NESTcc Data Quality & Methods Framework
Public Comment Webinar

Agenda

- **Dr. Robbert Zusterzeel,** *MDIC/NESTcc*: NESTcc Overview and Data Quality & Methods Introduction
- **Dr. Lesley Curtis,** *Duke University School of Medicine*: NESTcc Data Quality Framework
- **Dr. Sharon-Lise Normand,** *Harvard Medical School*: NESTcc Methods Framework
- **All**: Audience members can submit questions through the Q&A feature

Dr. Robbert Zusterzeel
Data Network
Director, MDIC/NESTcc

Dr. Lesley Curtis
Chair, NESTcc Data
Quality Subcommittee

Dr. Sharon-Lise Normand
Chair, NESTcc Methods
Subcommittee

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NESTcc Data Quality & Methods Framework Public Comment Webinar

Robbert Zusterzeel, MD, PhD, MPH
Data Network Director, MDIC/NESTcc

Monday, June 3, 2019

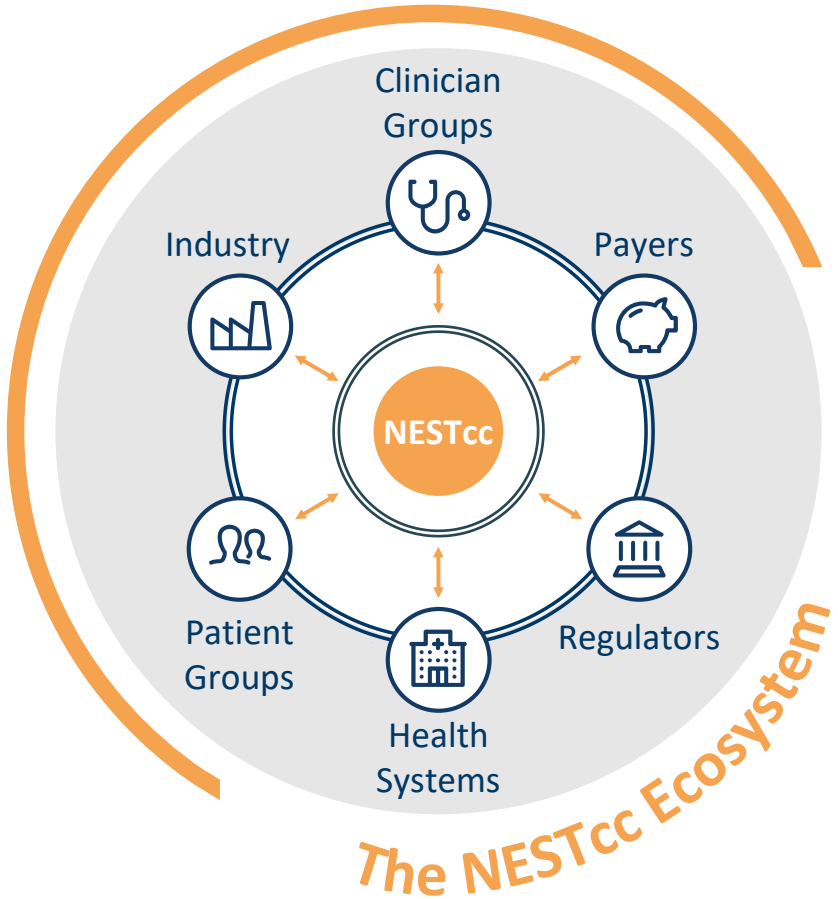
NESTcc Overview

Mission

To accelerate the development and translation of new and safe health technologies, leveraging Real-World Evidence (RWE), and innovative research.

Vision

To be the leading organization within the health technology and medical device ecosystem for conducting efficient and timely high-quality Real-World Evidence (RWE) studies throughout the Total Product Life Cycle (TPLC).



