EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

EMA perspectives on ICH M4Q(R2) and digital regulatory assessment

CMC strategy forum, Brugge, 17-19 October 2022

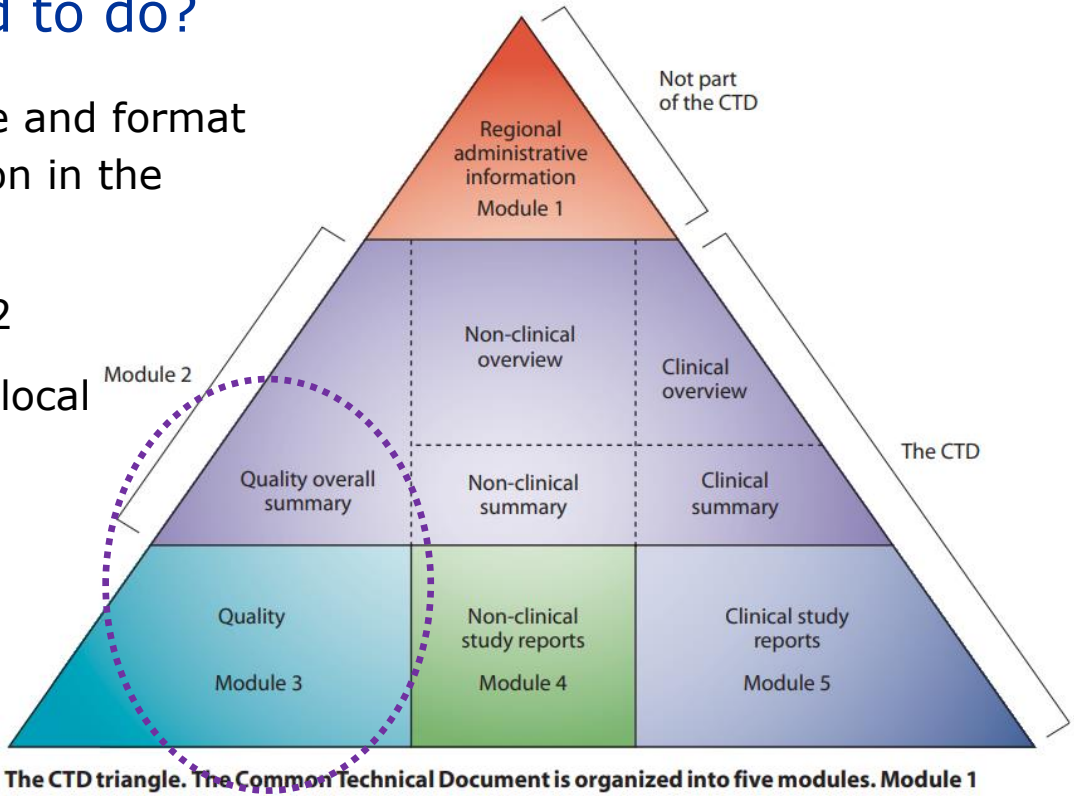
Klara Tiitso, Pharmaceutical Quality Senior Specialist, European Medicines Agency

Presentation outline

- Introduction
- M4Q(R2) roadmap
- Concept paper
  - Problem statement
  - Issues to be resolved
  - Objectives
- Structured Product Quality Submissions
- EU digitalisation overview
- What are the benefits?

