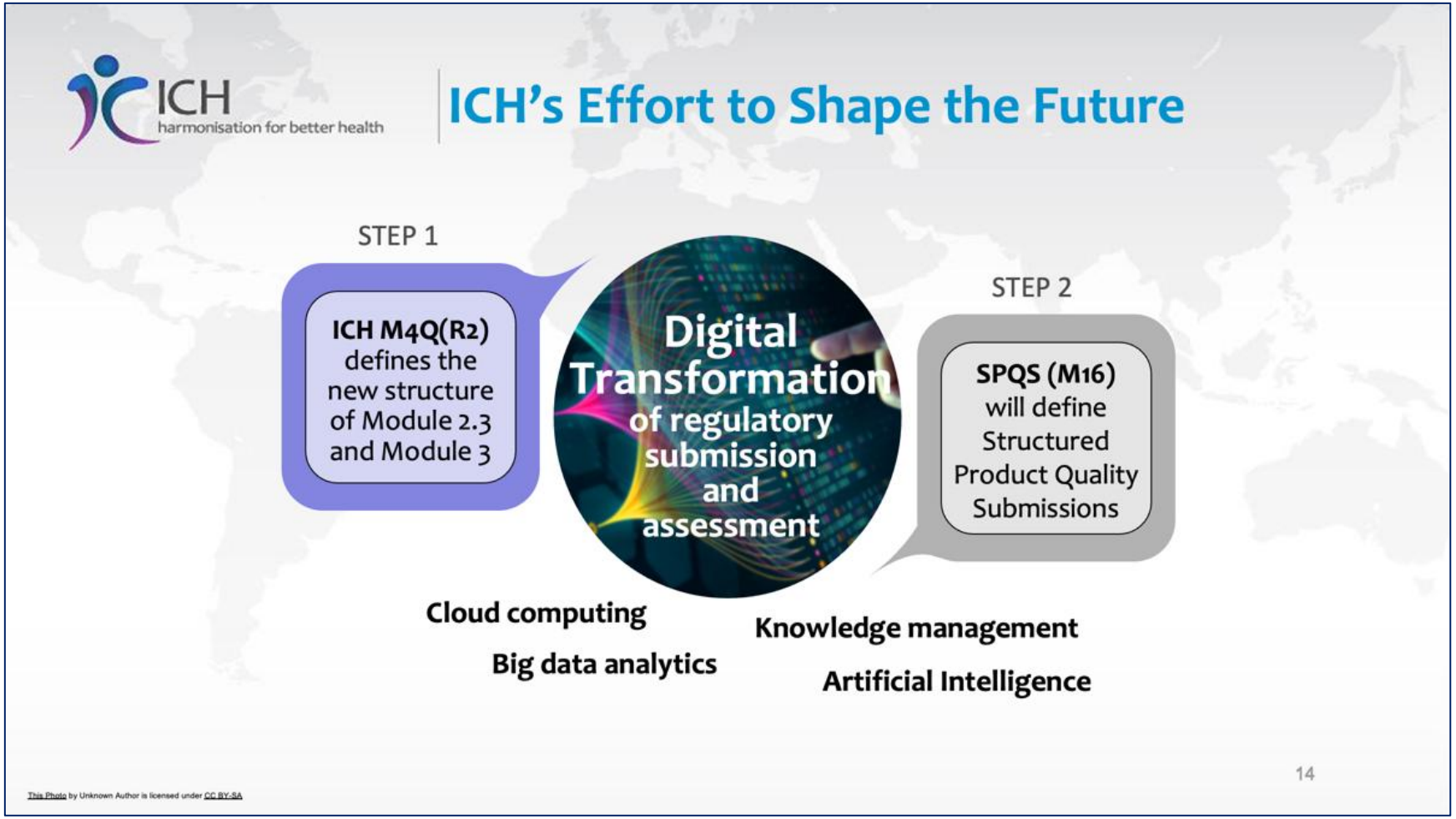


Percentage of Approvals After First Submission



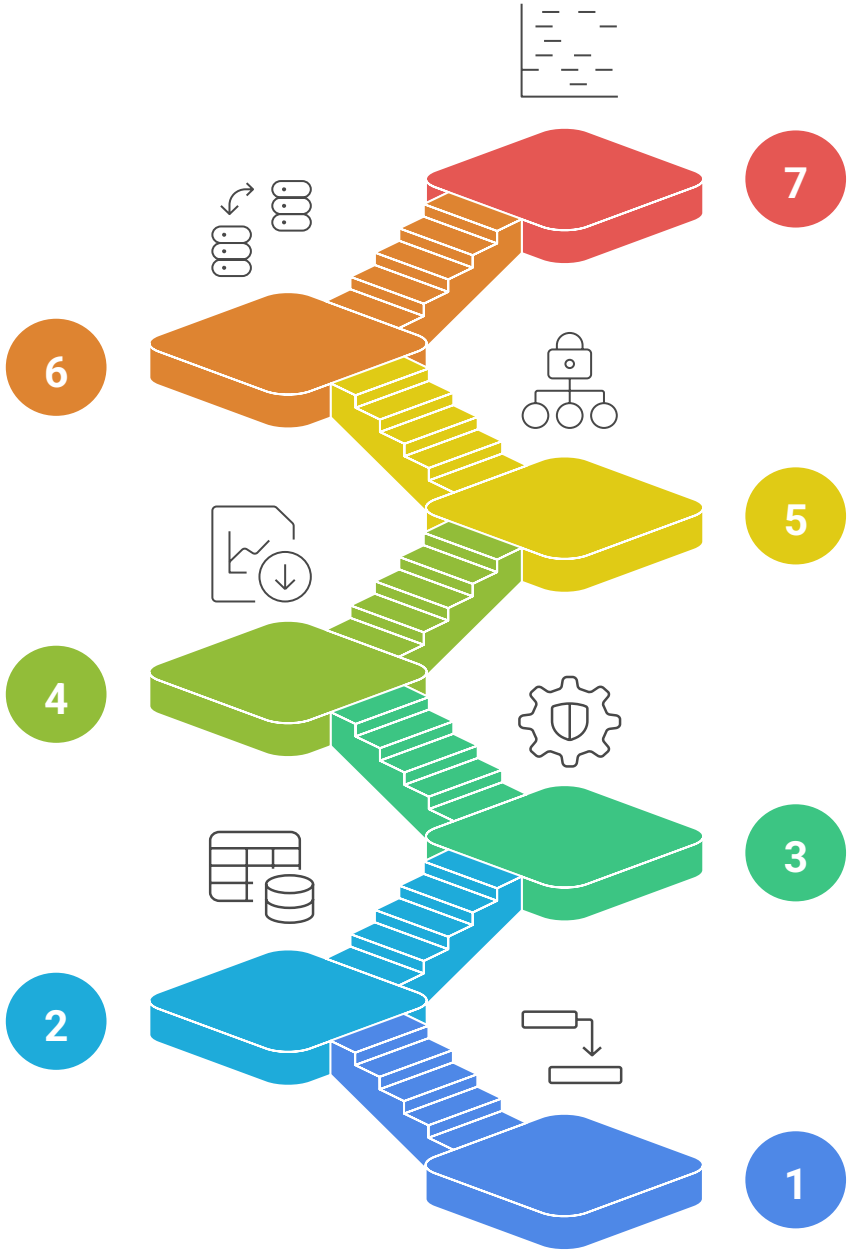
ICH is Working to Standardize Structured Data For CMC

Each company needs to carefully consider a strategy for implementation



Company Transition to End-to-End CMC Structured Submissions

These capabilities need to be established internally to effectively author, manage, publish, submit and monitor regulatory data and content



7 AI, Analytics & Insights

Leverage AI and advanced analytics to improve efficiency and compliance of regulatory and downstream processes

6 HA CMC Data Exchange

Establish systems for direct structured CMC data exchange with HAs and Cloud Platforms

5 Outgoing CMC Data & Publishing

Portfolio of structured regulatory content and data to support internal processes and meet diverse Health Authority requirements

