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: New Drugs Regulatory Program Modernization: Integrated Assessment of Marketing Applications and Integrated Review Documentation; Request for Comments (Docket No. FDA-2024-N-3878)

To the Food and Drug Administration:

The RWE Alliance appreciates the opportunity to respond to the Request for Comments on the "New Drugs Regulatory Program Modernization: Integrated Assessment of Marketing Applications and Integrated Review Documentation" (the "Request for Comments"). 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.[1]

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

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

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.[2]

We appreciate FDA's Request for Comment on the Agency's review template used to communicate the Agency's assessment of safety and efficacy for new drug product marketing applications. We agree with FDA that the Integrated Review should provide sufficient detail about the FDA's benefit-risk assessment, including the evidence used to establish efficacy and the scientific reasoning underlying FDA's regulatory decisions. We offer our comments on ways to improve the Integrated Review documentation in response to the Request for Comments, below.

In Response to Question #2: "We are interested in specific recommendations about any areas of the Integrated Review documentation of the Integrated Assessment that can be improved to meet the needs of stakeholders."

We recommend that FDA include a dedicated section summarizing the RWD/E submitted and reviewed as part of an original or supplemental drug product marketing application in the Interdisciplinary Assessment or Additional Analyses and Information sections, where applicable, along with an overview in the Executive Summary. We recommend that the Integrated Review address any analyses of RWD, whether previously published or unpublished, that is conducted by the sponsor or an external party and is intended to support the assessment of clinical effectiveness or safety. FDA should state how FDA considered the RWD/E as part of the marketing application, including with respect to the Agency's risk-benefit assessment that informs regulatory decision making. At a minimum, FDA should describe, for each study involving RWD that is considered in FDA's review of a marketing application:

(1) the source and type of RWD;

(2) FDA's evaluation of the study design and analysis methods, including information about how RWD contributed to the study (this could consider, e.g., data for endpoint assessment, data for an external control arm, safety data necessary for an NDA/BLA approval or to satisfy a postmarketing requirement or commitment, or other uses of RWD); and

(3) the role of the study involving RWD in FDA's review of the application (e.g., whether the study contributed to substantial evidence of effectiveness, evidence of safety, or other contextual or supportive evidence).

We suggest that FDA also include a description of the Agency's engagement with the sponsor on the real-world study design.

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

Clinical researchers will be better equipped to use RWD to generate clinical evidence of effectiveness and safety with more information from FDA on the use and evaluation of RWD/E in medical product applications. Transparency and explanation by FDA about the role of RWE in marketing applications are critical for advancing increasingly sophisticated methods of data collection and analysis and can facilitate uses of RWD/E when traditional trials are not feasible, such as for rare diseases affecting small populations. Adding a dedicated section for RWD/E may also facilitate greater consistency among FDA reviewers and review divisions in their assessment of RWD/E in marketing applications. We encourage FDA to continue to engage with the RWE ecosystem to identify other information on RWD/E or innovative clinical development approaches that would help ensure stakeholders understand how FDA considers RWD/E in the regulatory decision making process.

The RWE Alliance appreciates the Agency's efforts to update its Integrated Review to facilitate more clarity on FDA's regulatory decision making. 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,

The RWE Alliance