EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

EMA Update: Clinical Trials

Fergus Sweeney (EMA) on 17 May 2019
EUFEMED Annual Conference

- CT Regulation update
- Departure of UK from EU
- EUNTC and clinical trials
- ICH GCP Renovation
- EMA Regulatory Science Strategy

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Clinical Trials Information System (CTIS)

- The Clinical Trial Regulation* and its implementation require the development of a range of IT functionalities by the European Medicines Agency.
- These functionalities form the system collectively known as the Clinical Trials Information System (CTIS).
- CTIS is a regulatory system for use by Member States supervisory authorities and sponsors of clinical trials.
- CTIS will become the single entry point for submitting clinical trial information in the EU, including clinical trial applications and safety reports concerning these trials.

*REGULATION (EU) No 536/2014 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC

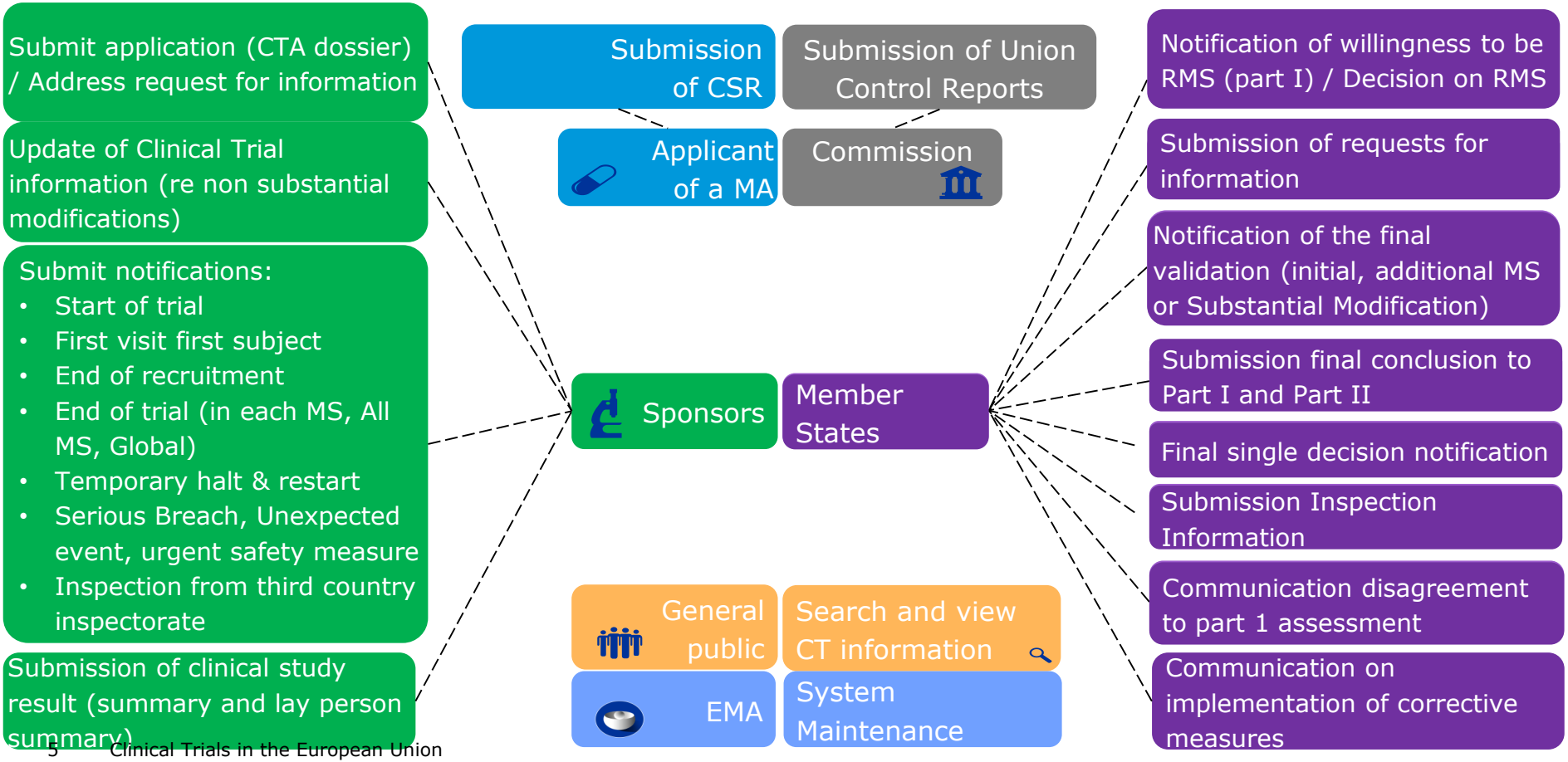
A real opportunity for EU to innovate and to lead

