TIME COALITION IN RANGE

May 23, 2023

Re: Time in Range Coalition Comments to Docket No. FDA-2022-N-3319: Framework for the Use of Digital Health Technologies in Drug and Biological Product Development

Dear Sir/Madam,

On behalf of the Time in Range Coalition (TIRC), thank you for the opportunity to comment on the Food and Drug Administration's (FDA) proposed Framework for the Use of Digital Health Technologies in Drug and Biological Product Development (Framework). We appreciate your fulfillment of this important commitment under the Prescription Drug User Fee Act VII and thank you for your recognition of the need to facilitate the use of digital health technologies (DHTs) in the development of new therapies for patients. For individuals living with diabetes, DHTs – many digital devices and especially continuous glucose monitors (CGMs) – are an essential tool in achieving the appropriate Time in Range (TIR) as part of daily diabetes management. The incorporation of CGM-derived TIR metrics into drug development and regulatory decision-making is critical to maximizing the benefits of TIR in improving health outcomes and reducing health disparities and as such, is a priority for members of TIRC. Please know we stand ready to serve as a resource for you and your colleagues as you undertake this important body of work.

About Time in Range Coalition

TIRC is a global effort led by The diaTribe Foundation and comprised of 26 nonprofit associations, patient advocacy organizations, professional societies, and industry members committed to driving awareness and adoption of TIR (including times above and below) measured through the use of a CGM as an actionable metric for daily diabetes management and a means to improve long-term health outcomes. TIRC works to achieve this by educating individuals with diabetes, health care providers, and regulators about the science of TIR and by working to establish TIR as an essential part of diabetes management and to make TIR accessible to all people with diabetes.

Reflecting its importance to the quality of life and health outcomes for individuals living with diabetes, a central goal of TIRC has been for CGM-derived TIR data to be used in regulatory decision-making, specifically for TIR to serve as an endpoint to support diabetes drug approvals, as a complement to HbA1c, and for TIR data to be incorporated into the product prescribing information to support the clinician's treatment decision. As diabetes management is increasingly reliant on DHTs such as CGMs, greater regulatory clarity on the utilization of DHTs in clinical trials will make a profound impact on the ability to advance TIR and innovation in diabetes treatments.

The Critical Role of DHTs in Diabetes Management

Thirty-seven million Americans are impacted by diabetes, a chronic condition that requires proactive daily management of glucose levels. High blood glucose levels can lead to serious and life-threatening acute complications, such as ketoacidosis or death; and over time severe long-term complications including heart and kidney disease, strokes, crippling amputations, and blindness. On the opposite end of the spectrum is hypoglycemia, or low blood glucose levels, which in severe cases can include disorientation, seizures, difficulty speaking, loss of consciousness, coma or death. As such, ensuring that people with diabetes have access to the real-time information they need to manage this disease can help prevent and reduce negative health outcomes.

TIR can provide actionable information to improve people's daily diabetes management. People with both type. 1 and type 2 diabetes can use the data generated by a CGM including alarms to avoid dangerous blood glucose levels and to help make real-time adjustments to stay within a healthy range. According to the "Validation of Time in Range as an Outcome Measure for Diabetes Clinical Trials" study led by Drs. Roy Beck and Rich Bergenstal, as one's TIR increases, the risk of microvascular complications decreases. Even for those who don't need to use a CGM device continuously 24 hours per day 7 days per week, TIR and other CGM derived metrics are still an important tool to improve diabetes care. In addition, the CGM data collected through daily CGM wears plays a key role in assisting clinicians in choosing the most appropriate treatment option for each individual patient.

TIRC's Efforts to Advance the Use of CGMs in Clinical Trials

TIRC has recognized that as diabetes technology continues to advance, the collection, analysis and reporting of CGM data in clinical trials needs to be standardized so clinicians, scientists and regulators across the globe can incorporate it into their decision-making to the benefit of individuals living with diabetes. To that end, in 2022, TIRC, along with The diaTribe Foundation and Advanced Technologies & Treatments for Diabetes (ATTD), convened a group of international experts to discuss the role of TIR and CGMs in clinical trials for diabetes treatments. The result of this convening was a historic consensus that includes 22 recommendations for optimizing CGM-derived glucose data in clinical studies, including the parameters and specific glucose metrics researchers should evaluate and report, collection of baseline data and timing, information on clinically relevant changes in key glucose metrics over time, and training for both trial staff and participants.

