CLINICAL TRIALS TRANSFORMATION INITIATIVE

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RCT Approval process – international perspective FDA, EMA and ICH

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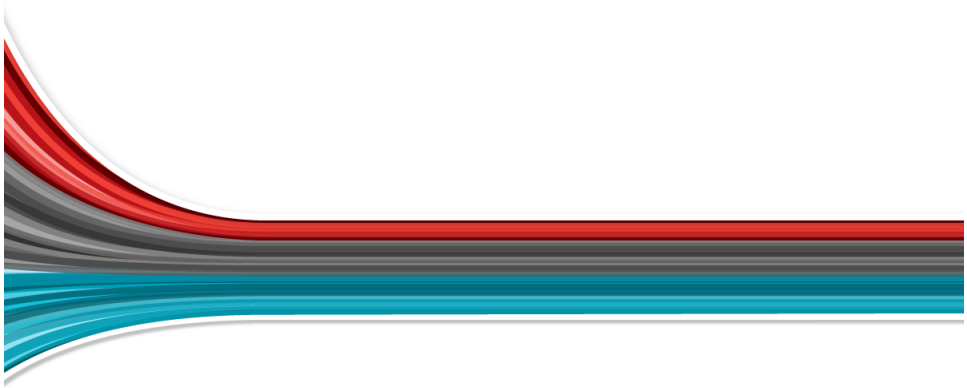
Disclaimer

- The views and opinions expressed in this presentation are those of the individual presenter and do not necessarily reflect the views of the Clinical Trials Transformation Initiative.
- Pamela Tenaerts is an Employee of Duke University. Salary support comes from pooled membership fees of the Clinical Trials Transformation Initiative and from FDA grant R18FD005292.

A few International Perspectives

- FDA
  - PDUFA/21CC
  - CDER/OCE
- EMA
  - Regulatory Science 2025
- ICH renovations



Food and Drug Administration

FDA Mission (Mar 28, 2018)

- The **Food and Drug Administration** is responsible for **protecting the public health** by ensuring the safety, efficacy, and security of **human and veterinary drugs, biological products, and medical devices**; and by ensuring the safety of our nation's **food supply, cosmetics, and products that emit radiation.**
- **…Tobacco products…**
- Advancing the public health by helping to **speed innovations** that make medical products more effective, safer, and more affordable….
- Significant role in the Nation's counterterrorism capability…
  - security of the food supply
  - public health threats.

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FDARA

- On August 18, 2017, the President signed into law the Food and Drug Administration Reauthorization Act (FDARA) extend the user-fee programs for drugs, medical devices, generic drugs, and biosimilar biological products, and for other purposes.
  - PDUFA, MDUFA, GDUFA
- Initial law passed by the United States Congress in 1992
- PDUFA VI

https://www.congress.gov/115/plaws/publ52/PLAW-115publ52.pdf

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PDUFA VI

- *Enhanced Review Transparency and Communication*
- *Promoting Innovation through Enhanced Communication*
- *Ensuring Sustained Success of Breakthrough Therapy Program*
- *Early Consultation on the Use of New Surrogate Endpoints*
- *Advancing Development of Drugs for Rare Diseases*

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PDUFA VI

- *Advancing Development of Drug-Device and Biologic-Device Combination Products*
- *Enhancing Use of Real World Evidence (RWE) for Use in Regulatory Decision-Making*
- *Capturing the Patient Voice in Drug Development*
- *Advancing the Use of Complex Innovative Trial Designs and Model Informed Drug Development*
- *Enhancement and Modernization of the FDA Drug Safety System*

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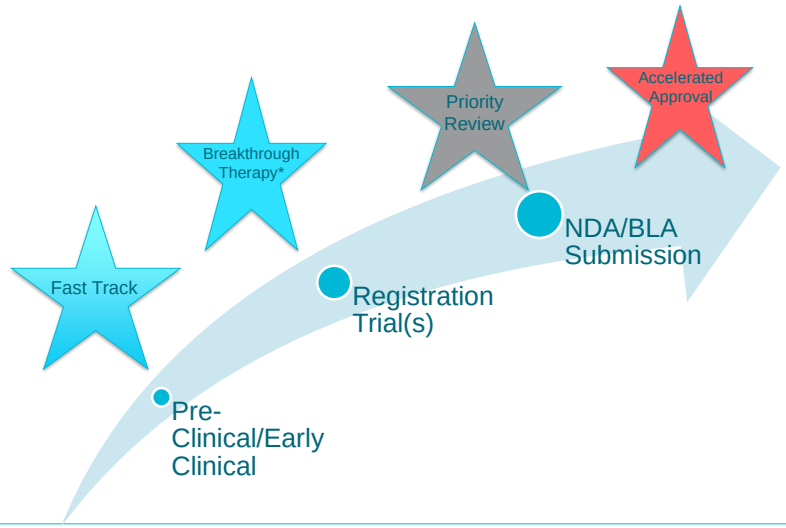
FDA Expedited Programs



