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: Docket No. FDA-2025-N-0129: Electronic Study Data Submission; Data Standards; Clinical Data Interchange Standards Consortium Dataset-JavaScript Object Notation; Request for Comments

To the Food and Drug Administration:

The RWE Alliance appreciates the opportunity to respond to the Request for Comments titled "Electronic Study Data Submission; Data Standards; Clinical Data Interchange Standards Consortium Dataset-JavaScript Object Notation" (the "Request for Comments").[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

[1] 90 Fed. Reg. 15251 (Apr. 9, 2025).

[2] 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.[3]

We support FDA transitioning to Dataset-JSON for the submission of electronic study data. The use of Dataset-JSON will result in several benefits associated with the submission of RWD to FDA. First, JSON is a modern, structured, and API-friendly format that supports automation, reuse, and downstream analytics—core enablers for efficient handling of large and heterogeneous RWD. Second, RWD sources like electronic health records ("EHRs") and medical claims are increasingly ingested and processed through systems built on Fast Healthcare Interoperability Resources ("FHIR") or the Observational Medical Outcomes Partnership ("OMOP"). Converting these into Study Data Tabulation Model ("SDTM") or Analysis Data Model ("ADaM") in Dataset-JSON can streamline the transformations involved in preparing regulatory submissions using these standards. Third, Dataset-JSON allows for richer, full-variable metadata by supporting the inclusion of labels, units, and controlled terms, relative to XPT's more limited capacity to show variable names, types, and lengths. Fourth, Dataset-JSON can facilitate submission consistency by standardizing and simplifying integration with define.xml, and by improving traceability, reproducibility, and alignment with Study Data Standardization Plans ("SDSPs"). Fifth, the move to JSON is aligned with the Agency's Technology Modernization Action Plan by mirroring FDA's focus on cloud-based, scalable, machine-first technologies. This proposed transition thus would improve the Agency's ability to receive and process regulatory submissions, including those with RWD.

While we support the transition to Dataset-JSON, FDA should account for potential integration and implementation challenges associated with the adoption of Dataset-JSON for submission of electronic study data. Many companies in the life sciences ecosystem have deeply embedded workflows and validated systems built around SAS XPT. Companies will need to develop, qualify, and validate new tools and processes to generate, read, and validate Dataset-JSON for regulatory compliance. Companies also will need to invest in training statistical programmers, data managers, and regulatory operations teams on the nuances of Dataset-JSON generation, error handling, and troubleshooting. For instance, technical experts within the industry will need to pay attention to potential technical issues with the use of Dataset-JSON, including concerns associated with file size, parsing performance, and transmission times for large clinical datasets compared to the more compact binary XPT format. It also will be important for there to be careful versioning and governance of Dataset-JSON specifications.

FDA's transition to Dataset-JSON using a phased implementation approach in accordance with FDA's guidance titled "Providing Regulatory Submissions in Electronic Format—Standardized Study Data" will allow the RWE ecosystem to integrate and validate the new standard. FDA's implementation period, during which FDA will support

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

Dataset-JSON in parallel with existing XPT-submissions, will permit industry to implement needed changes according to the guidance's implementation timeline.

We appreciate FDA's engagement with stakeholders, to date, to explore Dataset-JSON. To support implementation of Dataset-JSON, we recommend that FDA take several steps in advance of or during the implementation period. FDA should offer guidance, reference implementations, and detailed examples covering SDTM, ADaM, Standard for Exchange of Nonclinical Data ("SEND"), and other applicable data standards and formats, including any data standards the Agency is considering adopting in the future. FDA also should define validation expectations for Dataset-JSON submissions (e.g., structure, content, and integrity checks) and metadata expectations for Dataset-JSON used in studies involving RWD.

The RWE Alliance appreciates the Agency's commitment to exploring new and updated data standards and facilitating the submission of data collected from RWD sources to inform 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