Innovative Evidence Generation: OCE Project Pragmatica

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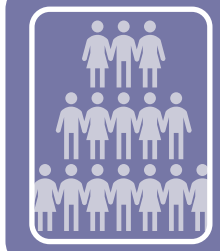
Current State

Complex and Restrictive



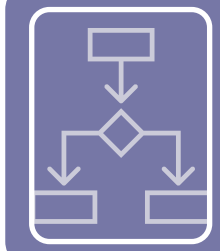
Resource Intensive

Highly Burdensome

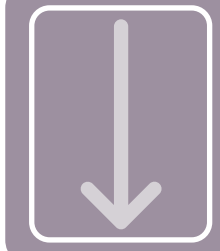
- Patients
- Providers

Future State

More Streamlined and Generalizable



Targeted Objective-focused Approaches



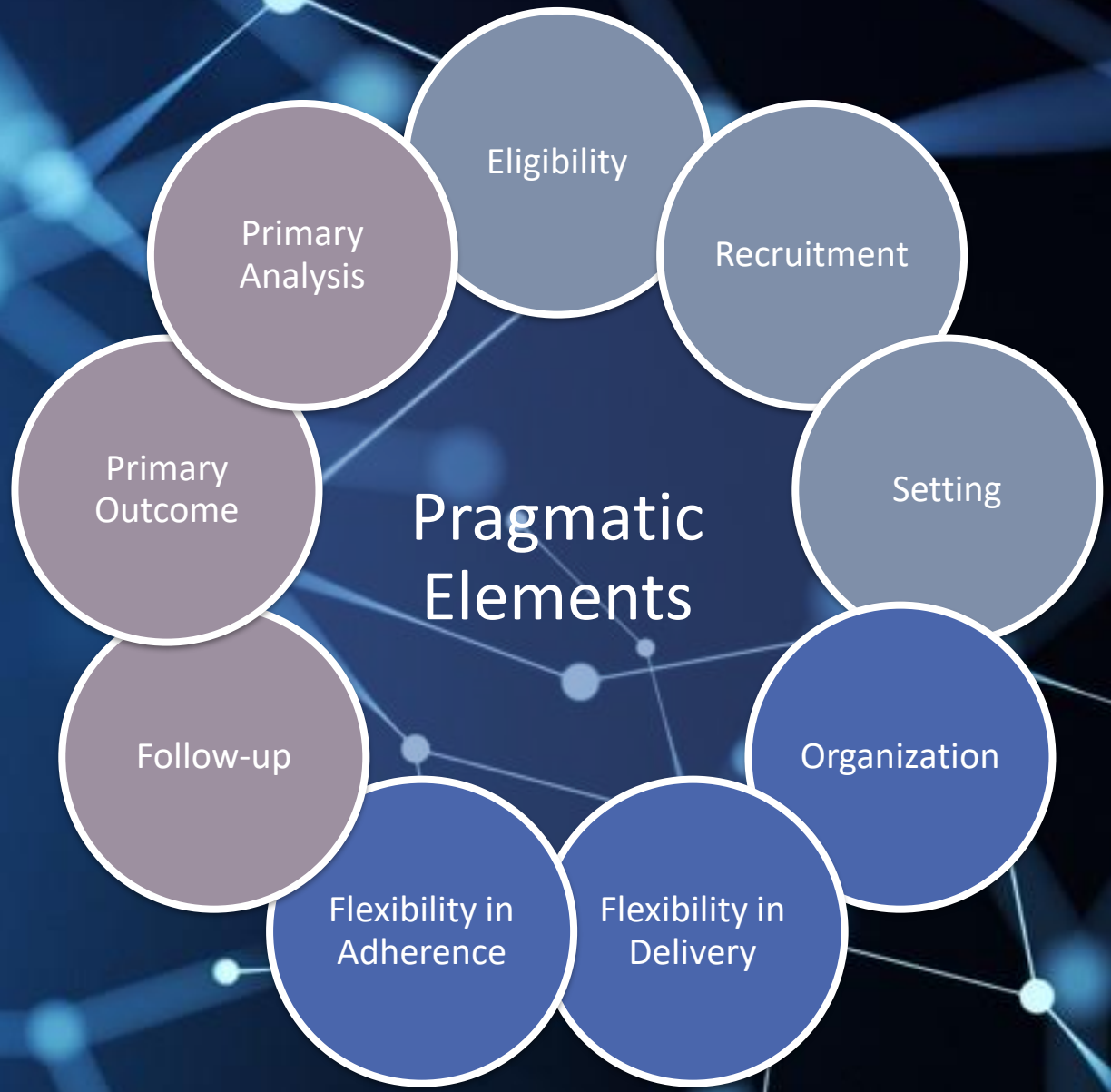
Closer to Routine Care

- Increased Access
- Appropriate Flexibilities

OCE Project Pragmatica

Objective

Advancing evidence generation for approved oncology medical products by exploring innovative trial design approaches that introduce functional efficiencies and patient centricity through integration with real-world routine clinical practice.



What is a **Pragmatic Clinical Trial?**