Source: FDA/OCE

*2012 Food and Drug Administration Safety and Innovation Act

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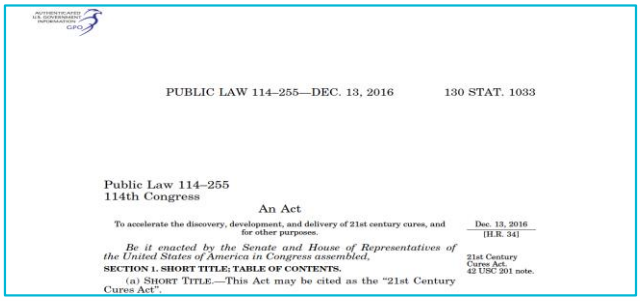
The 21st Century Cures Act

To accelerate the discovery, development, and delivery of 21st century cures, and for other purposes

- Landmark, bipartisan legislation, signed into law on Dec. 13, 2016
- Virtually all aspects of biomedical research, medical product development and the regulatory approval process
  - NIH
  - FDA
  - CMS



PUBLIC LAW 114–255—DEC. 13, 2016 130 STAT. 1033

Public Law 114–255
114th Congress

An Act

To accelerate the discovery, development, and delivery of 21st century cures, and for other purposes.

Dec. 13, 2016
[H.R. 34]

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled,

21st Century Cures Act.
42 USC 201 note.

SECTION 1. SHORT TITLE; TABLE OF CONTENTS.

(a) SHORT TITLE.—This Act may be cited as the "21st Century Cures Act".

https://www.congress.gov/114/plaws/publ255/PLAW-114publ255.pdf

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21CC: Food and Drug Administration

- Sec. 3002: Patient-focused drug development guidance
- Sec. 3011: Qualification of drug development tools
- Sec. 3021: Novel clinical trial designs
- Sec. 3022: Real-world evidence
- Sec. 3042: Limited population pathway (antibacterial & antifungal drugs)
- Sec. 3060: Clarifying medical software regulation
- Sec. 3072: Hiring authority for scientific, technical, and professional personnel

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CDER Program Modernization

Grow scientific expertise and clarify pathways to regulatory approval	• Address unmet medical need • Proactively collaborate with academic medical scientists and patient/disease advocates, evaluate scientific gaps, and strategically foster drug development
Submissions meets statutory and regulatory requirements	• Develop a more integrated, cross-disciplinary document to foster collaboration and reduce redundant information. • Assessments will be rigorous, risk-based, and clinically relevant; focus on the key issues; and incorporate the patient perspective
Benefit-Risk Monitoring	• Unified post-market safety surveillance framework. • Protect the American public, we will systematically monitor the benefits and risks of approved drugs across their lifecycles.
Talent	• 21st Century Cures Act: recruit and retain technical, scientific and professional experts, and eliminate backlog of vacant positions
Operational Excellence	• Enhance ability to address OND's workload through greater process standardization and better defined roles and responsibilities. • Improving operational efficiency and enable scientists to focus on science, not ancillary tasks
Knowledge Management	• Make it easy for staff to find and use scientific and regulatory precedents.

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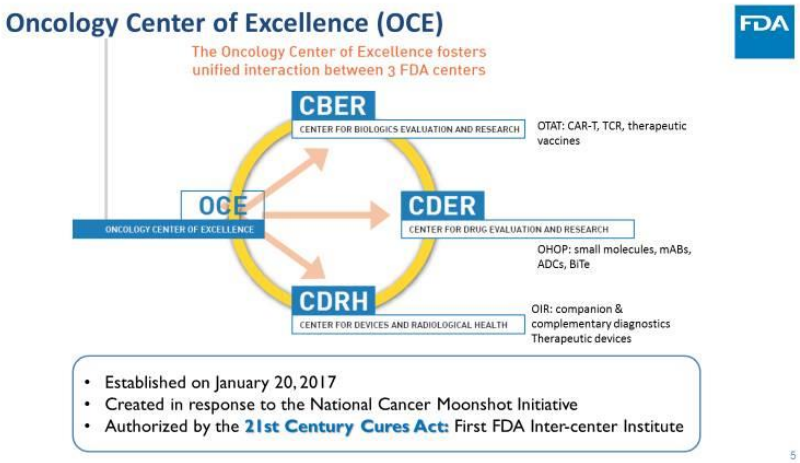
FDA: Oncology Center of Excellence



Source: FDA/OCE

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European Medicines Agency
Responding to the needs of the 21st century patient:
Addressing challenges and opportunities across the European Regulatory Framework

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Why now?