- in clinical trial regulation and
- in innovation of new medicines and better use of existing medicines,

Streamlined, coordinated, proportionate and transparent

- Single electronic submission of data and documents to cover trial application, modification, registration and results reporting
- Streamlined and coordinated clinical trial between and within MS, using best expertise in the MS concerned
- Streamlined safety reporting,
- Proportionate supervision of clinical trials,
- Transparency supporting public confidence, participation and critique and enabling innovation.

Activities in the system



EU portal and database project – business context view

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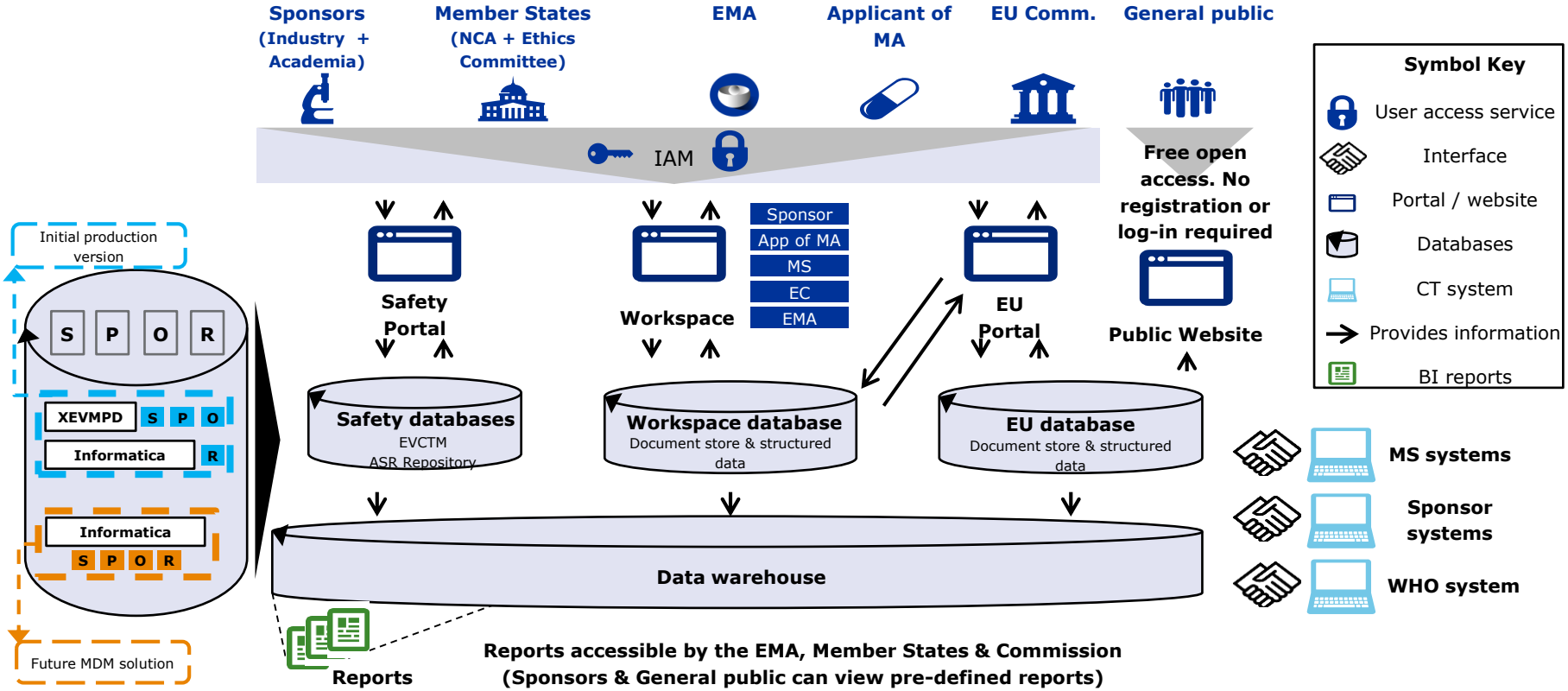
This diagram depicts the To-Be system architecture for the clinical trial systems:



