



PHYSICIAN CLINICAL REGISTRY COALITION

February 20, 2024

VIA ELECTRONIC SUBMISSION

Robert M. Califf M.D.
Commissioner of Food and Drugs
Food and Drug Administration
10903 New Hampshire Ave.
Silver Spring, MD 20993

Re: Draft Guidance for Industry and Food and Drug Administration Staff—*Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices* (Docket No. FDA-2023-D-4395)

Dear Commissioner Califf:

The undersigned members of the Physician Clinical Registry Coalition (“Coalition”) appreciate the opportunity to provide comments to the Food and Drug Administration (“FDA”) on its draft guidance, *Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices*. The Coalition is a group of medical society-sponsored clinical data registries that collect, analyze, and report clinical outcomes data submitted by physicians, hospitals, and other providers to identify best practices and improve patient care. We are committed to advocating for policies that encourage and enable the development of clinical data registries and enhance their ability to improve quality of care through the analysis and reporting of clinical outcomes. Although the focus of our comments is the use of clinical data registries, we understand the FDA is not endorsing or encouraging one type of real-world data (“RWD”) over another. Additionally, we believe it is important to establish the study questions before determining the study design and the appropriate RWD sources suitable for the specific study questions.

Clinical data registries are a major source of RWD and critical partners in the generation of real-world evidence (“RWE”) for evaluating the safety and effectiveness of various medical procedures, drugs, and devices. The Coalition applauds the FDA’s continuing recognition that RWE can be used to inform agency decision-making across the regulatory lifecycle of medical devices. As the draft guidance acknowledges, RWD from registries can and has been used in a variety of contexts including:

- **As sources of clinical evidence to support new device authorizations and expand label indications.** RWD from clinical data registries can be used to enhance or supplement data from traditional clinical trials, form external controls, or generate clinical evidence. For example, data from The Society of Thoracic Surgeons’ (“STS”) and the American College of Cardiology’s (“ACC”) TVT registry was used as the sole source of clinical evidence to expand

the indication of an approved heart valve and data from a second STS registry, the Adult Cardiac Surgery Database, was used as a comparison metric to support the approval of a new valve system. In addition, data from the American Academy of Ophthalmology was used with other data sources to demonstrate that performance of intraocular lenses (“IOLs”) in adult patients younger than 60 years old was comparable to performance in adult patients older than 60 years old for expanded label indications for IOLs. Boam AB, Eydelman MB, Lum FC, Silverman PM, Apple DJ, Werner L, Pandey SK. Retrospective evaluation of intraocular lenses in adults younger than 60 years. *J Cataract Refract Surg.* 2003 Mar;29(3):575-87. doi: 10.1016/s0886-3350(02)01845-x. PMID: 12663027.

- The Coalition welcomes the FDA’s clarification that an Investigational Device Exemption (“IDE”) trial is not required to collect RWD or generate RWE from the off-label use of devices in the course of normal medical practice or pursuant to an Emergency Use Authorization (“EUA”). We agree that an IDE should only be required when data collection “impact[s] how the device is administered” and where “the process for gathering the data would influence treatment decisions.” This framework provides sponsors and registries with the flexibility— with respect to extant data or data that can be collected without influencing clinical care—to tailor their collection and abstraction practices around new or evolving research needs.
- **As sources of postmarket data to support surveillance and post-approval requirements.** Like medical device registries, the Coalition’s society-sponsored registries can be used to collect postmarket RWD to provide ongoing evidence of safety and efficacy using preexisting, scalable, and reusable infrastructure. For example, postmarket surveillance through the STS/ACC TVT registry has been imposed as a condition of approval for multiple new heart valve devices and for expanding the indication of multiple approved devices. We agree that using postmarket evaluation and controls to balance premarket requirements, where appropriate, can support innovation and improve patients’ access to safe, timely, and effective care.

The Coalition supports the FDA’s focus on relevance and reliability as key factors in assessing whether RWD is fit-for-purpose to support regulatory decision-making. Clinical data registries are already designed to collect credible and accurate RWD as a function of their quality improvement objectives and their participation in quality improvement programs. Furthermore, registries often have unique advantages compared to other RWD sources when used to support research initiatives, including:

- **Relevance of Registry Data:** Clinical data registries typically collect a wide range of data elements in the course of advancing their quality improvement objectives. Some of these data types—including longitudinal data, patient-reported outcomes data, and experience data—can be collected more systematically by registries compared to other RWD sources. The robust data pool provided by clinical registries can be used to streamline or facilitate clinical trials and accelerate regulatory approvals.
 - The Coalition appreciates the FDA’s acknowledgment that, in addition to analyzing extant data, registries can be retooled to answer specific study questions and to

prospectively collect fit-for-purpose data regarding outcomes, covariates, or other relevant study considerations.

- We appreciate the FDA’s observation that data within registries may be missing study-relevant data elements, may not be representative of a device’s intended use population, or may contain elements of bias; we also appreciate the inclusion of Appendix A to help registries, sponsors, and FDA staff assess and address these relevance considerations using methods like linking across multiple RWD sources. However, we note that the salience of these relevance factors depends in large part on how RWD from registries is used in conjunction with data from other RWD sources to generate RWE and/or with data from investigational trials. We support the FDA’s proposed approach of assessing data sources both “individually and together in the aggregate” and encourage the Agency to provide more clarity on how the existence of complementary data can inform its fit-for-purpose assessment of a specific RWD source. For example, Appendix A instructs sponsors and FDA staff to “[e]nsure study sample is representative and generalizable to RWD source” but omits the possibility that data sources may be aggregated to generate more representative and generalizable RWE for a device’s intended use population.
- **Reliability of Registry Data:** Clinical data registries are designed to collect reliable data and will typically have established processes and procedures concerning data accrual, quality, and integrity. These existing systems align substantially with the reliability considerations described in the draft guidance and should facilitate the FDA’s fit-for-purpose assessment. For example, qualified clinical data registries (“QCDRs”) engaged in developing and testing quality measures for payment purposes under the Centers for Medicare and Medicaid Services’ (“CMS’s”) Merit-based Incentive Payment System (“MIPS”) must conduct data validation audits and, if needed, targeted audits. Such audits assess the impact and root cause of each deficiency or data error and correct such deficiencies or data errors prior to the submission of data for that MIPS payment year. In addition, QCDR measures must undergo certain measure testing requirements pursuant to CMS regulations. Registries may also have experience supporting regulatory decisions within other FDA centers or under international regulatory authorities such as EU MDR. The Coalition encourages the FDA to elaborate upon when and how registries’ preexisting data management and quality assurance methodologies can be leveraged to facilitate the Agency’s assessment of RWD/E developed thereunder.

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The Coalition appreciates your consideration of our comments. If you have any questions, please contact Leela Baggett or Jason Qu at Powers Pyles Sutter & Verville, PC (Leela.Baggett@PowersLaw.com or Jason.Qu@PowersLaw.com).

Respectfully submitted,

American Academy of Dermatology
American Academy of Ophthalmology
American Academy of Otolaryngology–Head and Neck Surgery
American Academy of Physical Medicine and Rehabilitation
American Association of Neurological Surgeons
American College of Gastroenterology
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