McKesson Corporation
6535 State Hwy 161
Irving, TX 75039

Pete Slone
Senior Vice President, Public Affairs

MCKESSON

www.mckesson.com

February 4, 2022

Dr. Janet Woodcock
Acting Commissioner
U.S. Food and Drug Administration (FDA)
Dockets Management
5630 Fishers Lane, Rm 1061
Rockville, MD 20852

Submitted via regulations.gov

Re: Data Standards for Drug and Biological Submissions Containing Real-World-Data: Guidance for Industry (FDA-2021-D-0548)

Dear Acting Commissioner Woodcock:

On behalf of McKesson Corporation ("McKesson"), we appreciate the opportunity to provide feedback on the U.S. Food and Drug Administration (FDA) draft guidance on "Data Standards for Drug and Biological Submissions Containing Real-Word Data (FDA-2021-D-0548)."

About McKesson

McKesson is a mission-driven company, focused on working with our customers and partners to advance health outcomes for *all*. Together, we are charting a course to better health in every setting — one product, one partner, one patient at a time. For over 180 years, McKesson has led the industry in the delivery of medicines and healthcare products. We deliver vital medicines, medical supplies, care management services and health information technology (IT) solutions that touch the lives of over 100 million patients in healthcare settings that include more than 50,000 retail pharmacies, 5,000 hospitals, 200,000 physician offices, nearly 12,000 long-term care facilities, and 2,400 home care agencies.

McKesson is also a leader in pharmacy solutions. Our Health Mart franchise is the fourth largest pharmacy network in the U.S. with more than 4,900 independent pharmacies. Our RelayHealth Pharmacy Solutions manages the nation's most reliable pharmacy connectivity network, executes more than 18 billion pharmacy transactions annually and connecting more than 50,000 retail pharmacies with key healthcare stakeholders. In addition, CoverMyMeds is a leader in electronic prior-authorization solutions that automate the prior-authorization process for more than 500 electronic health records systems, 49,000 pharmacies, 700,000 providers, and most health plans and pharmacy benefit managers (PBMs). Our RxBenefit Clarity solution provides patient-centric data that empowers providers and their patients with prescription price transparency data that goes above and beyond the patient's benefit, and leverages cash options as well as patient assistance programs. McKesson also develops and administers custom programs to help patients overcome

McKesson Corporation
6535 State Hwy 161
Irving, TX 75039

Pete Slone
Senior Vice President, Public Affairs

www.mckesson.com

barriers to medication initiation and adherence.

McKesson's unique 360-degree view of the healthcare system provides us with a distinctive vantage point. We monitor and engage in regulatory activities that present both opportunities and challenges for our company, our customers, and the patients they serve. Our company strives to ensure that our views on better healthcare prioritize what's best for the patient. Our public-policy platform is driven by the core belief that the ***Patient Comes First***.

About McKesson's Oncology Ecosystem

McKesson is a leader in advancing clinical cancer research and improving cancer care. We support **The US Oncology Network** (The Network), one of the nation's largest and most innovative networks of community-based oncology physicians. These practices serve more than 1.2 million patients, including 160,000 new cancer patients annually, across nearly 400 sites of care and represent more than half of the participants in the Centers for Medicare and Medicaid Services (CMS) Innovation Center's Oncology Care Model. Additionally, we support physicians participating in payer quality and performance programs, including CMS' Quality Payment Program. We also support US Oncology Research (USOR), an industry-leading research organization that has been conducting Phase 1-IV clinical trials across many indications, including rare tumor types. USOR has played a role in the approval of more than 100 therapies and has enrolled over 87,000 cancer patients to approximately 2,000 oncology clinical trials, including more than 3,200 patients into Phase I trials.

Ontada® is our oncology real-world data and evidence (RWD/E), clinical education, and provider technology business dedicated to transforming the fight against cancer. Ontada's non-interventional research is designed to accelerate life science drug discovery, development, and commercialization.

Ontada's value is strengthened by our proprietary provider technology solutions, including the oncology-specific iKnowMed electronic health record (EHR), that are utilized at the point of care and support clinical and operational excellence, generating structured and unstructured oncology data across more than 2,700 oncology providers in 40 states. This enables Ontada to serve as a connecting point to pull in data from the largest community oncology network and utilize our unique access to claims, reimbursement, and labs data to reveal important insights for our life sciences and provider partners.