A clinical trial designed to efficiently inform decision-making on the benefits, burdens, and risks of health interventions in representative populations by including **pragmatic elements** that

1) are partially or fully integrated into routine clinical practice and/or
2) that streamline trial design and conduct.

Pragmatic Elements

Design features that can be integrated into a clinical trial, including but not limited to ≥1 of the following:

- broad eligibility criteria
- simplified recruitment and follow-up
- flexibility in delivery of the intervention (e.g., community settings)
- flexibility in assessment frequency
- measurement of outcomes relevant to the population

Adapted from Califf RM, Sugarman J. Exploring the ethical and regulatory issues in pragmatic clinical trials. Clinical Trials. 2015;12(5):436-441.doi:10.1177/1740774515598334

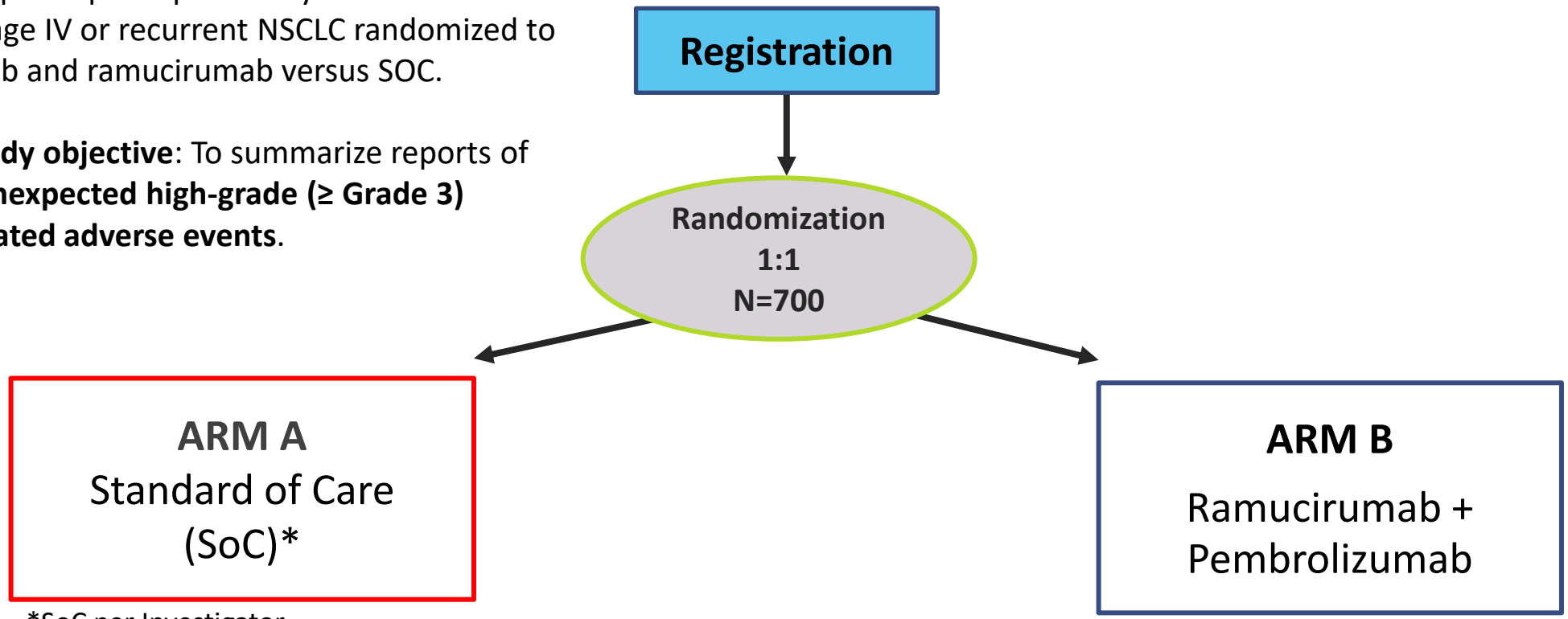
Pragmatic Domain	Pragmatic Element	*Traditional* RCT ⟷ *Fully* PCT
Recruitment: Patients and Investigators	Eligibility	**Who is selected and how representative are patients to intended use population?**
	Recruitment	**How are patients recruited and how may it differ than typical?**
	Setting	**Where is the trial being conducted and what health systems are included?**
Trial Intervention and Delivery	Organization	**What expertise, resources, and systems are conducting the trial?**
	Flexibility in Delivery	**What flexibilities are being permitted in care delivery?**
	Flexibility in Adherence	**How is monitoring and adherence being measured?**
Measurement	Follow up	**How is follow-up being done and what are the expected differences?**
	Primary Outcome	**How relevant is the primary outcome to patients?**
	Primary Analysis	**To what extent are all data included, available, and auditable?**