NESTcc DEVELOPMENT BEGAN IN 2012

Ensuring High-Quality Data & Analysis Methods

ADVANCING DATA QUALITY & METHODS

In 2018, NESTcc established multi-stakeholder subcommittees to support its efforts to conduct real-world evidence studies for medical devices, leveraging ongoing initiatives including expertise from MDEpiNet, PCORnet, and Sentinel.

DATA QUALITY SUBCOMMITTEE

- Chaired by Dr. Lesley Curtis, Duke University School of Medicine
- 12-person subcommittee includes representation from:
  - 6 health systems, including Network Collaborators
  - 3 medical device manufacturers
  - FDA

METHODS SUBCOMMITTEE

- Chaired by Dr. Sharon-Lise Normand, Harvard Medical School
- 9-person subcommittee includes representation from:
  - 3 health systems, including Network Collaborators
  - 4 medical device manufacturers
  - FDA

DATA QUALITY & METHODS SUBCOMMITTEES

NESTcc has established Data Quality and Methods Subcommittees to support its efforts to conduct real-world evidence studies for medical devices.

Methods Subcommittee

Member Name	Organization
Jesse Berlin	Johnson & Johnson
Mitchell Krucoff	Duke University Medical Center/Duke Clinical Research Institute (DCRI)
Heng Li	U.S. Food and Drug Administration (FDA)
Nilsa Loyo-Berrios	U.S. Food and Drug Administration (FDA)
Joao Montiero	Medtronic
Didier Morel	Becton Dickinson
Sharon-Lise Normand*	**Harvard Medical School**
Nilay Shah	Mayo Clinic
Scott Snyder	Cook Research Incorporated

*Subcommittee Chair

Data Quality Subcommittee

Member Name	Organization
Jeffrey Brown	Harvard Pilgrim HealthCare Institute/Harvard Medical School
Lesley Curtis*	**Duke University School of Medicine**
John Laschinger	U.S. Food and Drug Administration (FDA)
Aaron Lottes	Cook Research Incorporated
Keith Marsolo	Cincinnati Children's Hospital Medical Center
Frederick Masoudi	University of Colorado Anschutz Medical Campus
Joe Ross	Yale University
Art Sedrakyan	Weill Cornell Medicine
Kara Southall	Medtronic
James Tcheng	Duke University Health System
Karen Ulisney	U.S. Food and Drug Administration (FDA)
Charles Viviano	U.S. Food and Drug Administration (FDA)

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NESTcc Data Quality Framework

Lesley Curtis, PhD, MS

Duke University School of Medicine

Monday, June 3, 2019

Charge & Vision

- Develop Data Quality Framework for NESTcc Network Collaborators
- Design a process by which NESTcc Network Collaborators can demonstrate their aptitude with the NESTcc Data Quality Framework
- Develop first, simple, pragmatic, iteration of NESTcc Data Quality Framework that will apply to a “first wave” of NESTcc Network Collaborators

Data Quality Framework Overview

- Initial version lays out the foundation for the capture and use of high-quality data for post-market evaluation of medical devices
- Grounded in the use of real-world data (RWD) gleaned from the clinical care setting and the electronic health record (EHR)
- Data Quality Framework will evolve for a “second wave” of data vendors or similar collaborators with large de-identified datasets