- To monitor and sign-post emerging and future trends in science and technology
- To identify key priorities where new or enhanced engagement is essential to the continued success of the Agency's mission
- To prioritise use of resources and external collaborations to strategically advance regulatory science
- To shape and influence the vision for the EU Medicines Agencies Network (EMRN) Strategy 2020–25

https://www.ema.europa.eu/en/about-us/how-we-work/regulatory-science-2025

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How does EMA define Regulatory Science?

Regulatory science is defined as a range of scientific disciplines that are applied to the quality, safety and efficacy assessment of medicinal products and that inform regulatory decision-making throughout the lifecycle of a medicine.

It encompasses basic and applied medicinal science and social sciences, and contributes to the development of regulatory standards and tools.

https://www.ema.europa.eu/en/about-us/how-we-work/regulatory-science-2025

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Vision—EMA Regulatory Science to 2025

"To underpin its mission of protecting human health, EMA must catalyse and enable regulatory science and innovation to be translated into patient access to medicines in evolving healthcare systems."

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https://www.ema.europa.eu/en/about-us/how-we-work/regulatory-science-2025

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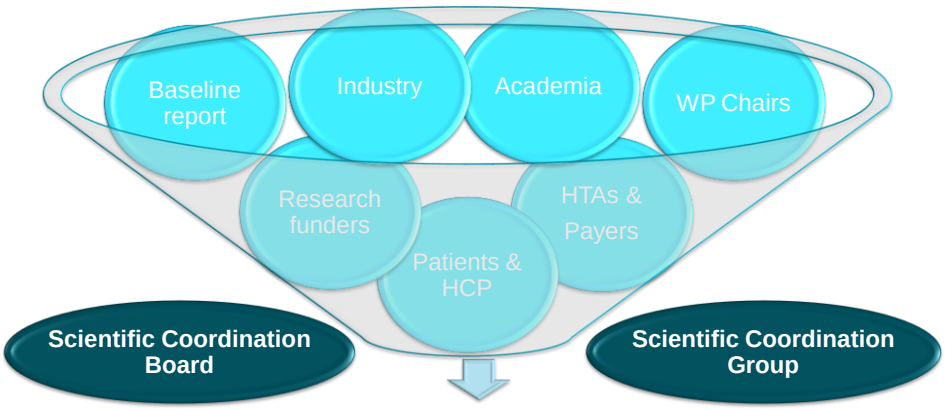

Regulatory Science to 2025

https://www.ema.europa.eu/en/about-us/how-we-work/regulatory-science-2025

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Regulatory Science 2025: Goals

Strategic goal 1
To catalyse the integration of science and technology in drug development.

Strategic goal 2
To drive collaborative evidence generation to improve the scientific quality of evaluations.

Strategic goal 3
To advance patient-centred access to medicines in partnership with healthcare systems.

Strategic goal 4
To address emerging health threats and availability/therapeutic challenges.

Strategic goal 5
To enable and leverage research and innovation in regulatory science.

https://www.ema.europa.eu/en/about-us/how-we-work/regulatory-science-2025

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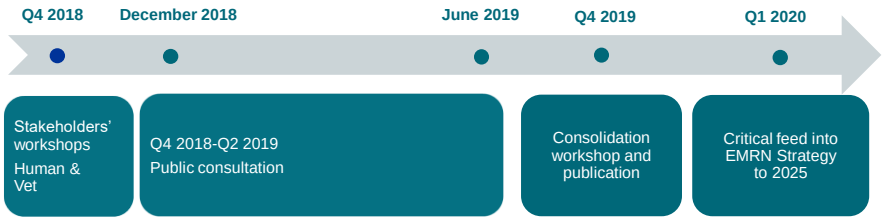
EMA Regulatory Science to 2025—Timeline



Legislation follows science, not the other way round:
implication for future EU legislation?