Status of CTIS development

- CTIS includes several components that are currently under development: the EU portal for submission including a safety reporting module, an EU database for document repository and a public register for publication of trial information.
- At present, most functionalities have been delivered that facilitate the processing of a clinical trial and related application (CTA):

Preparation and submission of CTA by a sponsor and related safety information	Evaluation by the concerned Member State(s)	Submission of the clinical study report by the applicant
Evaluation by the concerned Member State(s) concerned	Regulatory supervision	Publication of clinical trial information

Further development of CTIS

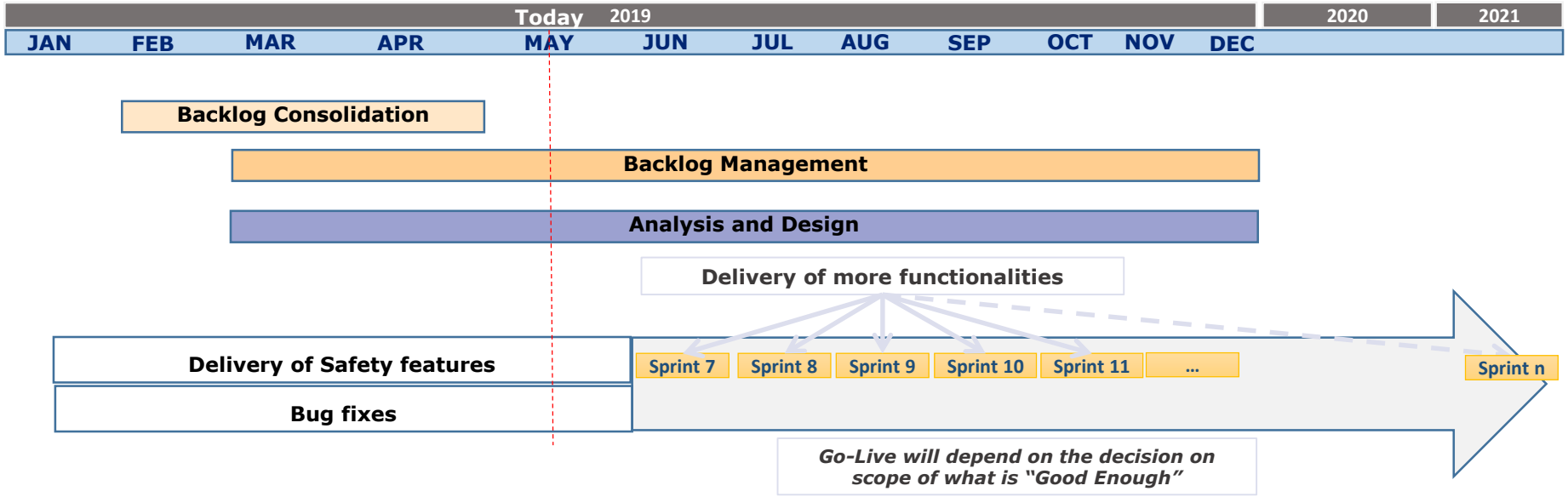
The continued development engages business experts from various stakeholder groups to ensure that CTIS is fit for purpose.

From June 2019, the delivery model follows a fast-paced and short-cycled way of working.

Areas that require further development include

- Document management, enhanced submission and identification of changes made to an application.
- Facilitation of Member States oversight, cooperation and supervision through improved sharing of information and features to facilitate scientific and regulatory review and monitoring.

Schedule for development



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Operational preparedness update – Industry stakeholders guidance

European Council agreed to a further extension of the **date for the UK's withdrawal** which will last as long as necessary and, in any event, **no longer than 31 October 2019**.

