REAL-WORLD EVIDENCE ALLIANCE

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ICH Secretariat
Route de Pré-Bois, 20
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Re: ICH Reflection Paper: International Harmonisation of Real-World Evidence Terminology and Convergence of General Principles Regarding Planning and Reporting of Studies Using Real-World Data, with a Focus on Effectiveness of Medicines

Dear ICH Assembly and Management Committee Representatives:

The RWE Alliance appreciates the opportunity to comment on ICH's reflection paper titled "International Harmonisation of Real-World Evidence Terminology and Convergence of General Principles Regarding Planning and Reporting of Studies Using Real-World Data, with a Focus on Effectiveness of Medicines" (referred to here as the "Reflection Paper").[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 patients' lives. 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 generated in everyday clinical practice and everyday life through electronic health records ("EHRs"), administrative claims and billing data, product and disease registries, personal devices, wearables,

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[1] ICH Reflection Paper: International Harmonisation of Real-World Evidence Terminology and Convergence of General Principles Regarding Planning and Reporting of Studies Using Real-World Data, with a Focus on Effectiveness of Medicines (2023), https://admin.ich.org/sites/default/files/2023-06/ICH_ReflectionPaper_Harmonisation_RWE_Terminology_Endorsed-ForConsultation_2023_0613.pdf.

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

and health applications will be used to generate evidence that complements clinical trial data to inform regulatory decisions. To achieve this goal, 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]

The RWE Alliance appreciates ICH's efforts to enhance global regulatory harmonization and convergence for RWD/E and to establish a dialogue with stakeholders on this topic. We share ICH's goals of informing and advancing the regulatory landscape for RWD/E, as these efforts will ultimately foster innovation and benefit patients. The RWE Alliance offers the following comments for consideration, centered on three themes: (1) ICH's development work on RWD/E; (2) interconnectivity of ICH Guidelines; and (3) stakeholder engagement.

I. We support the ICH Guideline development work to advance regulatory use of RWD/E.

The RWE Alliance commends ICH for the Reflection Paper on RWE terminology and convergence of general principles regarding planning and reporting of studies using RWD, with a focus on effectiveness of medicines. We are encouraged by ICH's focus on prospective planning for guideline development and stakeholder engagement to promote harmonization as the role of RWD/E in supporting the development and use of medicines across the globe continues to evolve rapidly. Notably, the International Coalition of Medicines Regulatory Authorities (ICMRA) statement[4] on international collaboration to enable RWE for regulatory decision making highlights the need for harmonization of terminologies and convergence on guidance and best practices for RWD and RWE. The RWE Alliance supports ICH's uptake of these priorities and efforts to advance international regulatory guideline development work. We also believe that beginning harmonization with (1) "RWD/RWE terminology, metadata, and assessment principles and" (2) "RWD/RWE protocol & report format, and study transparency" principles is an appropriate starting point for ICH guideline development work. These topics will allow ICH members to participate meaningfully in the development of this area of regulatory science and to pave a solid foundation for convergence in years to come.

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

[4] ICMRA statement on international collaboration to enable real-world evidence (RWE) for regulatory decision-making, https://www.icmra.info/drupal/sites/default/files/2022-07/icmra_statement_on_rwe.pdf.

II. We support interconnection of RWD/E-related Guidelines across the ICH portfolio.

While the Reflection Paper outlines new topics for ICH to develop in the future, it is important to acknowledge that ICH has already developed several guidelines that incorporate concepts related to the use of RWD/E in medical product development and regulatory decision making. ICH should ensure that existing ICH guidelines that reference RWD/E concepts, including any guidelines currently under development, are taken into consideration during the development of future ICH guidelines anticipated through this reflection paper. To that end, we suggest ICH prioritize integrating the anticipated guidelines on RWD/E with existing and upcoming guidelines and articulate integration as a distinct, standalone objective of its harmonization approach. Doing so will help to achieve ICH's goal of promoting harmonized technical requirements that support the development of higher quality RWD/E able to substantially contribute to the body of evidence supporting the benefit-risk profile in regulatory decision making.

For example, guidelines relevant to RWD/E and the effectiveness of medicines within the ICH portfolio include the ICH GCP Renovation Reflection Paper[5]—specifically ICH E6(R3) Good Clinical Practice (GCP) and its Annexes[6]—and ICH E8(R1) General Considerations for Clinical Studies.[7] Additionally, the ICH M14 Guideline in development on "General principles on plan, design, and analysis of pharmacoepidemiological studies that utilize real-world data for safety assessment of medicines"[8] should also be taken into account as ICH develops future RWD/E guidelines to ensure harmony in the description of RWD/E terminology and concepts with a focus beyond the effectiveness of medicines.

We also recognize that ICH has a demonstrated interest in measuring and promoting consistent regulator implementation of ICH guidelines.[9] We recommend that ICH

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[5] ICH Reflection Paper on "GCP Renovation": Modernization of ICH E8 and Subsequent Renovation of ICH E6 (revised 2021), https://admin.ich.org/sites/default/files/2021-05/ICH_ReflectionPaper_GCPRenovation_2021_0519.pdf.

[6] ICH Harmonised Guideline, Good Clinical Practice (GCP) E6(R3) (2023), https://database.ich.org/sites/default/files/ICH_E6%28R3%29_DraftGuideline_2023_0519.pdf.

[7] ICH Harmonised Guideline, General Considerations for Clinical Studies E8(R1) (2021), https://database.ich.org/sites/default/files/ICH_E8-R1_Guideline_Step4_2021_1006.pdf.

[8] Final Concept Paper (Apr. 5, 2022), https://database.ich.org/sites/default/files/M14_ConceptPaper_2022_0405.pdf.

[9] ICH Guideline Implementation (last visited Sept. 29, 2023), https://ich.org/page/ich-guideline-implementation.

consider how RWD/E concepts that will be included in future ICH guidelines could be incorporated in related ICH training materials and programs for regulators, industry, and other stakeholders. This is particularly important for ICH E6(R3) given its status as an ICH Tier 1 Guideline.[10] As existing and future ICH regulators advance and implement RWE frameworks in their jurisdictions, such training efforts will ultimately bolster global regulatory convergence of RWD/E and help drive forward access to innovative treatments and cures.

III. We suggest including RWE organizations in the development of ICH RWD/E Guidelines.

The RWE Alliance looks forward to the development of future ICH guidelines articulated in the ICH RWE Reflection Paper, including on best practices for data quality and data standards for RWD. While the ICH Assembly includes a diverse set of global stakeholders, it is primarily composed of regulatory authorities and industry associations that are typically not involved in the direct collection and curation of RWD. We suggest that ICH consider including RWD organizations in development efforts as well to leverage these entities' insights from their direct involvement in RWD collection and utilization and work with biopharmaceutical sponsors and health authorities. RWD organizations may be in a position to offer unique perspectives and use cases that are distinct from other ICH members and observers that can accelerate ICH's goals for convergence.

IV. Conclusion

The RWE Alliance appreciates ICH's commitment to informing the regulatory landscape in this evolving area and looks forward to continued engagement. 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

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[10] Implementation of ICH Tier 1 Guidelines (i.e., ICH Q1 Stability Testing Guidelines, ICH Q7 Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients, and ICH E6 Good Clinical Practice) is a minimum criteria for new regulators to become members of the ICH Assembly. The eligibility criteria for becoming an ICH Member or Observer are detailed in the ICH Articles of Association (Articles 11, 12 and 17) and in the ICH Assembly Rules of Procedure (Sections 1 and 2). See details of the ICH application process here: https://www.ich.org/page/application-process.