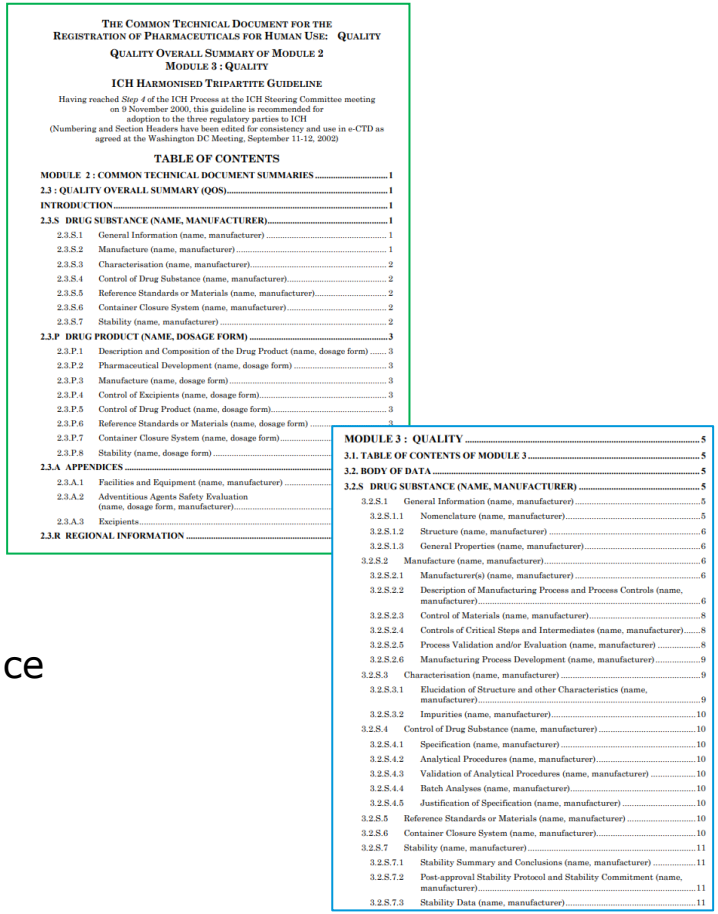
What is ICH M4Q designed to do?

- Provides a harmonised structure and format for presenting quality information in the CTD
- M4Q(R1) was developed in 2002
- Major improvement over paper/local submission formats



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.

Current ICH M4Q(R1)



THE COMMON TECHNICAL DOCUMENT FOR THE REGISTRATION OF PHARMACEUTICALS FOR HUMAN USE: QUALITY

QUALITY OVERALL SUMMARY OF MODULE 2
MODULE 3 : QUALITY

ICH HARMONISED TRIPARTITE GUIDELINE

Having reached *Step 4* of the ICH Process at the ICH Steering Committee meeting on 9 November 2000, this guideline is recommended for adoption to the three regulatory parties to ICH
(Numbering and Section Headers have been edited for consistency and use in e-CTD as agreed at the Washington DC Meeting, September 11-12, 2002)

TABLE OF CONTENTS

MODULE 2 : COMMON TECHNICAL DOCUMENT SUMMARIES 1
2.3 : QUALITY OVERALL SUMMARY (QOS) 1
INTRODUCTION 1
2.3.S DRUG SUBSTANCE (NAME, MANUFACTURER) 1
2.3.S.1 General Information (name, manufacturer) 1
2.3.S.2 Manufacture (name, manufacturer) 1
2.3.S.3 Characterisation (name, manufacturer) 2
2.3.S.4 Control of Drug Substance (name, manufacturer) 2
2.3.S.5 Reference Standards or Materials (name, manufacturer) 2
2.3.S.6 Container Closure System (name, manufacturer) 2
2.3.S.7 Stability (name, manufacturer) 2
2.3.P DRUG PRODUCT (NAME, DOSAGE FORM) 3
2.3.P.1 Description and Composition of the Drug Product (name, dosage form) 3
2.3.P.2 Pharmaceutical Development (name, dosage form) 3
2.3.P.3 Manufacture (name, dosage form) 3
2.3.P.4 Control of Excipients (name, dosage form) 3
2.3.P.5 Control of Drug Product (name, dosage form) 3
2.3.P.6 Reference Standards or Materials (name, dosage form) 3
2.3.P.7 Container Closure System (name, dosage form) 3
2.3.P.8 Stability (name, dosage form) 3
2.3.A APPENDICES 3
2.3.A.1 Facilities and Equipment (name, manufacturer) 3
2.3.A.2 Adventitious Agents Safety Evaluation (name, dosage form, manufacturer) 3
2.3.A.3 Excipients 3
2.3.R REGIONAL INFORMATION 3

