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DiMe response to Methodological Challenges Related to Patient Experience Data

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Dockets Management Staff (HFA-305)
Food and Drug Administration
5360 Fishers Lane, Rm 1061
Rockville MD 20852

RE: Docket No. FDA-2023-N-1506:

The Digital Medicine Society (DiMe) is pleased to respond to the Food and Drug Administration's (FDA) request for comments regarding Methodological Challenges Related to Patient Experience Data in the context of benefit-risk assessments and product labeling.

Positioned at the intersection of healthcare and technology, DiMe has expertise in facilitating pre-competitive collaboration to provide community resources guiding development and deployment of digital measures in clinical research and care. DiMe is committed to developing clinical quality resources on a tech timeline, by engaging with experts and pursuing fit-for-purpose methodologies. We commend the FDA's efforts to understand methodological challenges related to patient experience data and take the opportunity to provide our comments based on the gaps we observe in the field and through our work engaged in this space. Specifically, we outline the potential to harness digital health technologies to support meaningful and higher resolution patient experience data, discuss challenges with analyzing intensive longitudinal data and novel measures, and propose precompetitive collaborations as a vehicle to characterize the landscape of challenges and work towards consensus solutions and standard methodologies.

The Opportunities for Digital Health Technologies to Inform Benefit-Risk Assessments

Digital health technologies (DHTs) present novel methods to capture patient experience data to inform the benefit and risk management strategies for drug development. DHTs can be utilized to measure digital biomarkers for personalized and real-time monitoring of a response to a drug, safety, and adverse events. In contrast to discrete clinic-assessments, digital measures can also capture aspects of patients' health in their daily life in contexts that matter and where treatments can provide meaningful benefit to how patients function, feel, or survive (electronic clinical outcome assessments; eCOAs). Equipped with continuous, longitudinal, and thus

higher resolution data from fit-for-purpose eCOAs or digital biomarkers, there is greater opportunity to make better informed decisions related to outcomes that matter to patients.

Methodological Challenges Related to Patient Experience Data Collected from Digital Health Technologies

Data collected from DHTs can produce intensive longitudinal data (ILD), characterized by high frequency, repeated measures able to capture daily patient behavior, experiences, and physiological responses, often in real-time. While ILD provides greater capability to understand risk and characterize benefits of a drug, methods to analyze continuous data remain under-utilized. Typically, when analyzing ILD, the wealth of information from continuous data is collapsed into summary scores such as an average calculated over a given time period. This can provide simplicity for researchers, who can compare average changes of a health outcome using traditional statistical methods (i.e., ANOVA, MMRM, and regression). For example, a study that may measure the change in the length of walking bouts (e.g. number of steps in a single continuous walking action before stopping) may assess the mean walking bout length over 28 days prior to the clinic visit and use this summary value in their longitudinal analysis model. By summarizing ILD to use in a longitudinal model, the variance associated with the summary score is not included. This means that valuable information is lost and valuable insights derived from this variability cannot be used, decreasing the ability to inform benefit and risk decisions.

The use of summary values also reduces the available data (in this example, a continuous signal captured over 28 days) down to a single data point, thus using only a portion of the available statistical power to detect an effect. Although many techniques exist for the appropriate analysis of ILD, implementation has been slow by a field that is not used to interacting with such data.

A second methodological challenge with analyzing data from DHTs include selecting appropriate reference measures for novel digital endpoints. The FDA Draft Guidance 'Digital Health Technologies (DHTs) for Remote Data Acquisition' provides clear direction on the technical evidence needed in support of the use of digital endpoints in drug development. Yet the clinical and regulatory science pertaining to digital clinical measures remains incomplete as neither the scientific community nor the regulatory policymakers have defined: (1) how to select the optimal reference measure(s) for novel digital clinical measures and endpoints and (2) performance requirements against these existing measures. Without methodological guidance

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developed collaboratively across multiple stakeholder groups, the extent of value from novel digital endpoints will not be fully realized.

Pathways Forward for Methodological Challenges

In response to these methodological challenges, DiMe suggests convening a multi-stakeholder group of experts in ILD analysis, data science, outcome development, and clinical research tasked to define the landscape of ILD methodologies and reference measures for novel digital endpoints, test approaches on simulated and real world data, recommend optimal solutions, and identify remaining research needed. DiMe looks forward to answering any questions and collaborating with the FDA in the pursuit of excellence in digital clinical measurement and harnessing innovation to better inform benefits and risks in drug development.

We thank the FDA for allowing the opportunity to comment on methodological challenges related to patient experience data.