Industry Highlights of IMDRF Clinical Definitions and Clinical Evaluation Process

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Further, Together

Outline

GOAL OF IMDRF AND CLINICAL EVALUATIONS

PRACTICAL APPLICATION

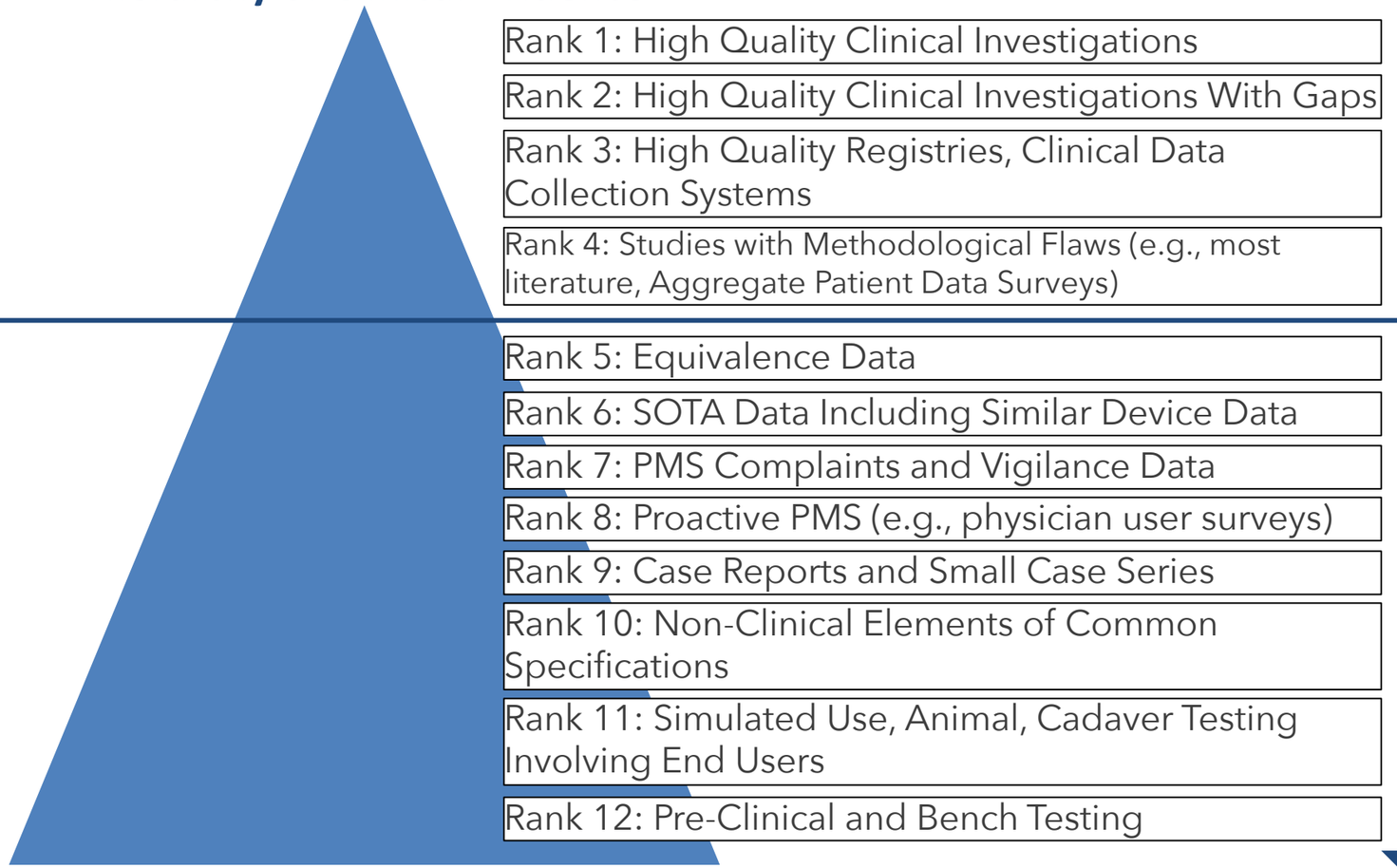
CLINICAL EVALUATION AND PRODUCT LIFECYCLE

Goal Of IMDRF On Clinical Evaluations

- Improve the effectiveness and efficiency of pre-market review by increased global harmonization
  - Leveraging and evaluating available clinical evidence
  - Reduce the number of **redundant** clinical trials
  - Integrate principles of post-market clinical follow and real-world evidence
  - **Accelerate** introduction of and effective medical devices/technologies to patients

Ranking of Clinical Evidence

Hierarchy of Clinical Evidence



- Rank 1: High Quality Clinical Investigations
- Rank 2: High Quality Clinical Investigations With Gaps
- Rank 3: High Quality Registries, Clinical Data Collection Systems
- Rank 4: Studies with Methodological Flaws (e.g., most literature, Aggregate Patient Data Surveys)
- Rank 5: Equivalence Data
- Rank 6: SOTA Data Including Similar Device Data
- Rank 7: PMS Complaints and Vigilance Data
- Rank 8: Proactive PMS (e.g., physician user surveys)
- Rank 9: Case Reports and Small Case Series
- Rank 10: Non-Clinical Elements of Common Specifications
- Rank 11: Simulated Use, Animal, Cadaver Testing Involving End Users
- Rank 12: Pre-Clinical and Bench Testing

Higher Bar for Clinical Evidence

Considerations:

- Higher risk class and/or implantable
- Novel features, technology or application (NOVELTY)
- New indication
- Known safety issues, open CAPAs
- Strong clinical claims

Lower Bar for Clinical Evidence

Considerations:

- Lower risk class, non-implantable
- Long market history with well-known safety profile
- Simple, stable design and indications
- Indirect clinical benefits
- Equivalency
- Well-Established Technology (WET)*
- Standard of Care (SOC) Legacy device*

**Does not eliminate need for subject device data collection in the PMCF space*

Practical Application

US regulators (FDA) fashioned new guidance on software as a medical device (SaMD) based on IMDRF principles.