MODULE 3 : QUALITY 5
3.1. TABLE OF CONTENTS OF MODULE 3 5
3.2. BODY OF DATA 5
3.2.S DRUG SUBSTANCE (NAME, MANUFACTURER) 5
3.2.S.1 General Information (name, manufacturer) 5
3.2.S.1.1 Nomenclature (name, manufacturer) 5
3.2.S.1.2 Structure (name, manufacturer) 6
3.2.S.1.3 General Properties (name, manufacturer) 6
3.2.S.2 Manufacture (name, manufacturer) 6
3.2.S.2.1 Manufacturer(s) (name, manufacturer) 6
3.2.S.2.2 Description of Manufacturing Process and Process Controls (name, manufacturer) 6
3.2.S.2.3 Control of Materials (name, manufacturer) 8
3.2.S.2.4 Controls of Critical Steps and Intermediates (name, manufacturer) 8
3.2.S.2.5 Process Validation and/or Evaluation (name, manufacturer) 8
3.2.S.2.6 Manufacturing Process Development (name, manufacturer) 9
3.2.S.3 Characterisation (name, manufacturer) 9
3.2.S.3.1 Elucidation of Structure and other Characteristics (name, manufacturer) 9
3.2.S.3.2 Impurities (name, manufacturer) 10
3.2.S.4 Control of Drug Substance (name, manufacturer) 10
3.2.S.4.1 Specification (name, manufacturer) 10
3.2.S.4.2 Analytical Procedures (name, manufacturer) 10
3.2.S.4.3 Validation of Analytical Procedures (name, manufacturer) 10
3.2.S.4.4 Batch Analyses (name, manufacturer) 10
3.2.S.4.5 Justification of Specification (name, manufacturer) 10
3.2.S.5 Reference Standards or Materials (name, manufacturer) 10
3.2.S.6 Container Closure System (name, manufacturer) 10
3.2.S.7 Stability (name, manufacturer) 11
3.2.S.7.1 Stability Summary and Conclusions (name, manufacturer) 11
3.2.S.7.2 Post-approval Stability Protocol and Stability Commitment (name, manufacturer) 11
3.2.S.7.3 Stability Data (name, manufacturer) 11