Ontada is part of a broader oncology ecosystem that leverages McKesson's 360º-degree view in oncology care delivery. This includes The Network, USOR, Biologics by McKesson (a specialty pharmacy for oncology and other therapeutic areas), and Onmark® and Unity Group Purchasing Organizations (GPOs). These partnerships enable Ontada's deep relationships with oncology providers and provides a unique understanding of the front lines of cancer care in the context of RWD/E generation, and collectively enable Ontada access to over 2.5 million patient records for research.

McKesson Corporation
6535 State Hwy 161
Irving, TX 75039

Pete Slone
Senior Vice President, Public Affairs

www.mckesson.com

General Comments

We applaud FDA's ongoing commitment to implementing the 21st Century Cures Act by establishing a robust real-world evidence (RWE) program to advance the use of real-world data (RWD) to support regulatory decision-making. We appreciate the opportunity to provide comments on the need to standardize study data to improve the use of RWD in regulatory decision making. This guidance is timely as the life sciences industry and researchers seek to embrace new ways of generating RWD to support trials and clinical advancements.

Since the passage of the Cures Act, our healthcare ecosystem has experienced a proliferation of innovations in the field of data science. COVID-19 only fueled this trend, forcing researchers to embrace new ways of conducting trials. From trial recruitment to virtual clinical visits, investigators implemented novel approaches to ensure clinical research programs continued with minimal disruptions. For the life sciences industry and regulators, this period has provided fertile ground for rapid progress in the utilization of RWD in clinical and regulatory decision-making.

Conforming RWD to currently supported FDA study data standards is essential to increasing the use of RWD to inform regulatory decision-making. Our response below contains some high-level observations of the guidance, followed by our specific recommendations on how we believe the guidance as written could be improved.

High Level Summary Observations

- ***FDA should play larger role in closing divergence of data domain terminologies and to the extent feasible, should work with other agency partners to encourage harmonization where possible:*** We appreciate FDA's recognition that nearly every data domain contains a "wide divergence in the terminologies used and their precise meaning between RWD sources and FDA-supported data standards," and note that the guidance touched upon some of the most tangible examples of these types of variations, such as gender and race/ethnicity. We are currently accounting for these nuances in our iKnowMed EHR; however, we believe FDA has an important role to play in helping the industry drive towards greater harmonization of data standards for common data elements. In our appendix, we provide examples of common data elements where FDA may want to consider driving greater standardization.

- ***Additional guidance needed to support use of the Data Standards Catalog and the role of prospective studies***: We support FDA's intention to issue further guidance and/or update the Data Standards Catalog with standards for study data derived from RWD sources. We would also like to see additional guidance from the agency on the use of RWD in prospective studies, as well as prospective studies leveraging EHRs. The agency could start with standards highlighting study outcomes measures, such as mortality, progression, and response. Establishing a common data model for known study elements will encourage harmonization.

McKesson Corporation
6535 State Hwy 161
Irving, TX 75039

Pete Slone
Senior Vice President, Public Affairs

www.mckesson.com

- ***FDA's role in shaping a sponsor's data dictionary****:* FDA cites the importance of sponsors developing data dictionaries to help map RWD to FDA-approved study data elements. While we are aligned with the importance of this step, we believe FDA is in a unique position to use industry submissions and offer greater specificity around common data elements of a data dictionary that can further harmonize data across different data sources.

- ***Addressing data missingness in data transformation****:* There are research methods for managing missing data and we would like to see FDA reference these methods in guidance. It would be helpful for FDA to provide recommendations or thresholds of willingness for acceptance of missing data (i.e., transparency in reporting percent of missing data, any minimum necessary completeness thresholds, appropriateness/acceptance for imputations, etc.).

- ***Guidance lacks specificity around the process to perform mapping of RWD to study data submission standards:*** While the guidance references the need for sponsors to perform a mapping of RWD to study data submission standards, we would like to see this guidance provide more clarity as to "how" the mapping should be performed. A prescribed process by the FDA will be helpful to the agency and sponsors to further minimize the potential for errors when mapping RWD to study data standards.