Loudon K et al. The PRECIS-2 tool: designing trials that are fit for purpose *BMJ* 2015; 350 :h2147 doi:10.1136/bmj.h2147

Pragmatica Lung Trial S2302 Design

Primary study objective: To compare **overall survival (OS)** between participants previously treated with PBC and I/O for Stage IV or recurrent NSCLC randomized to pembrolizumab and ramucirumab versus SOC.

Secondary study objective: To summarize reports of **serious and unexpected high-grade (≥ Grade 3) treatment-related adverse events**.



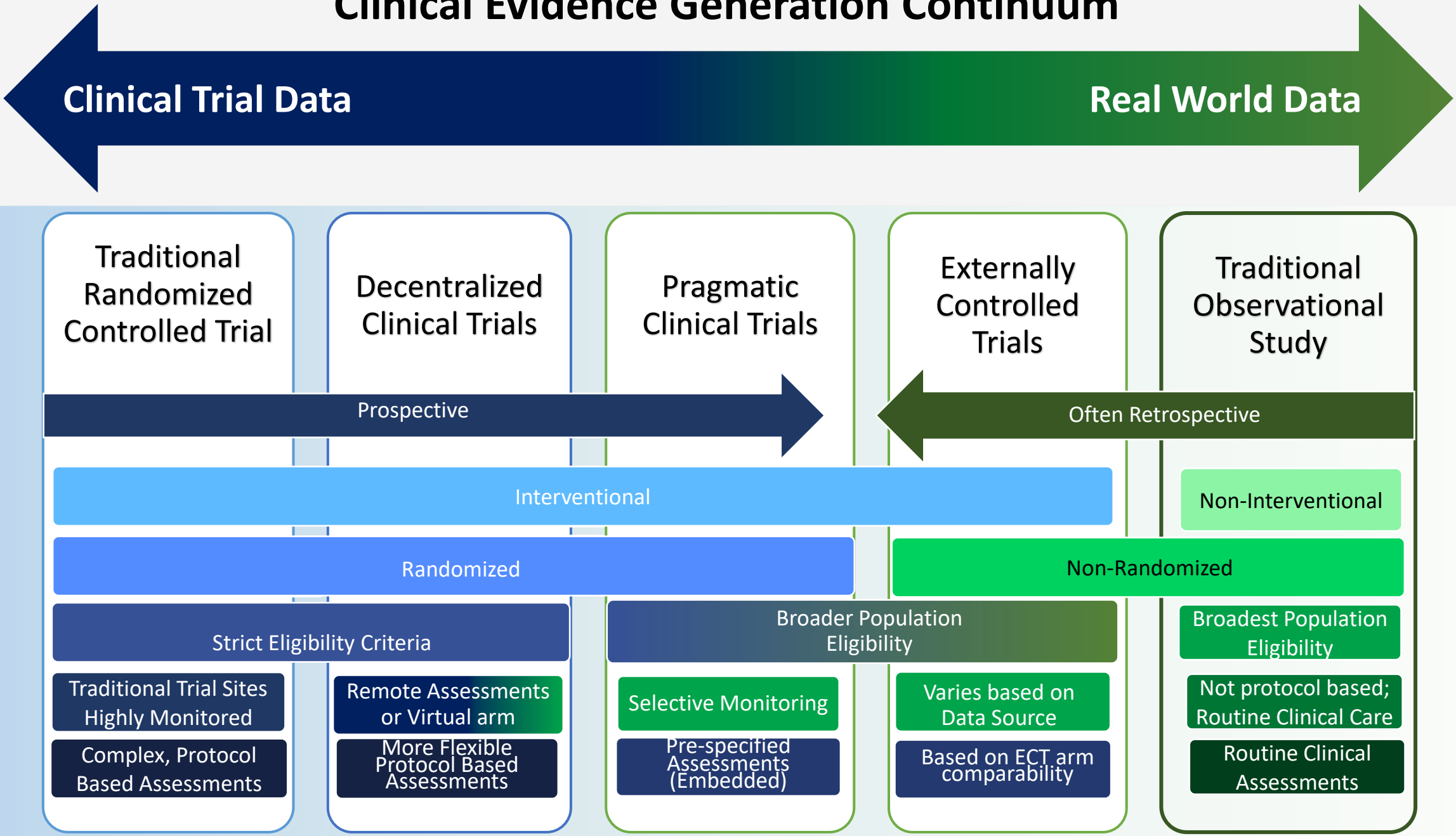
*SoC per Investigator. Recommended to be based on NCCN guidelines and should not be an investigational therapy.

Slide modified from Karen Reckamp, MD: LungMAP S1800A Future Directions

Example: Pragmatica LUNG

Pragmatic Domain	Pragmatic Element	*Traditional* RCT ⟷ *Fully* PCT
Recruitment: Patients and Investigators	Eligibility	Broadened Eligibility Criteria
	Recruitment	Use of NCORP Sites, Community Engagement and Enhanced outreach
	Setting	Community, Health System, and Academic US sites
Trial Intervention and Delivery	Organization	SWOG Coordination, NCI, NCTN, and Sponsors
	Flexibility in Delivery	Routine Clinical Care; Dosage Per Labeling
	Flexibility in Adherence	Routine Clinical Monitoring
Measurement	Follow up	Routine Clinical Practice
	Primary Outcome	Overall Survival
	Primary Analysis	Efficacy Data; Limited Required Safety Data