4 Data Quality Monitoring

Data Quality indicators and monitoring systems to ensure the integrity, accuracy, and usability of regulatory submissions.

3 Regulatory Information Management

Managing key regulatory data and content in RIM, ensuring data availability and accessibility

2 Manage Content & Data Lifecycle

Robust systems and processes to author and manage structured content and data changes over time.

1 Incoming Regulatory Ready CMC data

Incoming reusable structured data and content assets compliant to ISO IDMP, M4Q (R2) and SPQS

ICH Structured Data Implementation Timeline (personal guess)

External drivers are only part of the wider business case for data-driven CMC regulatory

Company Implementation Approach

Early Adopter

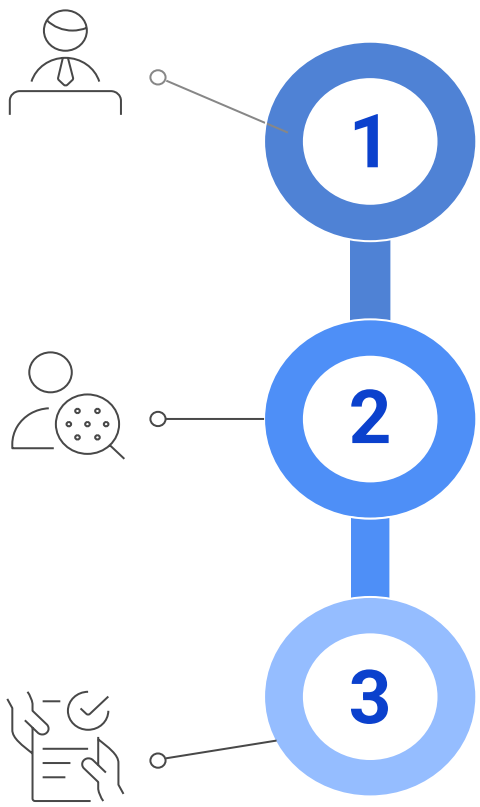
Leads digital transformation, influencing standards and capturing early benefits but accepting higher risk