The UK **remains a Member State** for the duration of the extension

EMA calls on all **pharmaceutical companies** in the EU to **continue their preparedness** for the UK's withdrawal

UK continues to be a Member State of the EU

- Involved in clinical trial process, completing EudraCT, part of CTFG etc
- Involved in design and testing of the Clinical Trial Information System for CT Regulation

UK withdraws from EU

- EC Notice To Stakeholders – Withdrawal of the UK and EU rules in the field of clinical trials 6 September 2018 https://ec.europa.eu/info/sites/info/files/notice_to_stakeholders_brexit_clinical_trials_final.pdf
  - UK will then become a third country
  - Subject to any transitional arrangement that may be contained in a possible withdrawal agreement,
    - Supply of investigation medicinal products – rules on import apply
    - Establishment requirements for the sponsor or the legal representative – establishment in a EU Member State
    - Submission of clinical trial information to EudraCT – protocol information no longer submitted for trials authorised as of withdrawal date, results summaries required if due before withdrawal date – except where present in a PIP

Science and Research are international

Clinical trials conducted in EU also involve clinical trial sites outside of EU, may be anywhere in the world

ICH standards are applied internationally

Clinicial trial results accepted in EU MAAs so long as they meet scientific and ethical standards equivalent to those applying in EU

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About the EU Network Training Centre

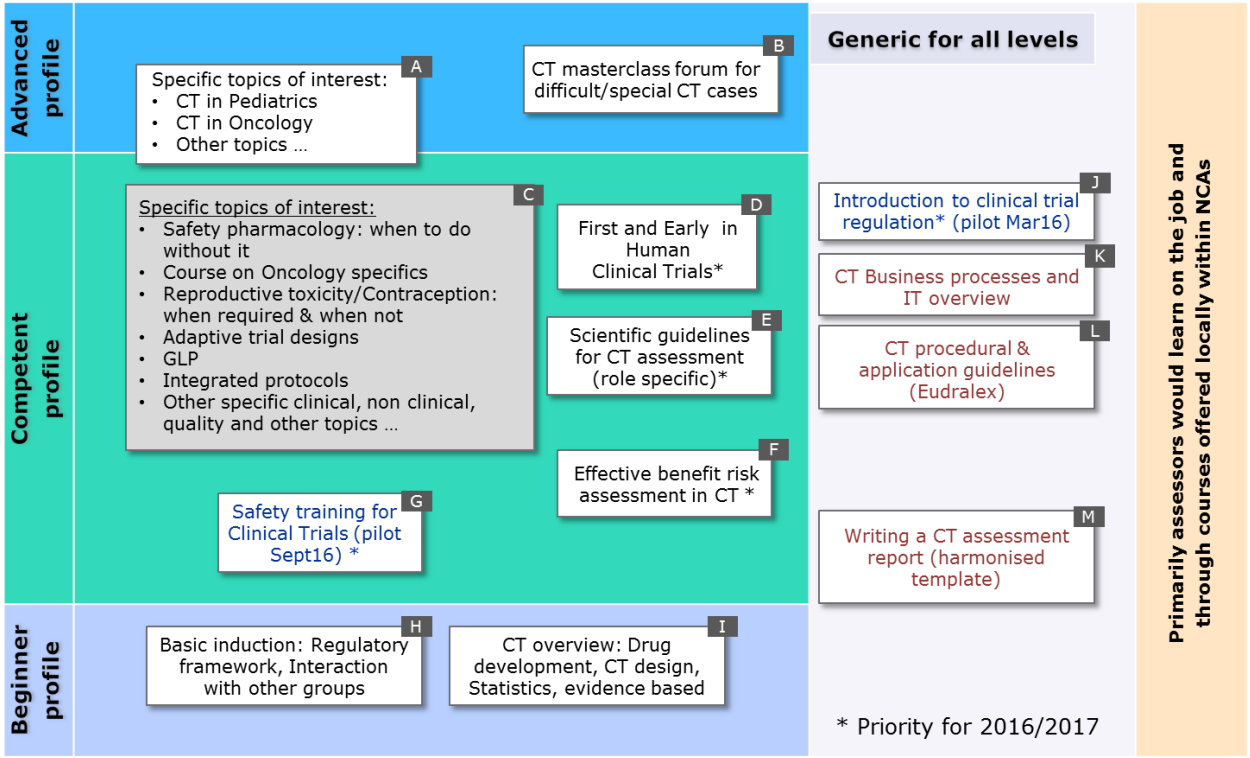
The EU Network Training Centre is a joint HMA & EMA initiative

