REAL-WORLD EVIDENCE ALLIANCE

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Dockets Management Staff (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

Re: Diversity Action Plans To Improve Enrollment of Participants From Underrepresented Populations in Clinical Studies; Draft Guidance for Industry; Availability (Docket No. FDA-2021-D-0789)

To the Food and Drug Administration:

The RWE Alliance appreciates the opportunity to comment on the draft guidance titled "Diversity Action Plans to Improve Enrollment of Participants from Underrepresented Populations in Clinical Studies" ("Draft Guidance").[1] We are a coalition of real-world data ("RWD") and analytics organizations with a common interest in harnessing the power of real-world evidence ("RWE") to inform regulatory decision making to improve the lives of patients. Our members have deep knowledge and experience working with healthcare data across disease areas and patient populations, and we aim to bring these collective insights to bear in support of RWE policies.[2]

The RWE Alliance envisions a future in which data from electronic health records, administrative claims and billing records, product and disease registries, personal devices, wearables, and health applications will be used to generate evidence to support regulatory decision making related to medical product safety and effectiveness. To achieve these goals, the RWE Alliance advocates for policies that will (1) advance FDA's RWE Framework, (2) encourage the use of RWE to better understand treatment effects in underrepresented populations, (3) enhance opportunities for RWE organizations to consult with FDA, (4) increase communication on the generation and use of RWE, and (5) recognize the unique aspects of and opportunities for RWD/E.[3]

[1] 89 Fed. Reg. 54010 (June 28, 2024).

[2] For information about our members, please see our website, https://rwealliance.org/who-we-are/.

[3] Additional information about what we believe is available on our website, https://rwealliance.org/what-we-believe/.

We share FDA's commitment to enhancing diversity in clinical studies in pre- and post-approval settings to ensure that clinical studies appropriately evaluate safety and effectiveness in representative samples of a drug product's intended use population, and appreciate the opportunity to provide comments on the Draft Guidance on this topic.

I. Role and Value of RWD in Diversity Action Plans

As the Agency and industry have recognized, clinical trial study populations are not always fully representative of relevant patient populations in real-world settings. Underrepresentation in clinical studies can hinder the understanding of treatment effects for historically underrepresented populations[4] and can worsen health disparities. Better representation in clinical trials will help to advance biomedical research that improves the safe and effective use of medical products for *all* patients.

RWD can play a role in providing FDA, medical product sponsors, patients, healthcare providers, and other stakeholders in the clinical research community with information on treatment effects among underrepresented populations across therapeutic areas. RWD is an important component of the data used in various elements of diversity plan design and implementation because it can capture or elucidate the real-world distribution of valuable demographic and clinical characteristics in the intended use population—factors that are essential when setting clinical trial enrollment goals. We applaud FDA for adding registries and electronic health records as examples of possible data sources to advance these goals.

In addition, RWD can provide insights into potential differential outcomes in various subgroups of the intended population, identify potential recruitment barriers to inform actions that ensure enrollment of a representative sample is feasible,[5] and provide a more comprehensive view of a patient's clinical journey to uncover potential health disparities and underlying factors such as access to care. A fit-for-purpose and representative real-world dataset can help to generate evidence that enhances the generalizability of results across the intended use population and can accelerate equitable access to biomedical research discoveries and innovations.

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[4] *See* Policy and Global Affairs; Committee on Women in Science, Engineering, and Medicine; Committee on Improving the Representation of Women and Underrepresented Minorities in Clinical Trials and Research; National Academies of Sciences, Engineering, and Medicine 23–46 (Kirsten Bibbins-Domingo & Alex Helman eds. National Academies Press (US) 2022), https://www.ncbi.nlm.nih.gov/books/NBK584396/.

[5] For instance, RWD can support more inclusive trial eligibility criteria. Royce TJ, Zhao Y, Ryals CA. Improving Diversity in Clinical Trials by Using Real-world Data to Define Eligibility Criteria. *JAMA Oncol.* 2023 Apr 1;9(4):455–456.

In the final guidance, we encourage FDA to use the term "real-world data," as the Agency did in the 2022 draft guidance.[6] FDA should emphasize the value of RWD when seeking to characterize the incidence and/or prevalence of disease across populations historically underrepresented in clinical research. Specifically, we recommend inserting the phrase "including real-world data sources" in the paragraph starting on line 258, so that the opening sentence reads, "Whenever possible, sponsors should utilize appropriate available sources, including real-world data sources . . . ." An express reference to RWD will demonstrate FDA's commitment to the use of RWD and provide additional guidance to sponsors.

FDA also should highlight specific instances where RWD can add value. For instance, in lines 295–300 of the Draft Guidance, FDA notes the importance of capturing differences in disease characteristics, medical practice, and available therapies when designing globally conducted clinical development programs. Here, FDA should highlight that RWD can help to reveal these differences. Across its guidance, FDA should indicate the circumstances in which RWD can help sponsors set enrollment goals and rationales for such goals and identify considerations for the use of RWD.

The RWE Alliance appreciates the Agency's commitment to enhancing diversity in clinical trials. Thank you for considering these comments, and please let us know if you have any questions. We welcome the opportunity to discuss further.

Best regards,

RWE Alliance

[6] FDA, Draft Guidance for Industry: Diversity Plans to Improve Enrollment of Participants from Underrepresented Racial and Ethnic Populations in Clinical Trials at 7 (2022).