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Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, rm. 1061
Rockville, MD 20852
Submitted electronically via http://www.regulations.gov

RE: Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices; Docket No. FDA-2016-D-2153

AMIA is pleased to provide input that will inform the U.S. Food and Drug Administration's (FDA) current thinking on how to evaluate real-world data (RWD) to determine whether it may be sufficiently relevant and reliable to generate the types of real-world evidence (RWE) that can be used in FDA regulatory decision-making for medical devices.

AMIA is the professional home for more than 5,000 informatics professionals, representing front-line clinicians, researchers, educators and public health experts who bring meaning to data, manage information and generate new knowledge across the health and health care enterprise. As the voice of the nation's biomedical and health informatics professionals, AMIA plays a leading role in advancing health and wellness by moving basic research findings from bench to bedside, and evaluating interventions, innovations and public policy across settings and patient populations.

Real-World Evidence
AMIA convened a group of informatics experts in this field of study to review this draft guidance and provide feedback to the agency. As the FDA acknowledges in the draft guidance, routine clinical practice often involves the use of cleared or approved devices for uses or in patient populations not within the cleared or approved indications for use. However, the advances in knowledge that may result are often not realized because the data collected are not systematically characterized, aggregated, and analyzed in a way such that it can be relied upon to inform regulatory decision-making.

AMIA applauds the agency for recognizing the value of RWE as an important contributing factor for understanding and regulating medical devices, and for encouraging medical device researchers,

American Medical Informatics Association | AMIA
4720 Montgomery Lane, Suite 500 | Bethesda, Maryland

manufacturers, physicians, hospitals and other stakeholders to learn more from routine clinical care than we do today.

This draft guidance provides improved regulatory clarity and transparency around the methods used for assessing RWD and RWE as they apply to medical device approvals. FDA's attention to data generation, data quality, and the use of RWE to inform the development of devices will allow the agency to keep pace with the increasing amount of RWD generated by advancements made in the growing medical device industry.

Characteristics of RWD

The FDA does not endorse one type of RWD over another, but rather suggests that data sources be selected on the ability to address specific regulatory questions. As the FDA uses this guidance to inform regulatory decision-making going forward, AMIA recommends that the agency recognize social media data from sources such as patient networking forums in order to leverage patient-reported information on device usage. These sources of information have the potential to bolster medical device safety monitoring efforts and address important regulatory concerns.

Data Assurance – Quality Control

FDA proposes to evaluate data sources with respect to the data quality assessment (QA) plan and procedures developed for the data source itself. Since evaluation of RWD sources may not always permit specific item source verification, the agency outlines important factors for consideration, including

a. Assessments of data quality;
b. Adherence to source verification procedures and data collection and recording procedures for completeness and consistency;
c. Completeness;
d. Data consistency across sites and over time;
e. Evaluation of on-going training programs for data collection and use of data dictionaries at participating sites;
f. Evaluation of site and data monitoring practices; and
g. The use of data quality audit programs.

Based on the feedback from the team of AMIA reviewers with expertise in this field, AMIA recommends the addition of a data validation plan (DVP) to this list of factors in order to ensure data quality. Data validation is the process of testing the validity of data in accordance with protocol specifications. DVPs contain edit-check programs, which are embedded in the database and are written to identify the discrepancies in the entered data to ensure data validity.[1]

[1] Krishnankutty, B., Bellary, S., et al. Data management in clinical research: An overview. Indian J Pharmacol. 2012 Mar-Apr; 44(2): 168–172.

We note that recent works in clinical research and comparative effectiveness research have developed a set of field-tested best practices for data quality checking and validation,[2] as well as a harmonized data quality assessment terminology, organized into a logical framework.[3]

In addition, we urge FDA to encourage the use of consensus data standards whenever possible. We understand that it would not be appropriate to designate a specific standard in guidance such as this, but RWE founded in standard vocabulary, for instance, will improve the systematic collection of data, which would improve data quality.

Examples Where RWE Can be Useful

The draft guidance highlights various examples of RWE and RWD sources that might allow FDA to come to an appropriate regulatory decision without requiring additional clinical trial data, precluding delays in regulatory-decision making. FDA aptly notes that many RWD sources would have been designed to produce regulatory-quality data in addition to meeting research and quality improvement purposes, thus appropriate data quality checks and electronic controls would be a part of the initial design and implementation.

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We appreciate FDA's sentiments in the draft guidance and are excited about the possibilities this new pathway will have for bringing new and innovative therapies to American consumers. We look forward to working closely with the FDA, bringing the expertise of health informatics professionals to this paradigm.

Thank you for considering our comments. Should you have questions about these comments or require additional information, please contact Jeffery Smith, Vice President of Public Policy at jsmith@amia.org or (301) 657-1291. We look forward to continued partnership and dialogue.

Sincerely,

Douglas B. Fridsma, MD, PhD, FACP, FACMI
President and CEO
AMIA

[2] Brown, J., Kahn, M., Toh, S. Data quality assessment for comparative effectiveness research in distributed data networks. *Med Care*. 2013 August ; 51(8 0 3): S22–S29.

[3] Kahn, M., Callahan, T., Barnard, J., et al. A Harmonized Data Quality Assessment Terminology and Framework for the Secondary Use of Electronic Health Record Data. eGEMs (Generating Evidence & Methods to improve patient outcomes): Vol. 4: Iss. 1, Article 18