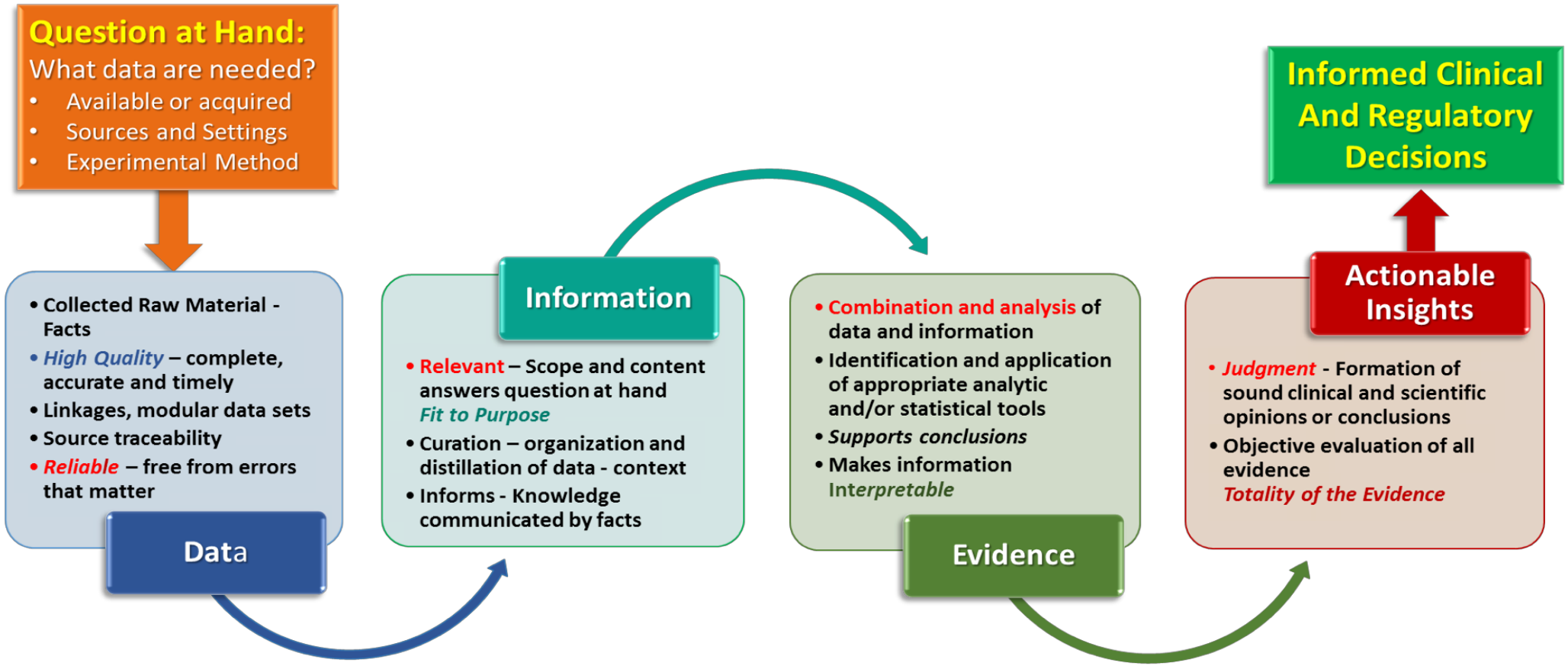
Framework Organization

1. Data Governance Principles
2. Characteristics of Data
3. Data Capture & Transformation
4. Data Curation
5. NESTcc Data Quality Maturity Model

DATA QUALITY: DATA GOVERNANCE PRINCIPLES

- Organizational transparency and integrity
  - Leadership, stewardship, patient-centered, stakeholder engagement, transparency, oversight
- Data access, management, linkage and aggregation, and use
- Submission, management, review, and acceptance of RWD/RWE requests
  - Clear criteria, transparent process, commitment to responsible research, efficiency, commitment to results reporting

DATA QUALITY: CHARACTERISTICS OF DATA



Evidence generation and evaluation: Actionable insights for informed clinical and regulatory decisions (adapted from Califf RM, Sherman R, What we mean when we talk about data. MassDevice. December 11, 2015. https://www.massdevice.com/44947-2/)

Data Capture and Transformation

- Improving data quality at the point of care and point of data entry should be the ultimate goal
- Understand how and why data of interest were originally obtained and processed
- Build quality control processes into each step of any ETL process

Data Curation

- Process should address conformance, completeness, plausibility
- Study-specific curation should augment foundational data curation
- Metadata about data provenance guides assessments of data fitness for purpose
- Iterative process that helps to improve data quality over time

NESTcc DATA QUALITY MATURITY MODEL

- The five stages of maturity reflect increasingly advanced and integrated levels of performance for health care systems to partner with the NEST ecosystem
- The stages are at least partially aligned with previous maturity models
- The model can indicate progress and help identify weaknesses and opportunities

