1399 New York Avenue, N.W.   202-378-2023
Suite 200
Washington, D.C. 20005

April 22, 2024

<u>Via Electronic Submission</u>

MedCACpresentations@ cms.hhs.gov

RE: Medicare & Medicaid Services' (CMS) Medicare Evidence Development & Coverage Advisory Committee (MEDCAC): Devices for Self-management of Type 1 and Insulin-Dependent Type 2 Diabetes

Abbott welcomes the opportunity to comment on the Centers for Medicare & Medicaid Services' (CMS) Medicare Evidence Development & Coverage Advisory Committee (MEDCAC) meeting which will be held on Tuesday, May 21, 2024.

In business for over 135 years, Abbott is a global healthcare leader that is creating life-changing technologies that are both accessible and affordable so we can help more people in more places live healthier and better lives. Our portfolio spans the spectrum of healthcare, with leading businesses and products in diagnostics, medical devices, nutritionals and branded generic medicines. Our 114,000 colleagues serve millions of people in more than 160 countries.

As a leading medical technology and nutrition manufacturer, we seek to ensure that Medicare policies promote beneficiary access to high-quality healthcare innovations that address unmet medical needs and improve health outcomes. Consistent with the proposed agenda, we therefore would like to offer our comments on the following topics:

- Surrogate markers/endpoints
- Health Outcomes
- Quality of life
- Device-related safety

We would also like to include the below key considerations which are relevant across the above topics:

- Continuous Glucose Monitor Accuracy
- Technological Innovation and Cybersecurity

1. Surrogate Endpoints

The impact of continuous glucose monitoring on glycemic endpoints has been extensively studied.

We agree with the expert's opinion that glycemic outcomes, A1C and percentage of time in acceptable range (TIR) should be primary endpoints for most studies. However, the choice of outcomes will depend on the specific research questions being asked. For example, if the primary aim is to study the impact of a technology on hypoglycemia, number of hypoglycemic episodes or percentage of time in hypoglycemia also called time below range (TBR) would be most appropriate as the primary outcome. Additionally, we agree with the expert's opinion that it is important to measure certain outcomes by time of day (e.g. time in hypoglycemia [<70 mg/dL]) as this can give us important insights into glycemic management overnight while many are asleep. Both IMPACT and REPLACE provided overall, daytime, and nighttime metrics on time in acceptable glucose range, time in hypoglycemia, and time in hyperglycemia.[1,2]

The table below summarizes the surrogate endpoints along with the minimally-clinically important difference (MCID) as appropriate mentioned in the MEDCAC notices and the clinical expert opinion.[3,4]

Given the pace of technological innovation, running long-term studies may not be appropriate.[5] Study durations of 3 – 6 months should be sufficient to assess impact of the technology on glycemic outcomes. Longer-term follow up has been studied through an extension of the primary study (e.g. REPLACE and MOBILE)[6,7] and through real-world analyses (e.g. COMISAIR and T1D Exchange).[8,9]

Surrogate Marker	Abbott Opinion	Proposed MCID
Impact on A1C	We agree that Impact on A1C is an important outcome. Additionally, achievement of A1C targets such as <7%, <8% and <9%, which align with goal for most people with diabetes from ADA[10] and the NCQA[11] targets for measuring care delivery quality. Not all patients will have an A1C goal of <7%; so, this target may not be appropriate.	While 0.5% has been proposed by CMS, 0.3% has been used as MCID in landmark studies. [12,13]
Percentage of time in acceptable glucose range (70-180 mg/dL)	This is an important outcome, which has been associated with long-term complications like A1C.[14] An advantage of this measure is that it is more sensitive to recent changes in therapy as this measure uses the past 2 weeks of glucose data versus being a measure of average glucose over 3 months. Additionally, while reduction in A1C only captures reduction in	Per the International Consensus on Time in Range by Battelino[14] et al, a 5% change in TIR is considered MCID.

	hyperglycemia, time in acceptable range can capture reductions in hypoglycemia as well.	
Number of hypoglycemic episodes (<70 mg/dL), especially episodes of Level 2 hypoglycemia (<54 mg/dL)	This is an important endpoint and should be considered at least as secondary depending on the research questions.	We are not aware of the MCID for this glycemic measure. In general, targets for hypoglycemia will depend on the general health of the individual.[15]
Percentage of time in hypoglycemia (<70 mg/dL)	This is an important endpoint and should be considered at least as secondary depending on the research questions.	We are not aware of the MCID for this glycemic measure. In general, targets for hypoglycemia will depend on the general health of the individual.[15]
Percentage of time in hypoglycemia (<54 mg/dL)	This is an important endpoint and should be considered at least as secondary depending on the research questions.	We are not aware of the MCID for this glycemic measure. In general, time in level 2 hypoglycemia (<54 mg/dL) should be minimized.[15]
Percentage of time in hyperglycemia (>180 mg/dL)	This is an important endpoint and should be considered at least as secondary depending on the research questions.	While the International Consensus[15] did not state an MCID for this outcome, we would propose 5% as MCID to correspond with the Percentage of time in acceptable glucose range (70-180 mg/dL) endpoint.