Molecule Driven

Adapts to digital regulation based on molecule strategy, balancing benefits & risk

Compliance Driven

Focuses on compliance, extending current practice and accepting delay in benefits of data-driven processes



	M4Q (R2)	SPQS
2026	**Address Public Comments**	**Kick-off Guideline Development**
2027	**Guideline Finalized**	Draft Completed
2028	Voluntary NDA/BLA Submission at FDA	Public Commenting and reach Step 4 for Phase 1
2029	Voluntary IMA Submission ICH founders	Voluntary Submission FDA for Phase 1, Reach step 4 for Phase 2
2030	Voluntary Submission First 10 countries	Voluntary Submission ICH founders for Phase 1, FDA for Phase 2
2032	Mandatory Submission ICH members	Mandatory Submission FDA, Voluntary ICH founders for Phase 1

Data-driven Regulatory will enable the scale-up of collaboration and reliance pathways to the benefit of patients

Faster Approvals: Accelerated assessment timelines across all markets

Lessen time & burden of the thousands of **filings and requests** industry prepares and regulators review

Accelerate adoption of latest electronic standards for MoW

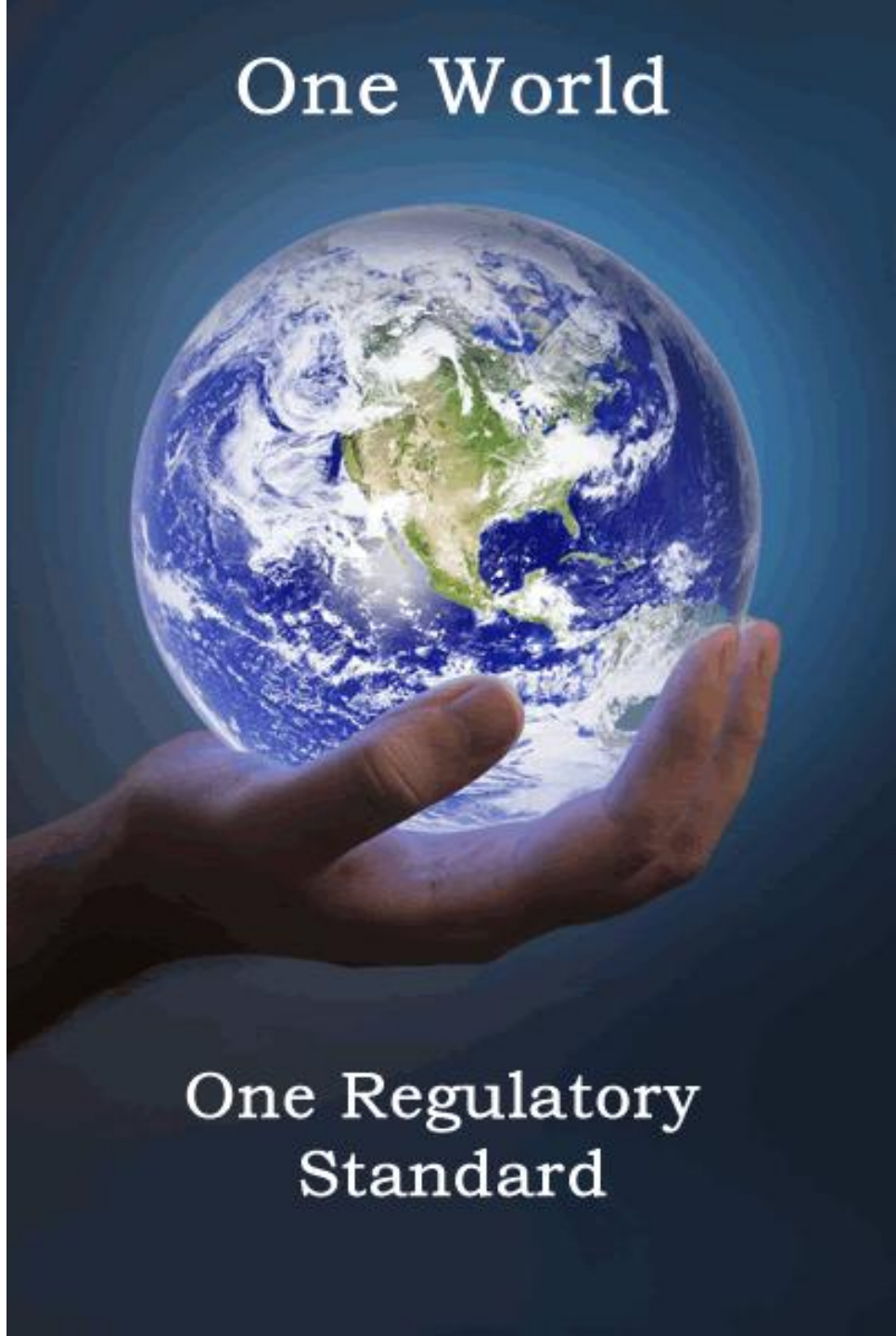
Optimize global safety and quality monitoring by sharing real-time information

Increase Supply Chain agility and resilience by enabling continuous improvement

Increase availability of medicines to patients

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