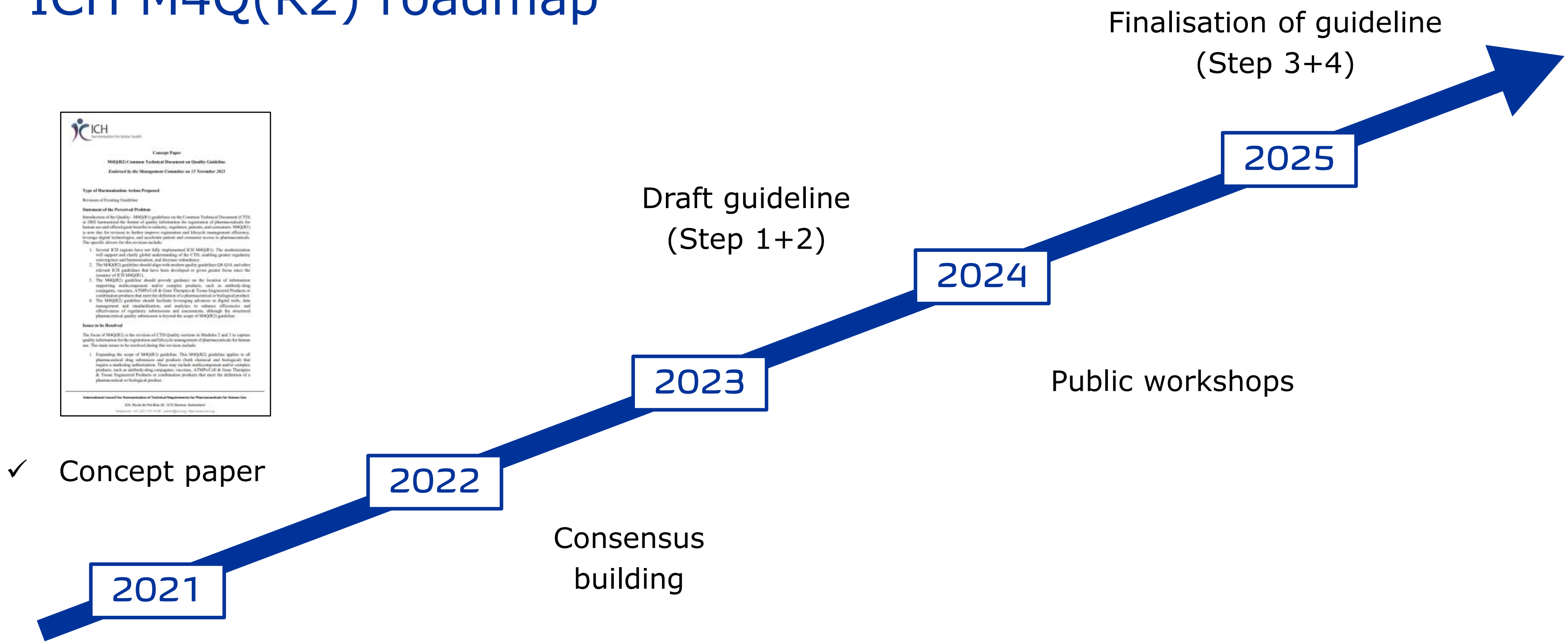
Module 2

Summaries of information from Module 3

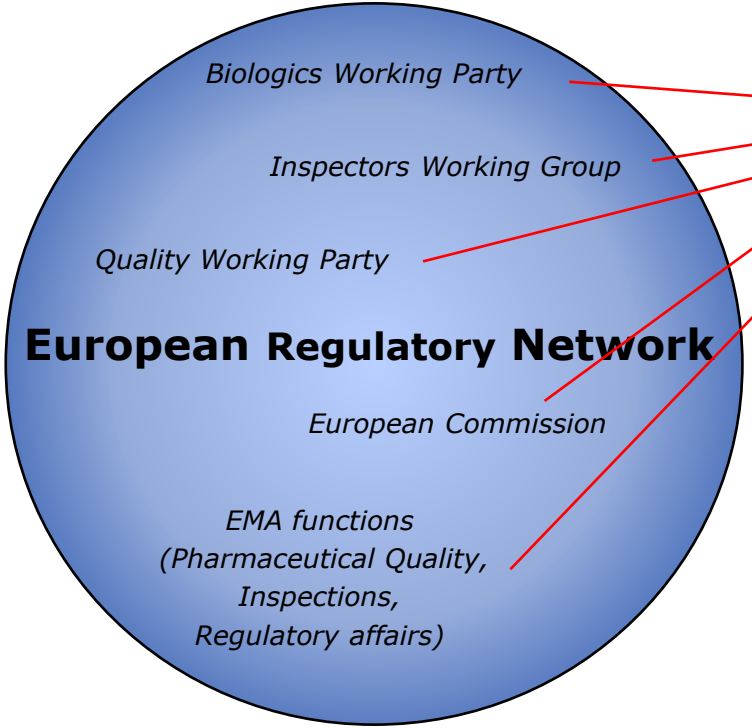
Module 3

Body of data pertaining to manufacturing, analytical methods, process development, specifications, reference standards, container closure system, and stability

ICH M4Q(R2) roadmap



EU input to ICH M4Q(R2)



M4Q(R2) EWG Revision of M4Q(R1)