2. Health Outcomes

Overall, we agree with the measurements proposed in the MEDCAC materials. Assessment of impact can be done using real-world types of studies through registries (prospective or retrospective) or retrospective research of other data (e.g. administrative payor claims data). The reason to prefer this modality, is that many of the health outcomes, such as diabetes-related emergency department (ED) visits may not occur frequently and would require long-term follow up or large sample sizes. Given the pace of change in diabetes technology, it will not be possible to keep all participants on the same device in long-term, large-scale studies.[5] Rather, real-world studies can allow us to capture this type of data with larger datasets (registries, payor administrative claims, health system records) over periods of time. A big advantage is that the data is in uncontrolled settings where participants are not compensated

for participation and obtain devices, medical care, and potentially medicines for free, representing a real-world use of the product. We can follow larger groups (>1000) over 6 months or longer.

We have performed several studies using claims data that have shown associations between acquisition of a FreeStyle Libre system and reductions in ED visits and inpatient hospitalizations.[16,17,18,19,20] There have also been several European registries, which have shown reductions in severe hypoglycemia, emergency department visits, hospitalizations, and restoration of hypoglycemia awareness in people who use FreeStyle Libre. [21,22,23]

The table below summarizes the health outcomes listed by the MEDCAC. We would recommend that the panel consider all-cause ED visits and hospitalizations.

Health Outcome	Abbott Opinion	MCID
Restoration of hypoglycemia awareness	This has been measured in registries and is an important endpoint depending on the population being studied. This may be an important	We are not aware of an MCID.
Cognitive function changes	It would be helpful to understand which instrument(s) that CMS is considering as each focuses on different aspects of cognitive function.[24]	MCID would depend on the exact instrument selected.
Diabetes-related emergency department visits	This is an important endpoint. Consider looking at all-cause events as well as the risk for some events may increase with high glucose (e.g. infections).[25]	We are not aware of an MCID and rather would look at the absolute and relative changes in rates.
Diabetes-related hospitalizations	This is an important endpoint. Consider looking at all-cause events as well as the risk for some events may increase with high glucose (e.g. infections).[25]	We are not aware of an MCID and rather would look at the absolute and relative changes in rates.
Complications of diabetes	This is an important endpoint.	We are not aware of an MCID for each outcome rather would look at the absolute and relative changes in rates.

3. Quality of Life

Diabetes is a chronic condition that can negatively impacts a patient's Health Related Quality of life (HRQoL) and results in long-term micro- and macro- complications. Therefore, the use of HRQoL is encouraged. HRQoL is an important measure of patients' assessment on health status including functioning and well-being in physical, mental, and social domains of life. Functioning includes physical functioning, such as self-care (e.g., bathing, dressing, walking); role functioning, such as work-related activities (whether paid or not) like housework and career; and social functioning, the extent to which one is able to interact with family and friends.[26]

It is important to select the diabetes-specific QoL instrument based on the domain of interest to be evaluated in relation to the research question and the patient population; given that HRQoL results are influenced by multiple patient and disease factors, particularly age, gender, and the presence and severity of disease complications and comorbid conditions.[27]

Each of the five HRQoL instruments assesses different domains from physical functional, mental, social domains of life and diabetes distress (Table 1).

When assessing the impact of self-management devices on patient-related QoL, it is important to consider that these devices will impact patient QoL in multiple ways. For example, continuous glucose monitoring systems are known to increase treatment satisfaction[28] and decrease fear of hypoglycemia.[i] The diabetes scales listed by the MEDCAC include those that focus on specific components, such as hypoglycemia fear (Hypoglycemia Fear Survey), patient treatment satisfaction (Diabetes Treatment Satisfaction Questionnaire [DTSQ]), diabetes-related distress (Diabetes Distress Scale), or more general components of diabetes-related emotional well-being. To fully assess impacts of self-management devices on quality of life, we recommend a study strategy that includes a psychological well-being measure such as the Diabetes Distress Scale in combination with treatment satisfaction measures such as the DTSQ to assess both patient perceived well-being (both positive, related to reduced burden or negative in the case of alarm fatigue) and their perception of their new treatment regimen. Both scales may produce meaningful results over a time period of at least six months, assuming sufficient patient numbers.[3,28,29] In terms of scales to not recommend, we note that there is some evidence that Diabetes Impact Measurement Scales (DIMS) has lower evidence of reliability in contrast to other scales that are being investigated by the MEDCAC.[7]

It is important to note that CGM as a tool may not show a difference in all of the domains in some of the HRQoL instruments such as DTSQ. Therefore, the HRQoL tool should be selected based on the research question to ensure that the domain will be appropriately evaluated. For example, the Fear of Hypoglycemia Survey could be suitable only when hypoglycemia events is one of the endpoints.