Our mission is to spread good scientific and regulatory practice across the EU Regulatory Network, by making more high quality training offers available to its members.

Why?

- To improve the quality, consistency and efficiency of the regulatory network and foster science based, pragmatic assessment, inspection, pharmacovigilance and decision making;
- To promote harmonised application of regulatory framework and guidelines.

Curriculum status update: Clinical Trials



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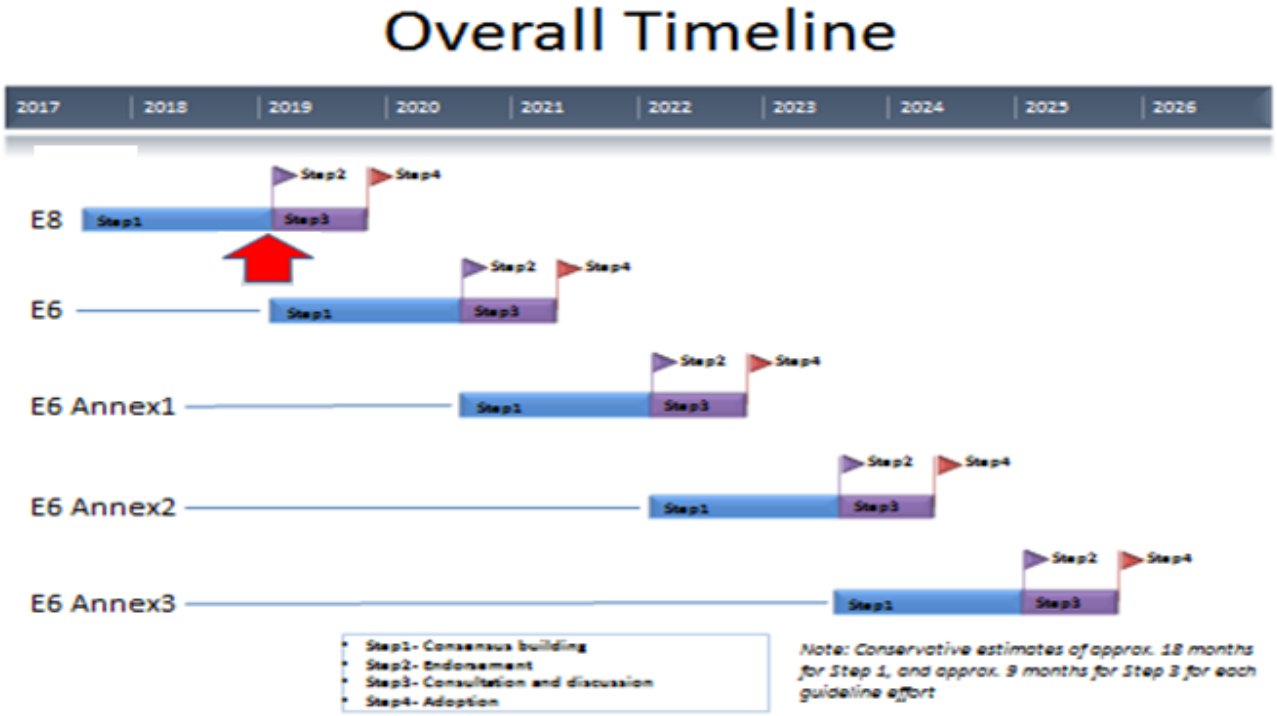
Key messages on ICH GCP Renovation

- *ICH E8 and E6 need modernising to prepare for the future – future medicines, future trial designs, future data sources*
- *Emphasise the role of achieving quality by good design*
- *Ensure the involvement of all parties up front in study planning, i.e.: sponsor, patients, trial subjects, investigators, HCPs, regulatory agencies*
- *Set the foundation for new study designs and data sources (RWE, etc.)*