- ***Guidance should elaborate on differences between structured and unstructured data*** While variations in terminologies exist across all domains, there is usually more internal standardization with structured data (EHR database, medical claims, etc.) domains than RWD obtained from unstructured domains (EHR progress notes, free text, etc.). The industry would benefit from more discussion from FDA on these differences.

Data Standards for Drug and Biological Submissions Containing Real-World Data – McKesson/Ontada Guidance Recommendations

Line Item	Text	Recommendation
95-103	*Documentation of processes for managing RWD.*	The FDA should provide more details on what documentation of the processes is acceptable.
108	*New guidance and/or to update the Catalog.*	Data standards described in the catalog (i.e., SDTM/CDISC) are not tailored for RWD sources, particularly for representing genomic, socio-economic, and patient-reported information and variables. In fact, in many cases the standards are still emerging to catch up with rapidly evolving science for genome markers, etc. To this end, FDA should follow a regular cadence to update the Catalog. We would also encourage further clarity around the level of specificity needed to represent

Line Item	Text	Recommendation
		data captured from real-world data and would request that FDA indicate when industry can expect further guidance.
139-145	*Documenting sex as a variable.*	FDA notes that sex as a variable may be codified in the Clinical Data Interchange Standards Consortium (CDISC's) terminology as a physical characteristic, whereas EHRs may use gender identity. Our EHR currently captures both physical characteristics and gender identity, and we will continue to do so; however, we believe data domains like sex are an area where FDA could leverage sponsor submission experience to provide guidance to industry on this type of data capture.
136-139	*Interpretation of health care records for vital measurement.*	Documenting Variation in Units: While FDA acknowledged that the interpretation of health care records for vital health care measurement can lead to variation, we would like to see the guidance discuss some of these issues in more detail. For example, when considering medical units and reference ranges, mapping routine data such as height, weight, body mass index (BMI) can vary regarding units used (e.g., metric system (kilograms, centimeters) vs. US imperial system (pounds, feet)). Additionally, when calculating conversions, there can be issues with rounding and decimals.
157	*Considerations for Data Transformation.*	We appreciate that the guidance notes examples of when sponsors may encounter challenges in transforming RWD into data that are consistent with FDA-supported data standards. FDA might consider including additional examples of when data missingness can occur in this process. Such additional data examples might include: • **Staging Shifts**: Mapping of data values to certain oncology disease stages when clinical guidelines evolve and standards of care change over time. • **Data Deidentification Process**: If date shifting occurs for data privacy (e.g., masking date of birth (DOB) or if

McKesson Corporation
6535 State Hwy 161
Irving, TX 75039

Pete Slone
Senior Vice President, Public Affairs

www.mckesson.com

Line Item	Text	Recommendation
		imputation occurs to address missingness of date fields).
185	*Data Curation*	Although the definition addresses application of standards, addressing variation in interpretation of the standards in a retrospective setting should be included.
242	*Source Data*	The source data definition includes a footnote to review the guidance, "Use of EHR Data in Clinical Investigations." This guidance document focuses on prospective studies and does not apply to post-market or feasibility studies, or registries. Considering use of RWD from the EHR is often retrospective and potentially supportive of pharmacovigilance, etc. Revised guidance in this area would be valuable.
258	*Appendix: Examples of Mapping Health Care Data to CDISC SDTM*	FDA standards should provide guidance on how to allow for incorporation of real-world variability in categories (e.g., for RWE, incorporation of multiple values for race). FDA does not provide guidance on how to perform data mapping, but rather states it should be performed to standards.

Conclusion

We appreciate the opportunity to provide comments on this draft guidance and FDA's ongoing commitment to advance the agency's thinking around the role of RWD/E in regulatory decision-making. We hope that the additional background information provided about Ontada, the Network and our RWD/E Framework will be helpful to FDA in understanding our interest in this space and future collaboration opportunities with your agency as the RWE program evolves. We look forward to continuing our partnership with HHS and the FDA and working with the Administration to promote a robust, patient-centered healthcare ecosystem that works for patients. If you have questions or need further information, please contact Fauzea Hussain, Vice President of Public Policy, at Fauzea.Hussain@McKesson.com.

Sincerely,

Pete Slone