EC, Europe
Klara Tiitso
Mr. Antonius (Ton) Johannes van der Stappen

EDA, Egypt
Dr. Sara Shatat

EFPIA
Henrik Kim Nielsen

FDA, United States
Dr. Ingrid Markovic
Dr. Susan Rosencrance

Global Self-Care Federation
Ms. Christelle Alliens-Müller

Health Canada, Canada
Dr. Hugo Hamel

IFPMA
Ms. Sheila Inada

IGBA
Mr. Javier Monvoisin

JPMA
Mr. Hiroki Ito
Ms. Tomoko Yamato

MFDS, Republic of Korea
Dr. Naroo Kang

MHLW/PMDA, Japan

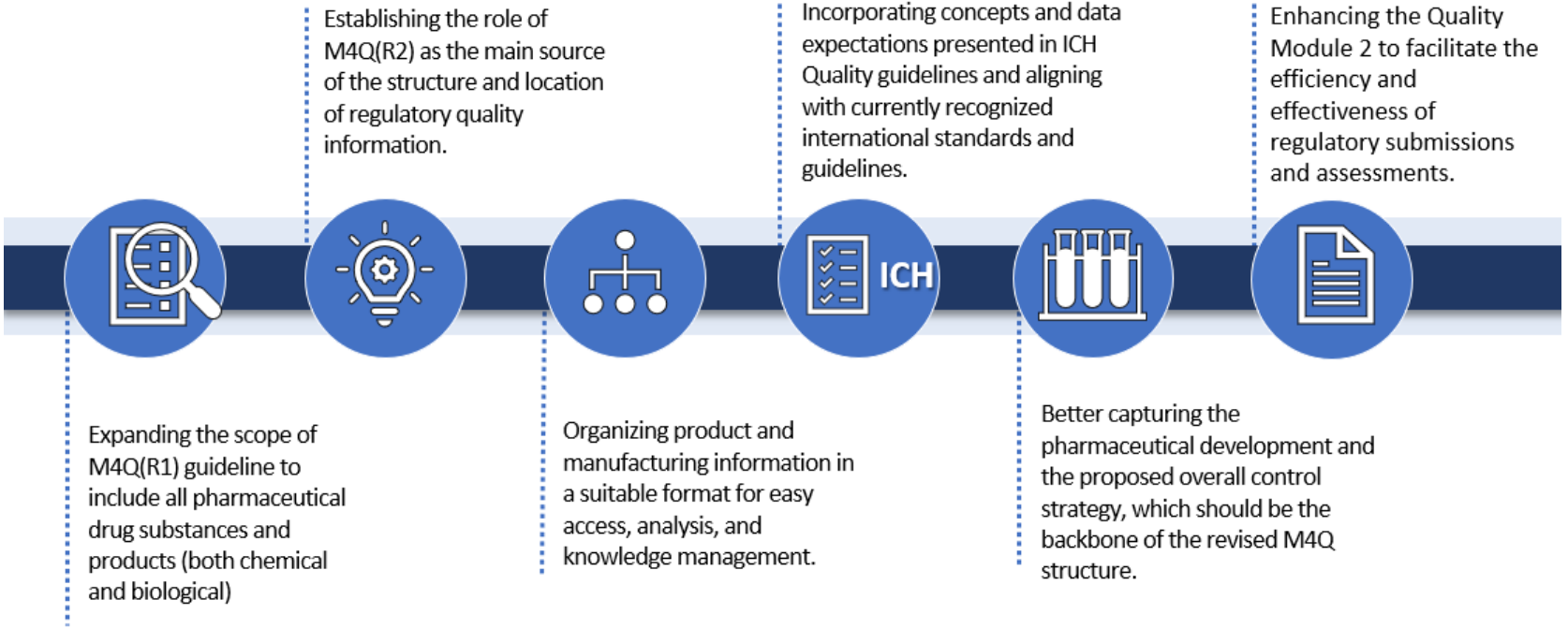
NMPA, China

Disclaimer: Expert Working Groups members are appointed by their nominating ICH Member or Observer party and are responsible for representing the views of that party, which may not necessarily reflect their personal views. Working Group experts do not respond personally to external inquiries but are directed to forward any inquiries they receive to their nominating party or the ICH Secretariat for a response on behalf of either their ICH party or the ICH Association as appropriate. For questions to the ICH Secretariat, please use the contact form on the ICH website.

M4Q(R2) concept paper - what are the perceived problems?

- Need to further support and clarify global understanding of the CTD, enabling greater regulatory convergence and harmonisation
- Lack of alignment with recent quality guidelines (Q8-14)
- Need to better support multicomponent and/or complex products
- Need to facilitate leveraging advances in digital tools, data management and standardisation, and analytics to enhance efficiencies of regulatory submissions and assessments

M4Q(R2) concept paper – what are the issues to be resolved?



M4Q(R2) concept paper – what are the objectives?

M4Q(R2) guideline will improve submission and assessment efficiency, resulting in accelerated access to pharmaceuticals by (6Es):

