November 29, 2021

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

Dear Dockets Management Staff,

The HIMSS Electronic Health Record Association (EHRA) member companies serve the vast majority of hospitals, post-acute, specialty-specific, and ambulatory healthcare providers using EHRs across the United States. Our core objective is to collaborate to accelerate health information and technology adoption, advance information exchange between interoperable systems, and improve the quality and efficiency of care through the use of these important technologies.

On behalf of the nearly 30 member companies of the EHRA, we appreciate the opportunity to provide feedback on the draft "Data Standards for Drug and Biological Product Submissions Containing Real-World Data" as well as the "Real-World Data: Assessing Electronic Health Records and Medical Claims Data To Support Regulatory Decision-Making for Drug and Biological Products" guidance for industry documents.

While much of the proposed guidance is focused on sponsors of clinical research and health sciences, real-world data (RWD) is most often obtained from EHRs for use in establishing real-world evidence through these sponsors, life-science research organizations and their technologies. The use of RWD from EHRs introduces challenges, which are well-recognized and acknowledged by the FDA. EHRs are focused primarily on enabling clinicians to document and coordinate care delivery; the collection of data for research, clinical trials, and subsequent drug and biological submissions, is secondary. EHR-sourced data provides substantial value. However, it sometimes must be complemented with data from other sources when the study at hand requires information not typically documented in an EHR, and may require further normalization when combined with data from multiple sources.

We appreciate that the FDA clearly establishes that research sponsors are responsible for data transformations and providing necessary documentation to justify approaches utilized in reconciling any challenges in the source data. However, the EHRA suggests that there is a clear opportunity to make

EHR-sourced real-world data increasingly available and valuable for research purposes while continuously improving on the end-to-end documentation that will benefit the delivery of care and coordination, through strong collaboration among critical stakeholders such as FDA, CMS, CDC, NIH, ONC, providers and their HIT suppliers.

Alignment on a clear set of standards to enable sharing of this data with a research environment is critical as it will help increasingly align on common vocabulary, structure, and relevant granularity in the source systems. **We suggest that targeted workshops may be a venue to convene relevant stakeholders to collaborate on key topics that enable alignment of the necessary standards**, as the SHIELD initiative has brought together all parties across the laboratory ordering and reporting continuum to improve on the consistent use of a standard vocabulary.

The EHRA has identified three areas where such collaboration can help raise the overall level of data quality, patient record completeness, and harmonization of documentation without unduly increasing clinician documentation burden.

Data Quality

We echo FDA's acknowledgement that real-world data provides tremendous opportunities to accelerate and enhance drug and biological product submissions, though the data comes from sources that may not be as complete and stringent as otherwise required for clinical trials. While clinical trial-quality data is not the expectation or the goal, increased focus on these uses of the data has the potential to advance data quality and completeness upstream in the documentation process. Alignment on standards is one aspect, further discussed below, that can further enable the quality of data. A particular example that would benefit from alignment is the need for traceability and the need for maintaining the provenance of data received by an EHR for the delivery of care. **We suggest that alignment on data requirements in the context of ONC's USCDI, which includes provenance, provides an opportunity to ensure consistency of approaches from initial capture through the various systems that data may flow before it is subsequently used for specific studies. We also recommend that guidance address the need for transparency about data that is escaped or excluded from use as part of data cleaning, normalization, or harmonization processes, as this can impact confidence in a study's findings.**

Patient Record Completeness

To ensure evidence is based on relevant real-world data, it must be complete for the patient cohort at hand. Patient matching and linking challenges must be addressed, especially as patients have been seen by multiple providers where one cumulative patient record cannot be expected to exist with any one of the providers involved. Depending on whether a study involves identifiable data or de-identified/pseudonymized/tokenized data introduces different considerations. When identifiable data is used, ostensibly the patient has provided the necessary consent and there typically is enough data available on the patient to enable record linking and further data normalization as data for the same patient is pulled from different data sources. However, when data is de-identified/pseudonymized/tokenized for the study, which is the more likely scenario for studies subject to the proposed guidance, record completeness will be a challenge as multiple data sources need to be aggregated. This underscores the need for being able to link data across data sources, while at the same time introduces the challenges of linking once data leaves the EHR as de-

identified/pseudonymized/tokenized data. If the necessary linking is not achieved before the data leaves the provider's stewardship and is de-identified/pseudonymized/tokenized, appropriate consent must be in place. **We suggest that appropriate guidance is provided on how to manage this consent process in the context of a clearly defined privacy framework.**

Standards Alignment

Enhancing data quality along the entire data collection and sharing chain can be substantially achieved through alignment of standards in three areas:

1. **Data model and data set definition alignment across data sources and the study to improve the normalization process and increase the study's data quality when gathering EHR data**

   The variety of data requirements across research and registry initiatives, including effective public health and quality measure reporting, creates a challenge to all stakeholders. As an example, we note that CMS' drive towards dQMs and "meaningful measures" will require more longitudinal data and outcome assessment, which is similar to the need for a common data model and data definition within and across data sources for real-world data for product submissions. We suggest two approaches to enable the necessary alignment across stakeholders:
   - Collaborate with ONC to utilize the USCDI process through the new USCDI+ extension approach to align alignment on the ePHI relevant to real-world, data-based research.
   - Align on the use of common data and data set definition expressions that certified HIT, such as EHRs, are already supporting and expanding (HL7 FHIR for APIs) or are actively developing with CMS (HL7 CQL).

2. **Consistent vocabulary standards adopted across stakeholders to satisfy care delivery and subsequent analysis and research**

   As previously noted, the EHRA suggests considering a corollary to the efforts of the SHIELD initiative to align vocabularies from diagnostic devices from LIS to EHRs to improve consistent data concept representations.

3. **Exchange standards alignment to minimize friction in the transmission and translation of data models deployed in EHRs vs. research databases**

   Currently, a variety of exchange standards are used across systems to share data, e.g., HL7 (v2, C-CDA, FHIR) or NCPDP (Script) to CDISC (ADaM, SDTM) or OMOP. We suggest alignment on those primarily used by the source systems would promote consistency of data contributions across data sources. We particularly suggest alignment on HL7 FHIR as it is emerging as a common approach beyond EHRs and as it is being progressed by the HL7 Vulcan initiative, including bulk data, supporting a variety of data sharing patterns. We suggest that guidance recommends these capabilities to study sponsors, and advocate for the creation of supplementary educational materials on the use of FHIR APIs in partnership with clinics and hospitals to retrieve clinical data to support studies. Lastly we suggest that FDA focuses on its

systems as well to accept data submissions via FHIR APIs. This would allow for data being contributed to study sponsors in FHIR format to be shared with FDA as needed and appropriate without further transformations, e.g. to CDISC (using SDTM or ADaM) as mapping fields to such standards can be highly manual and laborious. Allowing data in the FHIR format would ultimately reduce the burden on data sources and improve the overall rate of advancement in RWD.

Thank you for this opportunity to share our experiences and expertise. We appreciate the ongoing collaboration to leverage EHR data to accelerate medical product development and bring innovations faster and more efficiently to the patients who need them.

Sincerely,

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Cerner Corporation

David J. Bucciferro
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HIMSS EHR Association Executive Committee
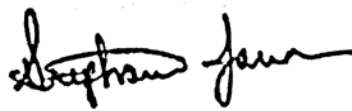
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