TIME COALITION IN RANGE

diaTribe

May 29, 2026

Re: Time in Range Coalition Comments to Docket No. FDA-2026-N-2476: Advancing the Use of Digital Health Technologies in Clinical Investigations for Drugs and Biological Products; Request for Information and Comments

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 or the Agency's) Request for Information and Comments on Advancing the Use of Digital Health Technologies (DHTs) in Clinical Investigations for Drugs and Biological Products (Request for Information). We appreciate FDA's recognition of the importance of facilitating the use of DHTs in the development of new therapies for patients.

For individuals living with diabetes, DHTs and, in particular, continuous glucose monitors (CGMs), are an essential tool in diabetes management, providing the kind of real-time, actionable data necessary to manage a complex 24/7 disease. The incorporation of CGM-derived metrics into drug development and regulatory decision-making is critical to maximizing the benefits of their use in improving health outcomes and reducing associated health care costs and, as such, is a priority for members of the TIRC.

About Time in Range Coalition

Spearheaded by The diaTribe Foundation, the TIRC is a diverse group of global diabetes stakeholders, including nonprofit organizations, professional societies, industry, and patient advocates working to drive awareness and adoption of TIR. Reliable measurement of TIR, which is the percentage of time a person spends within a target glucose range and is reported alongside time above range (TAR) and time below range (TBR), is now possible through advancements in continuous glucose monitoring. CGM technology empowers individuals living with diabetes to be aware of their glucose levels every few minutes, such that they can make real-time adjustments to their diet, activity, and medication dosing to improve health outcomes.

The Critical Role of DHTs in Diabetes Management

Over forty million Americans are impacted by diabetes, a chronic condition that requires proactive daily management of glucose levels.[1] 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, amputations, and blindness.[2,3] 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.[4] 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. Studies have shown that as one's TIR increases, health complications from the disease and associated healthcare costs decrease.[5–10]

TIR can provide actionable information to improve people's daily diabetes management. People with all types of 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. Care management has evolved such that guidelines now suggest the use of TIR alongside or in place of A1C to assess glycemic status, and a recent survey found that clinicians find TIR more helpful than A1C for identifying focus areas and observing the effect of a treatment change.[11,12] This reflects a major shift in clinical care, which now relies on rich CGM data, capturing variability and patterns that A1C cannot, to optimize treatment.

CGM-Derived Metrics in Clinical Trials

Reflecting its importance to 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, the TIRC has called for TIR data to be incorporated into product prescribing information to support clinicians' treatment decisions and for TIR to serve as an endpoint in clinical trials to support diabetes drug approvals.

The TIRC applauds FDA's recent approval of Awiqli, a once-weekly insulin that significantly reduces the burden of daily injections and, for the first time ever in the US, contains labeling that includes CGM-derived TIR metrics. Awiqli's labeling represents a major milestone in how we measure and communicate glucose control. The TIR metrics in the labeling will provide people with diabetes and clinicians with critical information for daily disease management—an advance made possible by the inclusion of DHTs in clinical trials.

As diabetes management is increasingly reliant on DHTs such as CGMs, regulatory clarity on the utilization of CGMs in clinical trials and the use of TIR as an endpoint will make a profound impact on the ability to advance innovation in diabetes therapies and to assist people living with diabetes in choosing the most appropriate treatment options.

Responses to Request for Information

TIRC appreciates the opportunity to provide input on the questions posed in the Request for Information. See below for our comments:

What regulatory challenges do DHT manufacturers, sponsors or other interested parties face regarding the use of DHTs in clinical investigations of drugs and biological products? What opportunities are there for CDER and CBER to support and facilitate the adoption of DHTs in clinical investigations of drugs and biological products?