Plan for E8 and E6 revisions



E8 R1 - General Considerations for Clinical Trials

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- Incorporate the most current concepts achieving fit-for-purpose data quality as one of the essential considerations for all clinical trials.
- Identify a basic set of critical-to-quality factors that can be adapted to different types of trials to support the meaningfulness and reliability of trial results and to protect human subjects;
- Address a broader range of trial designs and data sources (e.g. basket trials, umbrella trials, adaptive designs, prospective RCTs, observational studies… and data sources – eCRFs, EHRs, registries, RWE …)

This modernisation of ICH E8 is the first step towards the ICH GCP Renovation initiated in 2017.

ICH E8 R1 –published for consultation

https://www.ema.europa.eu/en/documents/scientific-guideline/ich-e-8-r1-general-considerations-clinical-studies-step-2b_en.pdf

08 May 2019
EMA/CHMP/ICH/544570/1998
Committee for Human Medicinal Products

ICH guideline E8 (R1) on general considerations for clinical studies

Step 2b

Transmission to CHMP	25 April 2019
Adoption by CHMP	25 April 2019
Release for public consultation	10 May 2019
Deadline for comments	30 September 2019

E8 (and E6) revision – goals and challenges

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Facilitate innovative approaches to clinical trials including:

- Quality by design processes
- Facilitating a broad range of study designs and data sources
- Upfront assessment of risks specific to a study design, protocol and procedures
- Proportionate management of the risks and controls focusing on critical study elements,
- use of technological tools to ensure robust conduct, oversight, and reporting.

- The greatest challenge is in Change Management – adjusting behaviors, attitudes – moving away from preconceived ideas and interests

- The greatest achievements will be by those who embrace new approaches and seek to make them work – there is no regulatory impediment per se

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Innovative medicines – challenges for regulators

- Novel technologies: e.g. genome editing
- Innovative manufacturing approaches: point-of-care manufacturing, release and control
- Borderline products: contribution of each component to clinical benefit-risk
- Data requirements: small patient populations / comparators / registries
- Evidence generation: approval / post-marketing / market access

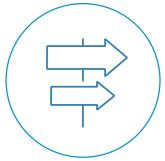
An evolving role for medicines regulatory agencies

To progress from R&D to patient access

Protecting patients and enabling innovation

Gatekeeper & Enabler

- Fostering scientific excellence in the **evaluation and supervision** of medicines



- **Supporting research and innovation** to stimulate the development of better medicines

- **Connecting stakeholders** together to bridge gaps

What are regulators doing to enable innovation?

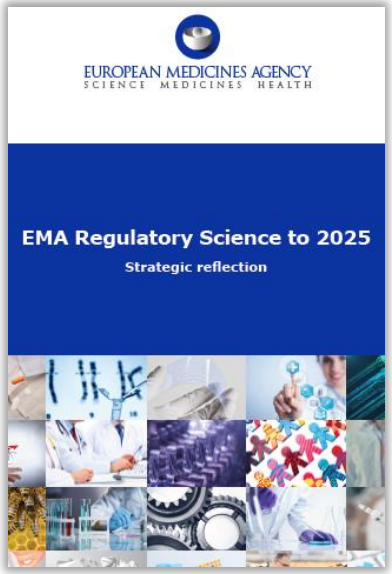
- Providing **regulatory guidance and support** to medicines developers / academia / healthcare professionals / investors
- Providing a **supportive scientific environment** and **standards**:
  - Adapt evidence standards to specific products and feasibility of studies
  - Contribute to the **progress of regulatory s**cience
  - **Qualification** of scientific **methods**
  - Collaborate with **HTAs** to define **data requirements for market access**

EMA's Regulatory Science Strategy

To build a **adaptive** regulatory system
that will encourage innovation in human and veterinary medicines

- Guidance on modernised medicines developments
- Facilitate the optimisation of regulatory science
- Assess benefits and risks of innovative therapies and diagnostics based on new technologies

Consultation to June 2019



Thank you for your attention

Further information

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