5

Table 1: HRQoL measures[3,31]

Name of Instrument Used	Title/Author/Year of Publication	Country	Domains of HRQOL Used	Strength and Weakness
Audit of Diabetes-Dependent QOL measure (ADDQOL)	The development of an individualized questionnaire measure of perceived impact of diabetes on quality of life.	United Kingdom	It has 13 Domains: Employment/Career Opportunities, Social Life, Family Relationships, Friendships, Sex, Life, Sporting, Holiday or Leisure Opportunities; The Ease with which I can Travel; Worries about my Future; Worries about the Future of my Family and Close Friends; Motivation to Achieve Things; Things I could do Physically and the Extent to which People would Fuss too much about Me	Diabetes-specific ADDQOL will be more sensitive to change and responsive to subgroup differences than a generic instrument such as the SF-36.
Diabetes Impact Measurement Scales (DIMS)	Measurement of Health Status in diabetic patients	United Kingdom	The items were grouped into four subscales: General Well-Being, Physical Symptoms, Social Functioning, and Diabetes-related Morale.	The Diabetes Impact Management Scales is an easily administered questionnaire with internal consistency and test–retest reliability. The questionnaire is simple and straightforward, comprising of items that are easily to understood; it covers a broad range of content relevant to diabetes impact
Problem Areas in Diabetes Scale (PAID)	Assessment of diabetes-related distress	United States of America	Not mentioned	The PAID is a brief and easy to administer instrument, which may serve as a clinical tool useful in the identification of patients who are experiencing high levels of diabetes-related distress.

Diabetes Distress Scale: 17-item scale that captures four critical dimensions of. distress: emotional burden, regimen distress, interpersonal distress and physician distress. The Type 2 Diabetes Distress Assessment Scale (T2-DDAS) is available in English and Spanish on this website, was developed in 2021 and its standardization sample included insulin-using and non-insulin-using adults with type 2 diabetes. It is the only DD assessment scale that was developed, validated and standardized specifically for T2D adults. Also, the T2-DDAS is unique in that it conforms more directly with the underlying theoretical premise of DD as a core emotional experience than either of the other two T2D measures currently available.

Diabetes Treatment Satisfaction Questionnaire: DTSQ comprises 8 questions, of which 6 (questions 1 and 4-8) are used to assess different domains of treatment satisfaction: (a) overall satisfaction, (b) convenience, (c) flexibility, (d) understanding of diabetes, (e) willingness to recommend current treatment to others, and (f) willingness to continue the current treatment, each of which is scored on a 7-point Likert scale from 0 (very dissatisfied) to 6 (very satisfied). Thus, the DTSQ treatment satisfaction score can range from 0 to 36 and represents the treatment satisfaction of the patient with their diabetes treatment. Two additional items, perceived hyperglycemia, and perceived hypoglycemia, are assessed through 2 questions (questions 2 and 3) on the frequency of hyperglycemia and hypoglycemia, using a 7-point scale from 0 (none of the time) to 6 (most of the time).

Hypoglycemia Fear Survey (HFS): The HFS is a validated instrument commonly used to measure fear of hypoglycemia in individuals with diabetes and their relatives. The HFS is composed of two subscales: behavioral[33] (i.e., actions carried out to avoid hypoglycemia) and worry (i.e., anxiety provoking) subscales. Higher scores indicate higher fears of hypoglycemia.[33] Elevated fear of hypoglycemia has been associated with suboptimal glucose control and higher risk of complications, and lower quality of life.[33]

4. Device-Related Safety

Safety endpoints are captured and reported as part of Good Clinical Practice. We would propose continuing to capture these endpoints as part of the usual practice. We note that continuous glucose monitoring systems have been associated with reduced diabetes-related hospitalizations, an important safety measure.[17]

It is also important to consider device accuracy in discussions of device-related safety. The MEDCAC's Clinical Expert had commented on accuracy of CGM devices. We agree with the opinion that accuracy is an important factor, especially at the low end of the glucose range. Accuracy in the hypoglycemic end is important; however, it is not clear what alternatives the expert is mentioning. For blood glucose monitoring, accuracy at the low end is measured as an absolute (e.g. 5 mg/dL difference at 50 mg/dL), instead of relative (e.g. 10% difference) level of

discrepancy. Laboratory calibrated glucose measurement similarly measure the absolute level of discrepancy at the lower end of the glucose measurement range (e.g. <70 mg /dL).