The 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 the 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.[13]

In addition to The diaTribe Foundation and members of the TIRC, the consensus statement was endorsed by the American Diabetes Association (ADA), Advanced Technologies & Treatments for Diabetes (ATTD) , JDRF (now Breakthrough T1D), the American Association of Clinical Endocrinologists (AACE), the 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), and the Japanese Diabetes Society (JDS) and published in *The Lancet Diabetes & Endocrinology* on December 6, 2022. This consensus statement has served as a valuable resource guiding and standardizing the use of CGM-derived metrics in clinical trials, now cited by over 700 publications including at least 45 clinical trials and the recent technical specifications document "Submitting Continuous Glucose Monitoring Data in Clinical Trials" [FDA-2017-D-6821] (Technical Specifications Document).[14] The standardized use of CGM, informed by this consensus, has facilitated detailed examination of innovative products, such as in the ONWARDS trial program which informed the recent approval of the first once-weekly insulin, and a recent phase 4 trial of a novel basal insulin-GLP-1 combination product.[15,16]

We urge FDA, in discussions with industry and researchers, to encourage the use of the approaches in the consensus statement to optimize and standardize CGM-derived glucose data collection in clinical studies.

In addition, we recommend increased coordination between FDA Centers to ensure that determinations by the Center for Devices and Radiological Health related to the accuracy of FDA-approved CGMs for life-saving insulin dosing are reflected in regulatory decision-making by the Center for Drug Evaluation and Research with regard to the use of CGMs in clinical trials. FDA should also increase transparency about how decisions are made across Centers and how the DHT Steering Committee ensures cross-Center consistency when handling DHTs.

What areas of guidance would support the use of DHTs in clinical investigations?

Clarity, consistency, and transparency to sponsors about the use of CGMs in clinical trials will facilitate progress toward approval of new therapies for individuals living with diabetes and improve the efficiency of the drug development process. The TIRC applauds the agency for the

publication of the recent Technical Specifications Document, which marks valuable progress in clarifying the agency's expectations for CGM device use in clinical trials and corresponding data submissions in support of drug or biologic applications.[14]

In 2023, FDA issued "Diabetes Mellitus: Efficacy Endpoints for Clinical Trials Investigating Antidiabetic Drugs and Biological Products: Draft Guidance" [FDA-2023-D-0625] (Draft Guidance), which would delineate the FDA's perspectives on efficacy endpoints for diabetes drugs, including the use of CGM-based metrics. To date, this Draft Guidance has not been finalized.[17]As noted in comments submitted by the TIRC, we welcomed the Draft Guidance as an important step forward.[18] In particular, we appreciated the Agency's acknowledgement of its willingness to consider including CGM-based metrics in Section 14 of the drug label as well as FDA's recognition of the advantages of CGM systems over self-monitoring of blood glucose test systems in clinical trials assessing hypoglycemia as an efficacy endpoint, among other advances. In our comments, we urged FDA to include the recommendations in the consensus statement in any final guidance as well as to provide additional specificity in several key areas to provide the necessary clarity and predictability to encourage incorporation of CGM-based metrics into drug development programs. Since, as noted above, the Agency has recently approved labeling that includes CGM-derived TIR metrics, additional specificity in the final guidance should include learnings from that approval, to allow the field as a whole to benefit from the achievement of this regulatory milestone. In addition, we would urge any final guidance to explicitly acknowledge the continued shift toward the use of TIR in clinical care and the value of CGM-derived metrics in daily disease management.

A final guidance can help to spur innovation in diabetes treatment and ensure that clinical trials deliver meaningful information on the efficacy of new therapies. We respectfully ask that FDA finalize this much-needed guidance prior to the end of calendar year 2026.

What specific DHT related topics, such as digitally derived endpoints in certain disease areas, would benefit from discussion in a public workshop?

We believe the following issues could be advanced by a public workshop:

- Considerations in advancing TIR metrics (including TIR, TAR, TBR, and potentially time in tight range 70–140 mg/dL—also called TITR) as endpoints in clinical trials of diabetes therapies
- Improving the efficiency and reducing the burden of collection of CGM metrics in clinical trials
- Opportunities for the use of CGMs in clinical trials to promote innovation, reduce trial duration and cost, and facilitate the participation of smaller biotech companies in addressing unmet needs in diabetes

Conclusion

The TIRC appreciates FDA's efforts to support the use of DHTs in drug development. We look forward to working with the agency to make progress toward our goal of further advancing the integration of CGM-derived TIR data into FDA's assessment of the safety and effectiveness of new therapies.

Respectfully,

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