NESTcc Stage	Description
1. Conceptual	Clinical processes capture data primarily in verbose documents, not as data
2. Reactive	Able to react to requests for analysis, respond to research requests
3. Structured	Clinical systems manage transactional data types (e.g., orders, transactions, laboratory results, medication prescriptions) as discrete data
4. Complete	Granular and complete clinical data based on standardized clinical CDEs captured in the processes of care, integrated into those care processes
5. Advanced	Data linkage and aggregation across systems enabled and open to external queries

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NESTcc Methods Framework

Sharon-Lise Normand, PhD, MSc

Harvard Medical School

Monday, June 3, 2019

Charge & Vision

- Develop a "living" Methods Framework for NESTcc addressing device-specific considerations in benefit/risk studies and safety signal detection.
- Develop a research agenda identifying critical issues in Methods for device, imaging, and other diagnostic technologies studies across the TPLC
- Consult on an ad hoc basis to NESTcc to ensure that NESTcc activities employ the most appropriate and rigorous methods of analysis

Methods Framework Overview

- Key: **pre-specification** of study design & analysis
- Develop a methodological framework to include device-specific considerations by **device stage**
- A single protocol is utilized for both randomized trials and observational studies

Framework Organization

1. Background: Disease, Available Therapies, and Device Risk
2. Device Description
3. Study Specific Objectives
4. Target Population and Patient Selection
5. Outcomes: Primary, Secondary, Procedural, and Device
6. Device Exposure
7. Study Design
    - 7.1 Specific Design
    - 7.2 Blinding (Masking)
    - 7.3 Units of Randomization and Observation
    - 7.4 Mechanism of Treatment Assignment
    - 7.5 Other Covariates
8. Study Procedures
    - 8.1 Patient Consent
    - 8.2 Randomization/Estimation
    - 8.3 Protocol Deviation Handling
9. Required Sample Size
10. Study Registration
11. Monitoring Plan
12. Statistical Analysis Plan

BACKGROUND, DEVICE DESCRIPTION, AND STUDY SPECIFIC OBJECTIVES

BACKGROUND

- Introductory material of the protocol should include:
  - Thorough discussion of the underlying disease
  - Available therapies
  - Unmet medical needs
- Goal: demonstrate that based on the information presented, there is a justified rationale for conducting the study

DEVICE DESCRIPTION

- Detailed device descriptions should be included in the protocol including details on each important:
  - Component
  - Ingredient
  - Material that will be in contact with tissues or body fluids of the study subject

STUDY SPECIFIC OBJECTIVES

- Protocols should include unambiguous statements of its objectives aligned with its overall purpose
- Objectives should be:
  - Relevant
  - Specific, based on measurable quantities
  - Attainable within a reasonable time-frame

Target Population and Patient Selection

- Provide a description of the population to which the results of the study will apply
- Research participants should closely reflect the population of intended use

Outcomes

- Primary outcomes are directly linked to the primary study objective
- Secondary outcomes provide additional information that are intended to support the primary hypotheses
- Procedural outcomes can include procedure time, physiological and biological data captures as part of the procedure, and procedure-specific data
- Device outcomes depend on risk of the device and could range from device performance to linking device performance mechanistically to outcomes in conjunction with determinations of effectiveness, safety, and benefit/risk
- Control outcomes are used to help justify the unmeasured confounder assumption

DEVICE EXPOSURE, STUDY DESIGN, AND STUDY PROCEDURES

DEVICE EXPOSURE

- The main goals of the underlying study should be used to define exposure and outcomes
- Exposure various by device types that are being studies

STUDY DESIGN

- Basic features of study design should include:
  - Number and type of comparison groups
  - Who is blinded to what when
  - Experimental unit of randomization
  - How the device assignment mechanism will occur
    - Randomized or observed