In addition to The diaTribe Foundation and members of the TIRC, the Continuous glucose monitoring and metrics for clinical trials: an international consensus statement was endorsed by the Advanced Technologies & Treatments for Diabetes (ATTD) American Diabetes Association (ADA), JDRF, the American Association of Clinical Endocrinologists (AACE), Association of Diabetes Care and Education Specialists (ADCES), DiabetesIndia, European Association for the Study of Diabetes (EASD), International Society for Pediatric and Adolescent Diabetes (ISPAD), Japanese Diabetes Society (JDS) and published in *The Lancet Diabetes & Endocrinology* on December 6, 2022. We hope this consensus statement can serve as a valuable resource for the FDA, industry, and researchers in the development of standardized approaches for other DHT-derived data in clinical trials.

FDA's Approach to Advancing the Use of DHTs in Medical Product Development Must Be Patient-Centered

We appreciate that a number of the approaches outlined in the framework envision providing the opportunity for public engagement in meetings, demonstration projects, and through comment periods in the development of guidance documents. Particularly with regard to efforts to advance the use of DHTs, including CGMs, to measure surrogate and clinical outcomes, we urge you to ensure that the perspective of individuals with diabetes is prioritized in the agency's undertaking of these activities, particularly any resulting regulatory guidance. As noted earlier, TIRC is eager to serve as a resource for the agency with regard to CGM-derived data and the importance of the recognition of TIR as an endpoint that is relevant and meaningful to individuals with diabetes and the clinicians who provide care to them. Including CGM-derived outcomes in the labeling of the disease-modifying medications would increase the access of individuals with diabetes to these medications and at the same time contribute to reducing current considerable disparities.

The Role of DHTs in Advancing Equity and Reducing Health Disparities

Minority communities bear a disproportionate burden of diabetes. Black (17.4%), Asian (16.7%), and Hispanic (15.5%) adults have higher prevalence rates than whites (13.6%) and Indigenous Peoples are twice as likely as whites to have diabetes. Diabetes also is disproportionately found among Americans with lower education and income levels. More than 13% of adults with less than a high school education have diagnosed diabetes compared to 9.2% of those with a high school education and 7.1% of those with more than a high school education. Adults with family incomes below the federal poverty level had the highest prevalence for both men (13.7%) and women (14.4%).

In addition, the most severe diabetes-related health complications are prevalent among minority populations. Black, Indigenous, and Hispanic individuals with diabetes have higher rates of blindness, end-stage kidney disease, and amputations than non-Hispanic white individuals with diabetes. Deaths from diabetes were also significantly higher among these populations – Indigenous Americans are three times more likely, Non-Hispanic Black Americans are 2.3 times more likely, and Hispanic Americans are 1.5 times more likely to die from diabetes than white individuals.

We very much appreciate the acknowledgment in the Framework of the potential for DHTs such as CGMs for increasing diversity among clinical trial participants. We believe that the use of CGM-derived TIR data in clinical care and regulatory decision-making, by giving individuals with diabetes the tools needed for themselves and their health care providers to better manage their disease, also has the potential to help address the racial, income, and geographic disparities in diabetes prevalence.

Conclusion

TIRC appreciates FDA's proposal to undertake a comprehensive approach and corresponding set of activities to support the use of DHTs in drug development. For people living with diabetes, increased access to the data CGMs provide has been proven to enable improved management of glucose levels for all people with diabetes and also to reduce health complications from this serious chronic condition. We look forward to engaging fully in the proposed activities and working with the agency to make progress toward our goal of advancing the integration of CGM-derived TIR data into FDA's assessment of the safety and effectiveness of new therapies along with HbA1c for individuals with diabetes, and through this increase the access to these new therapies and decrease current unacceptable disparities.

If we can be of any assistance to you as you implement the framework, please do not hesitate to contact me at julie.heverly@diaTribe.org.

Sincerely,

Julie Heverly
Senior Director

Time in Range Coalition
The diaTribe Foundation