The degree of clinical evaluation and evidence required of a SaMD would depend on the function it performs.

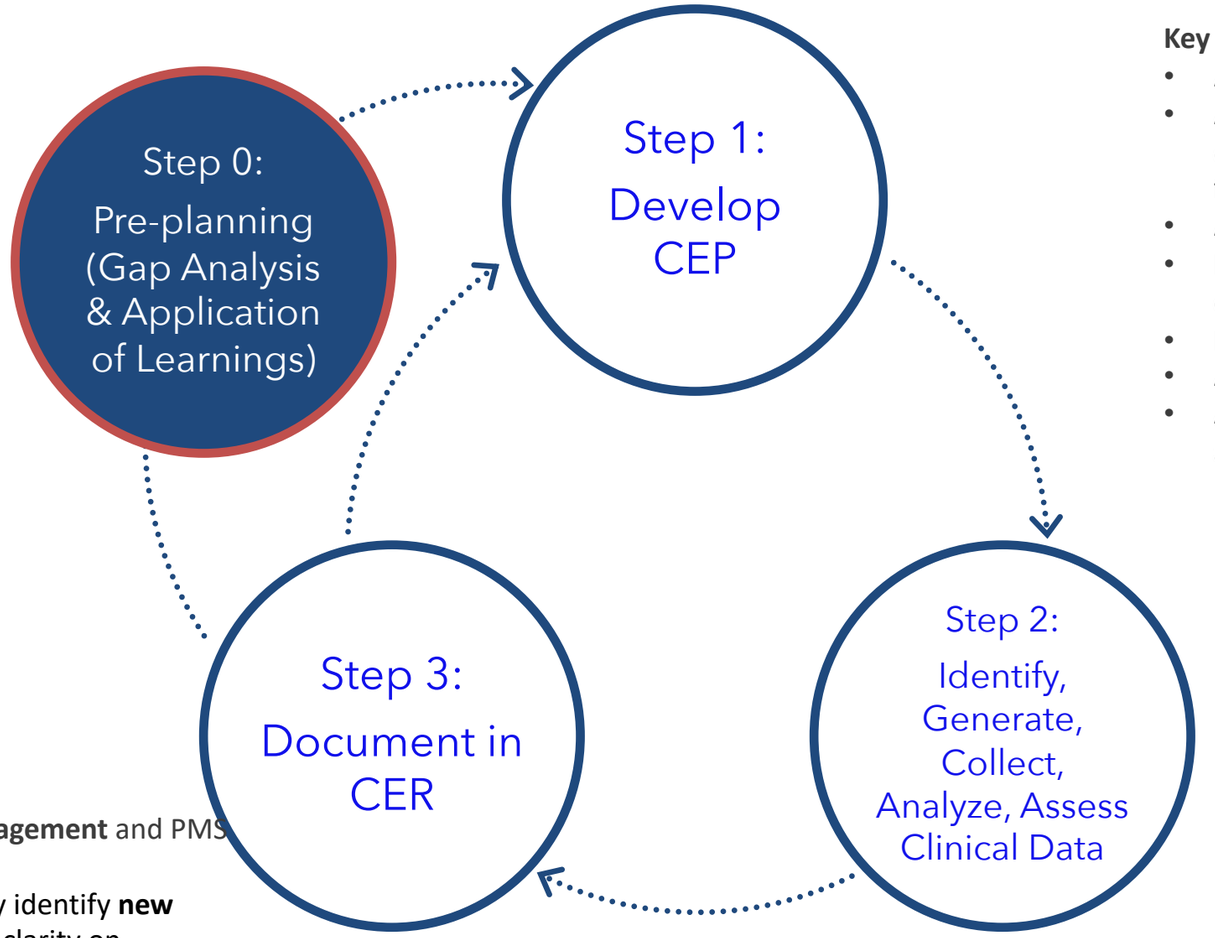
SaMD clinical evaluation should be able to support manufacturers' claims of safety, effectiveness and performance.

Clinical Evaluation is an Iterative Process!

PLAN, Identify, Generate, Collect, Analyze, Assess, Report, Apply Learnings, REPEAT

Gap Analysis for Clinical Evaluation:

- Process of determining **clinical evidence sufficiency** to allow for a qualified assessment of device safety, performance and acceptability of benefit-risk when used as intended
- Informs clinical data gaps so they can be appropriately remediated (e.g., narrower indications or additional data generation)



Key questions to be answered:

- Are the indications appropriate and supported?
- Are the clinical data of sufficient amount and quality to constitute "sufficient clinical evidence" for demonstration of conformity
- Are there new safety concerns?
- Informs submission strategy (e.g., SOC, equivalence, conformance adjacency)
- Informs potential PMCF activity/burden
- Allows us to be proactive!
- A lot of cross-functional involvement and alignment needed for successful cycle!

Clinical Evaluation Report:

- Feed output into **risk management** and PMS activities
- Data arising from PMS may identify **new risks** or provide additional clarity on indications and contraindications

Questions?