STUDY PROCEDURES

- Study procedures should include
  - How patients are approached and consented
  - How device assignment mechanism will be estimated
  - How data will be collected
  - Definitions of protocol deviations and how those will be treated
  - What constitutes subject withdrawal
  - What strategies will be adopted to minimize missing data

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- **Required Sample Size:** Sample sizes vary depending on the study, but basic principles include indicating the type of study design, describing the approach to evaluation, and describing and justifying additional features of the study that impact the sample size

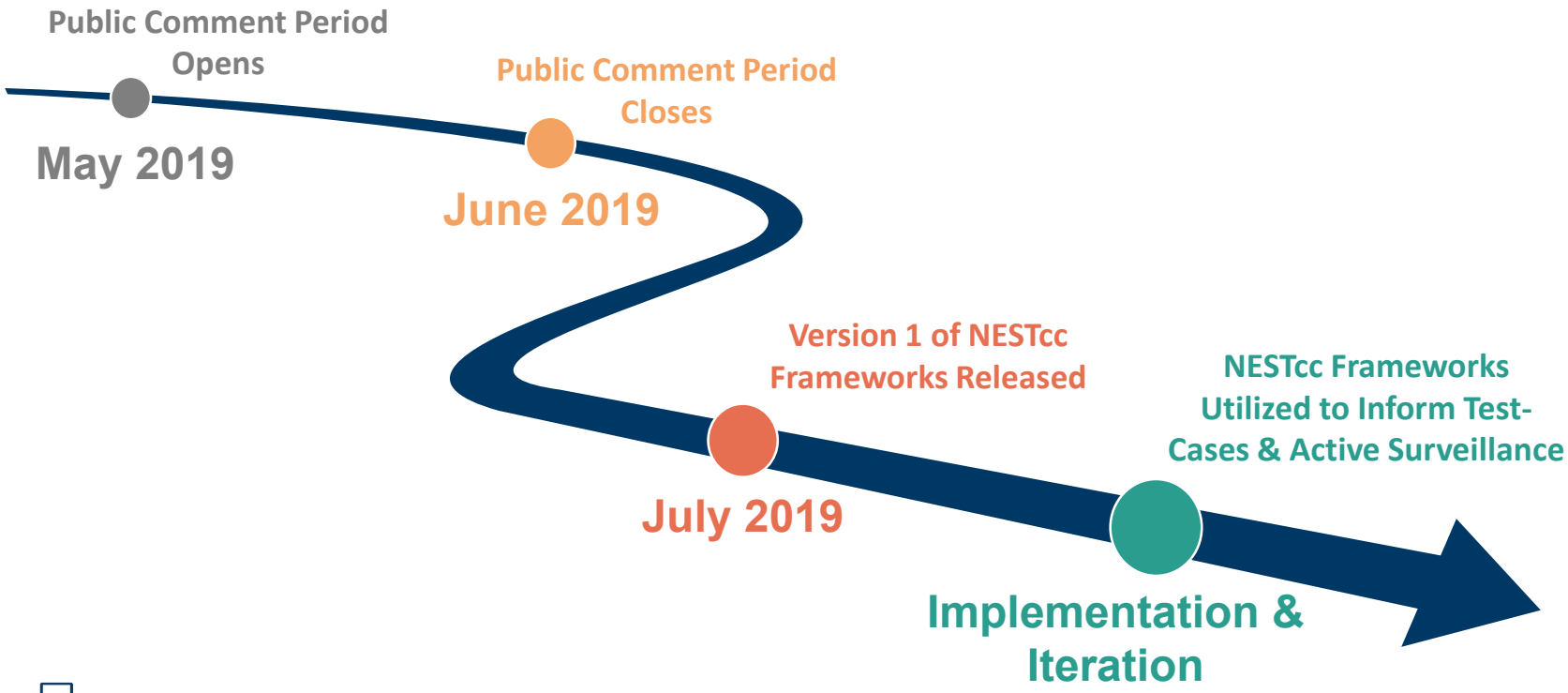
- **Study Registration:** Trials should be registered on www.clinicaltrials.gov prior to enrolling the first patient
  - While registration of observational studies is more controversial, registering selected observational studies is encouraged

- **Monitoring Plans:** Appropriate monitoring plans help ensure the protection of the rights, welfare, and safety of the human subjects, and the quality of the study data

- **Statistical Analysis Plan (SAP):** The SAP provides the detailed description of all statistical analyses, such as estimation of treatment effect, approach to missing data, etc., to be conducted once the data are available

NESTcc Data Quality & Methods Subcommittees' Framework development will include a public comment period before the first iterations are released.