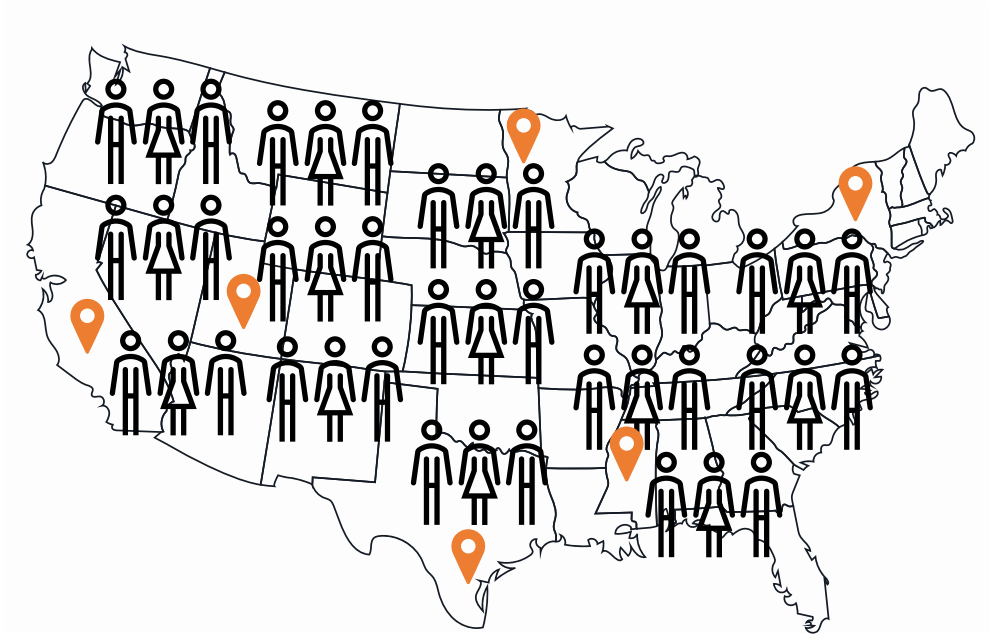
Clinical Evidence Generation Continuum



Enhancing Generalizability

Global Clinical Trials

US Real World Population



Integrating Clinical Trials into Routine Clinical Practice

Scientific advances and widespread use of EHRs provide new opportunities for the integration of clinical research + clinical care

Location

Bringing trials to places where patients receive their care

- **Improve convenience and accessibility** for participants
- Allow for enrollment of more **diverse populations**

Infrastructure

Leveraging established health care networks and existing clinical expertise

- Reduce **startup times**
- Increase **speed of enrollment**

Conduct

Agreements between sponsors and health care institutions

- **Mixture of trial-related activities**
  - Performed by local HCPs (not study personnel) and by study personal
- Provide instructions for data collection or measurement consistency

Modernizing Evidence Generation

Innovation	• Streamlining trials requires change in the ways or thinking and working
Inclusion	• Patient- centric trials include patients in trial design and development
Risk Mitigation	• Seek advice early and often from relevant review division

Modernizing Evidence Generation

Possibilities

- Enhanced Integration of Clinical Research and Clinical Practice
  - Example: USDCI+, rwResponse
- Understanding Drug Effects in
  - Underrepresented Populations
  - Rare Molecular Subsets
- Rapid Characterization of Emergent Public Health Needs
- Postmarket Treatment Optimization

Challenges (and Progress)

- Source Data and Quality
- Implementation of PCTs (incentives and risk)
- Causal Inference in Innovative Designs
- Integration and Access of Data Systems, Availability of Raw Imaging Data

OCE Project

Crowdsource oncology community to identify **5** clinically-relevant questions in oncology that can be answered through pragmatic trials over **5** years

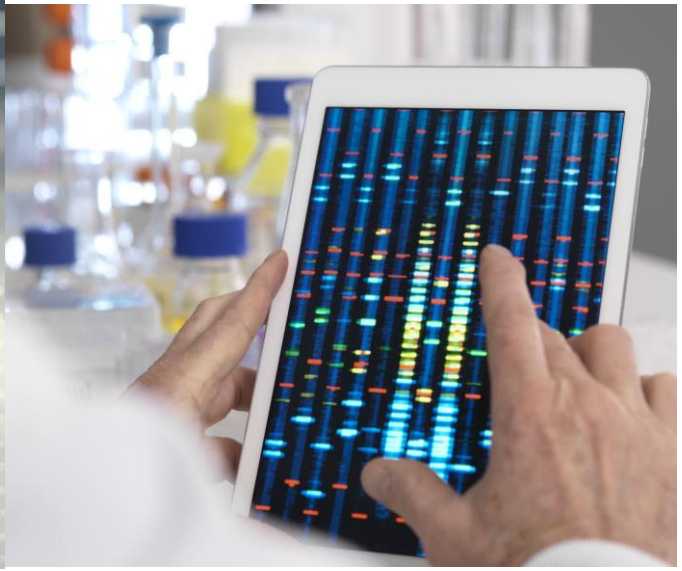
Launching on 5/5!

5 in 5

Envision the Future

Clinical Practice

Point of Care



Clinical Research

Thank you!

Additional Questions?

Please email OCERWE@fda.hhs.gov

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