Principles Regarding The Use of Real World Evidence

Medical device regulators have shown increased interest in the use of real world evidence ("RWE") in pre- and post- market regulatory decision making. As RWE collection methods are developed, and platforms become available to regulators, manufacturers, academics, and providers alike, we believe that certain foundational principles are necessary with respect to the use of RWE, and to guide the governance and operation of a system that may be established to collect, disseminate and evaluate RWE.

I. BACKGROUND

RWE has been defined as evidence derived from the aggregation and analysis of real-world data ("RWD").[1] RWD, in turn, has been defined as data collected from sources outside of traditional clinical trials. RWE may consist of information from many data sources, including but not limited to:

1. Registries;
2. Patient Communities;
3. Public and Private Health Plans;
4. Manufacturers;
5. Delivery Systems, including electronic health records (EHR);
6. Regulators;
7. Safety surveillance systems; and
8. Observational studies and scientific literature.

GMTA is committed to the principles of appropriate analysis of medical technologies. Stakeholders, such as patients, their caregivers, providers, payers, regulators, and manufacturers share in the commitment to improve the quality and increase the efficiency

[1] *See*, *e.g.*, U.S. Food and Drug Administration Draft Guidance: Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices (July 27, 2016), *available at* https://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm513027.pdf.

of healthcare. As medical device manufacturers, we recognize the need to ensure adequate and accurate information concerning the safety, effectiveness, and impact of medical interventions to guide healthcare decision-making. We further recognize there may be a number of benefits with respect to the use of RWE, including the following:

1. Improve patient care and outcomes;

2. Improve patient access to new therapies and diagnostics by efficiently collecting data to support regulatory submissions for expanded use and indications or expanded coverage;

3. Support device modifications;

4. Support patient access through expanded coverage, reimbursement, and value analysis based on RWD evaluation and collection;

5. Evaluate the "real-world" safety and/or effectiveness of products outside of randomized controlled clinical trials or other clinical study designs;

6. Meet regulatory requirements for post-market data collection;

7. Provide regulators with alternative methods to monitor the performance of technologies to reduce existing pre- and post- market data collection burdens;

8. Develop hypotheses for further clinical and economic evaluation; and

9. Aid in the development or assessment of care guidelines.

Although we recognize these potential benefits as possible outcomes, by definition RWD is not data collected from a clinical investigation. Therefore, it is important that this information be appropriately analyzed and validated prior to dissemination and use.

In addition, we believe protections must be in place to prevent the spread of incorrect, incomplete, biased or misleading information. The public health relies on the communication and dissemination of accurate and reliable information from public health agencies. In this regard, we provide below key principles with respect to the use of RWE, and to guide the governance and operation of a system that may be established to collect, disseminate and evaluate RWE.

II. PRINCIPLES

1. Systems designed to collect RWE must include a clear purpose, objective, and participation requirements for promoting the use of RWE to facilitate understanding of medical technology and innovation.

a. Criteria for an RWE system's partners and sources of data must be established to ensure partners providing information are committed to the system goals and that data are relevant and useful for RWE purposes.
b. RWE system partners must establish sufficient safeguards to ensure that RWE data are of appropriate quality for the intended use of the data.
c. An RWE system must be validated for each purpose before its intended use.
d. Data integrity and security must be maintained across an RWE system by system partners.
e. RWE system partners must agree to follow data governance standards.

2. **Before the launch of an RWE system, a data governance committee (that includes medical device manufacturers) must be formed and written procedures for data ownership, data access, data use, and participation must be established.**
    a. An RWE system must collect sufficient data to identify, consider and allow risk adjustment for modifiable risk factors such as social, demographic and disease-related factors, including changes in applicable evidence based practice guidelines over time.
    b. An RWE system governance committee must establish procedures for reviewing proposed research protocols that would use RWE or RWD obtained through the system.
    c. Findings derived from RWE or RWD obtained through an RWE system must be reviewed by a data governance committee or through an appropriate peer review committee prior to release. Manufacturers of the technologies studied must be part of the review process as the manufacturer may have relevant information to any conclusion. Manufacturers, however, do not need to approve the conclusion.
    d. An RWE system's data governance committee must establish a process to ensure transparency of the process for proposing, conducting, and releasing reports based on RWE.

3. **Regulatory authorities must have clear policies regarding the use of data from an RWE system, if applicable. Use of data from an RWE system to make a regulatory determination of device safety or effectiveness must only be conducted by regulatory authorities in accordance with their statutory authorities.**
    a. Regulatory authorities should seek input from and share relevant information with manufacturers prior to taking any regulatory action based upon data derived from an RWE system.
    b. Regulatory authorities should actively work with manufacturers to identify possible uses of RWE derived from an RWE system to address pre-market requirements in a least burdensome manner.
    c. In the interest of reducing healthcare costs, device surveillance systems derived from an RWE system should be developed to replace, rather than supplement, existing passive surveillance systems.
    d. An RWE system must make clear that RWD and RWE analysis plans are not clinical investigations.

e. Manufacturers should be able to communicate truthful and non-misleading information about analyses of RWD, provided research methods are sound and well-described.

4. **Access to data through an RWE system should be granted only upon request by qualified scientific, medical and economic researchers for purposes benefiting public health or patient care. Procedures should be developed and employed by a data governance committee to receive and review data access and dissemination requests prior to approving the release of any data.**
    a. Requests for data access must be based on clear criteria established by a data governance committee, including the validity of the hypothesis, whether the data requested and analysis plan will address the hypothesis, and the qualifications of the requestor.
    b. A data governance committee must establish a process for adequate data protection, including a process to ensure agreement from individuals granted system access not to transfer the data or information to parties not identified in the research proposal.
    c. An approved analysis plan must address how data on patient characteristics, patient medical conditions and co-morbidities, facility characteristics, physician experience, interventional technique and associated parameters, and device characteristics (including unique device identifiers, if applicable) will be used to identify potential factors that affect study conclusions.
    d. Research partners must define a prospective process for considering changes in the analysis plan after initiation, including items such as data collection and protocol revisions.
    e. Device manufacturers must be allowed full and timely access to data on their products.
    f. Data requesters may be charged reasonable fees.

5. **An RWE system must comply with all applicable laws and regulatory requirements.**
    a. Patient privacy must be protected, and any required consent must be obtained.
    b. All confidential manufacturer, physician, and hospital data must be identified as confidential and protected from release.
    c. Data provided to an RWE system does not absolve facility, physician or manufacturer obligations to file reports required under applicable laws or regulations.