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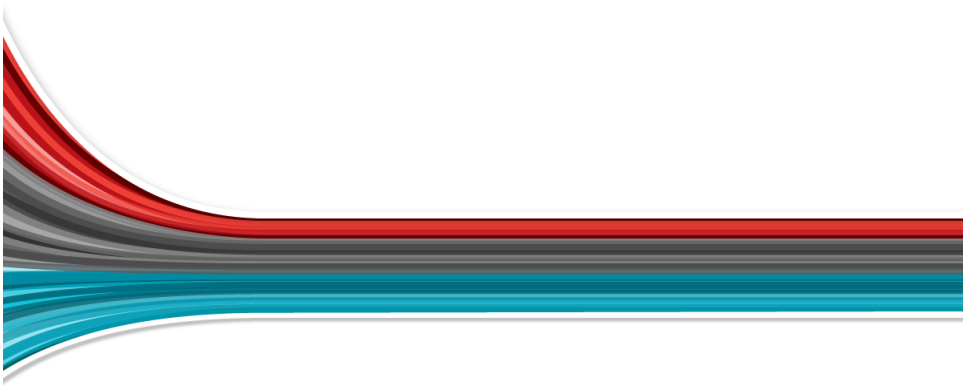

ICH guidelines

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ICH Members

Founding Regulatory Members	Regulatory Members
EC, Europe	ANVISA, Brazil
FDA, United States	MFDS, Republic of Korea
MHLW/PMDA, Japan	HSA, Singapore
	NMPA, China
Founding Industry Members	TFDA, Chinese Taipei
EFPIA	
JPMA	**Industry Members**
PhRMA	BIO
	Global Self-Care Federation
Standing Regulatory Members	IGBA
Health Canada, Canada	
Swissmedic, Switzerland	

Observers: Legislative or Administrative Authorities: TGA, Australia

https://www.ich.org/about/members-observers.html

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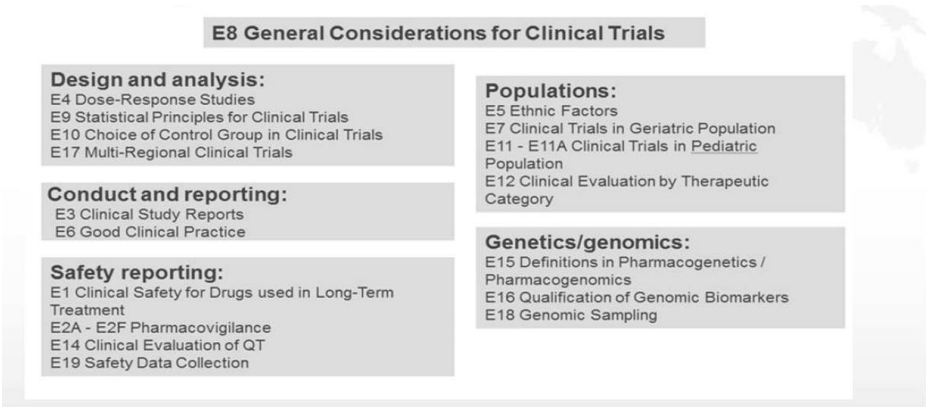
ICH E guidelines: need to be read together



https://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E8/ICHE8_R1__Step_2_Presentation_2019_0606.pdf

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ICH E8

- Published in 1997 and has not been revised until now. ICH Reflection on “GCP Renovation”: Modernization of ICH E8 and Subsequent Renovation of ICH E6 (2017)
- Proposed revision of E8 as 1st step towards a broader GCP renovation. E8(R1) will inform the development of future guidelines.
- E8(R1) has been signed off as a Step 2 document (08 May 2019) to be issued by the ICH Regulatory Members for public consultation.
- Anticipating finalization as a Step 4 document to be implemented in the local regional regulatory system: Jun 2020

https://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E8/ICHE8_R1__Step_2_Presentation_2019_0606.pdf

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ICH E guidelines

- The ICH Efficacy guidelines cover the design, conduct, analysis and reporting of clinical studies. The guidelines should be used in an integrated manner rather than one or other guideline or subsection being focused on in isolation of the others.
- E8(R1) provides an overall introduction to clinical development, designing quality into clinical studies and focusing on those factors critical to the quality of the studies
  - Quality by design
  - Development Planning
  - Design Elements for Clinical Studies

https://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E8/ICHE8_R1__Step_2_Presentation_2019_0606.pdf

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ICH E8 R(1) Key principles

- Protection of clinical study subjects is a shared responsibility (investigators, sponsors, IRB/IECs).
- Clinical studies should be designed, conducted, and analyzed according to sound scientific principles and reported appropriately.
- Consulting with patients and/or patient organizations in the design, planning and conduct of clinical studies helps to ensure that all perspectives are captured.

https://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E8/ICHE8_R1__Step_2_Presentation_2019_0606.pdf

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ICH E8 (R) Quality by Design Concepts

- Quality of a clinical study is fitness for purpose. The quality of the information generated should therefore be sufficient to support good decision making.
- The quality of a study is driven proactively by designing quality into the study protocol and processes.
- Critical to quality factors should be determined for each study
- Risks that threaten the integrity of the critical to quality factors should be identified and managed in a proportionate manner

https://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E8/ICHE8_R1__Step_2_Presentation_2019_0606.pdf

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THANK YOU.

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