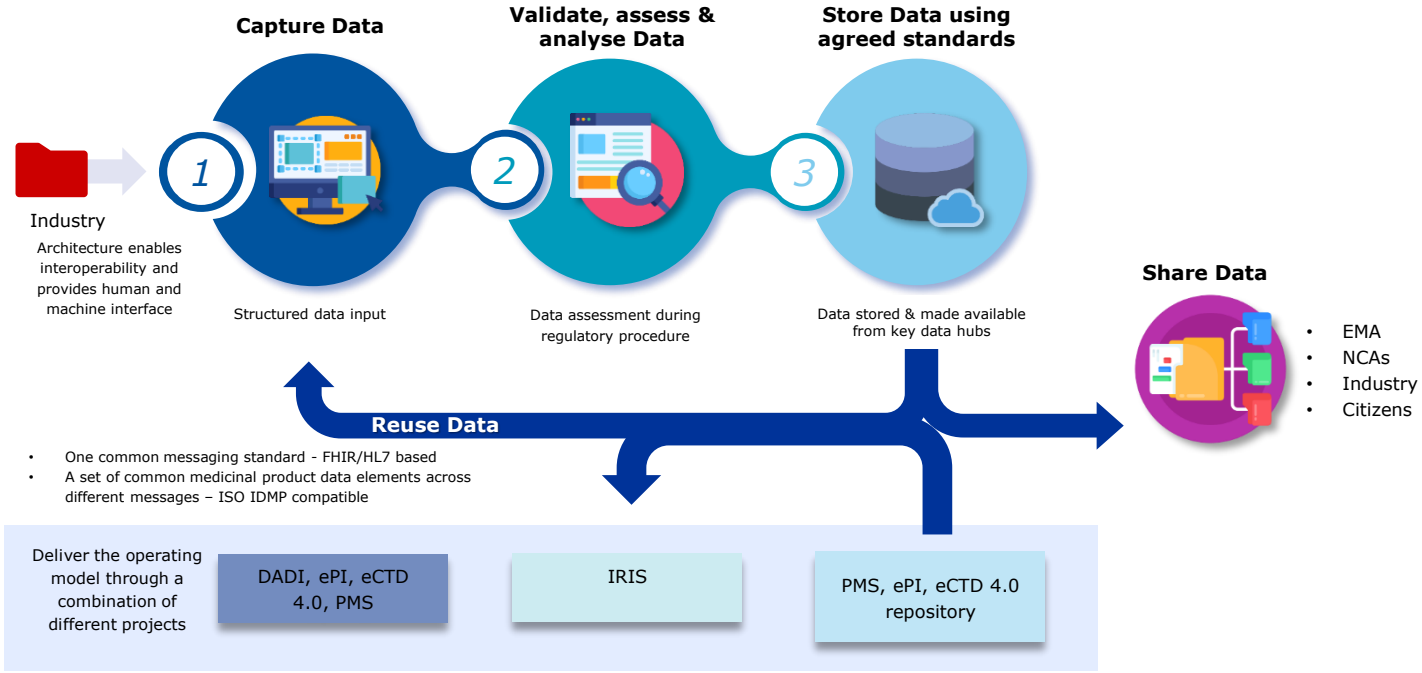
1. **Encouraging global convergence** of science- and risk-based regulatory approaches in the preparation of dossiers.
2. **Explaining** and defining the **organization and positioning of information** for Modules 2 and 3.
3. **Enriching communication** between regulators and applicants and enhancing lifecycle and knowledge management.
4. **Embracing** product and process **innovation**.
5. **Enabling efficient use of digital tools** for submission and assessment.
6. **Elucidating regulatory expectations** and supporting efficient assessments and decision-making.

Structured product quality submissions

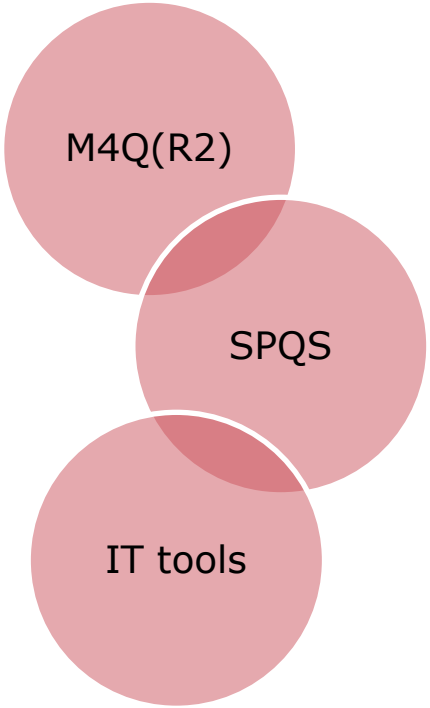
Structured data is highly organised and formatted, making it searchable and easy to collect, process, and analyse

- Implementation of structured data outside scope of M4Q(R2) – Structured product quality submissions (SPQS) agreed as separate ICH topic
- Stepwise approach: SPQS to start when M4Q(R2) reaches step 2

EU digitalisation → *Moving to a Data-Centric Target Operating Model*



What are the benefits?



- Improved access to data and information
- Effective knowledge management
- Use of intelligent data analysis and risk assessment
- Easy sharing of information

- Streamlined regulatory assessment
- Improved product oversight
- Increased consistency in regulatory decision making
- Enhanced B/R decisions
- Support regulatory convergence and reliance
- Improved communication with industry

Any questions?

klara.tiitso@ema.europa.eu

Official address Domenico Scarlattilaan 6 • 1083 HS Amsterdam • The Netherlands
Telephone +31 (0)88 781 6000
Send us a question Go to www.ema.europa.eu/contact

Follow us on **@EMA_News**