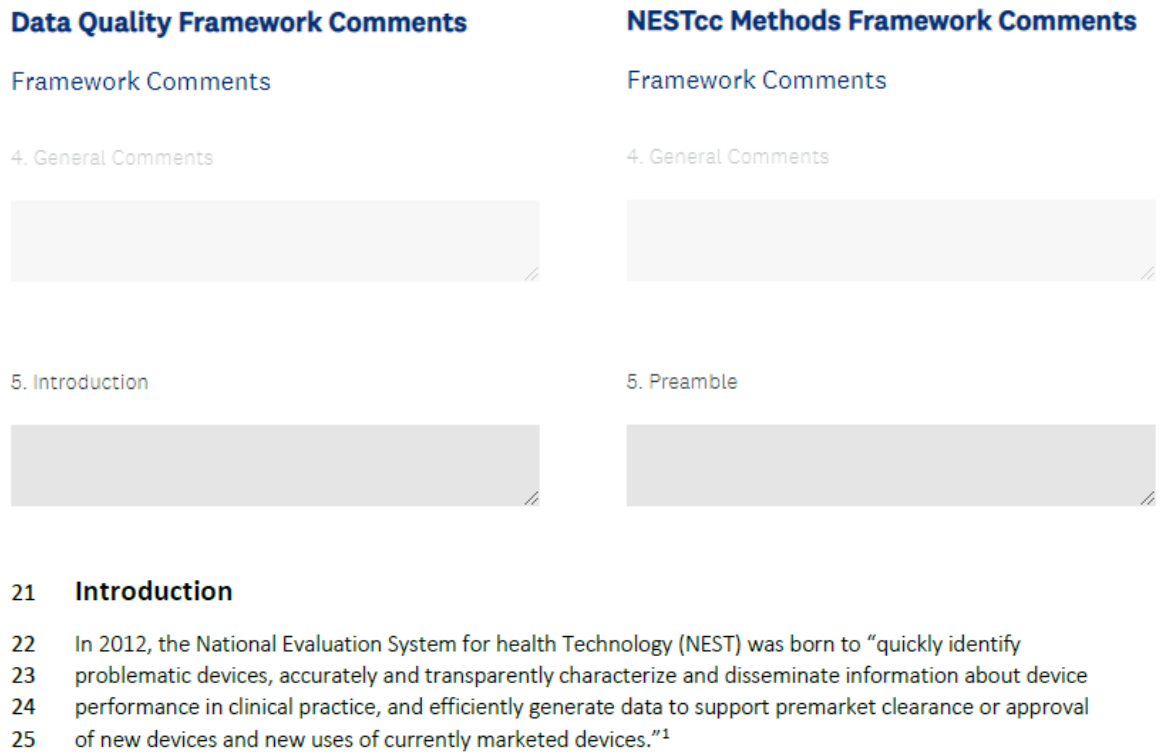
NESTcc Data Quality & Methods Frameworks Timeline



NESTcc Data Quality & Methods Frameworks were released for public comment (http://nestcc.org/opportunities) on **Tuesday, May 28**.

Comments are being collected through Survey Monkey

- Comments should be submitted for the appropriate section of the Framework
- Comments should refer to the line numbers in the Framework documents



Engage with NESTcc

CONNECT WITH NESTcc

Explore opportunities to connect with NESTcc online with the following resources:

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www.nestcc.org

@NESTccMedTech

nestcc@mdic.org