We propose that continuous glucose monitoring devices should report whether they meet the special controls related to accuracy that the Food and Drug Administration (FDA) set with the iCGM category requirements.[36] See table in the appendix. Especially when informing insulin dosing decisions or when paired with insulin pumps or closed-loop systems, CGMs must meet and maintain consistent, rigorous accuracy levels to mitigate the risk of diabetes-related complications and adverse events.

5. Technological Innovation and Cybersecurity

One additional area that was not included in the MEDCAC notice pertains to technological innovation and cybersecurity. These are important as they ensure that the CGM devices and other diabetes technologies are meeting future needs for people with diabetes. The special controls by FDA for iCGM requirements includes requirements for interoperability with other devices (e.g. automated insulin delivery devices) and cybersecurity.[36]

Cybersecurity and privacy continue to grow in importance especially as threats continue to grow in volume and skill.[37] Diabetes technologies and other medical devices must be designed to protect data and functionality to reduce the risk of attacks on confidentiality, integrity, and availability (CIA). These attacks can impact patient safety if critical services are interrupted or corrupted (i.e. leading or contributing to an incorrect treatment). As such, FDA has issued extensive guidance for cybersecurity including guidance on implementing a secure product development framework. Abbott Diabetes Care includes cybersecurity in its product design and has implemented the secure product development framework based on the HSCC Joint Security Plan and maintains security certifications as required by FDA and other regulators as well as payors around the globe.

* * * * *

We appreciate your consideration of our comments. Please feel free to contact me if you have any questions or if you need additional information.

Yours Truly,

DocuSigned by:

Mahmood Kazemi

5D0F5275EA99487...

Mahmood Kazemi, MD
DVP Medical/Scientific Affairs and Chief Medical Officer
Abbott Diabetes Care

References

1. Bolinder J, Antuna R, Geelhoed-Duijvestijn P, et al. Novel glucose-sensing technology and hypoglycaemia in type 1 diabetes: a multicenter, non-masked, randomized controlled trial. *Lancet*. 2016;388(10057):2254–2263. doi:10.1016/S0140-6736(16)31535-5

2. Haak T, Hanaire H, Ajjan R, et al. Flash glucose-sensing technology as a replacement for blood glucose monitoring for the management of insulin-treated type 2 diabetes: a multicenter, open-label randomized controlled trial. *Diabetes Ther*. 2017;8(1):55–73. doi:10.1007/s13300-016-0223-6

3. https://www.cms.gov/medicare-coverage-database/view/medcac-meeting.aspx?medcacid=81. Accessed 9 April 2024.

4. https://www.cms.gov/medicare-coverage-database/view/medcac-meeting.aspx?medcacid=80. Accessed 9 April 2024.

5. Rickson M, Wright EE, Bindal A, Ghonim L. Advancements in Diabetes Technology Are Outpacing the Evidence. *DTT* 2023;25(supplement 3):S35-S41. doi: 10.1089/dia.2023.0145

6. Haak T, Hanaire H, Ajjan R, et al. Use of flash glucose-sensing technology for 12 months as a replacement for blood glucose monitoring in insulin-treated type 2 diabetes. Diabetes Ther. 2017;8(3):573–586. doi:10.1007/s13300-017-0255-6

7. Aleppo G, Beck RW, Baily R, et al. The Effect of Discontinuing Continuous Glucose Monitoring in Adults with Type 2 Diabetes Treated with Basal Insulin. *Diabetes Care* 2021;44(12):2729-2737. Doi:10.2337/dc21-1304

8. Soupal J, Petruzelkova L, Flekac M, et al. Comparison of Different Treatment Modalities for Type 1 Diabetes, Including Sensor-Augmented Insulin Regimens, in 52 Weeks of Follow-Up: A COMISAIR Study. *DTT* 2016;18(9):532-538. doi:10.1089/dia.2016.0171

9. Foster NC, Beck RW, Miller KM, et al. State of Type 1 Diabetes Management and Outcomes from the T1D Exchange in 2016-2918. *DTT* 2019;21(2):66-72. doi:10.1089/dia.2018.0384

10. American Diabetes Association Professional Practice Committee. 6. Glycemic Goals and Hypoglycemia: Standards of Care in Diabetes–2024. *Diabetes Care* 2024;47(Supp 1):S111-S125. doi: 10.2337/dc24-S006

11. https://www.ncqa.org/hedis/measures/hemoglobin-a1c-control-for-patients-with-diabetes. Accessed 10 April 2024.

12. Lind M, Odén A, Fahlén M, Eliasson B. A systematic review of HbA1c variables used in the study of diabetic complications. *Diabetes Metab Syndr.* 2008;2(4):282-293. doi:10.1016/j.dsx.2008.04.006

13. Lind M, Polonsky, W, Hirsch IB, et al. Continuous Glucose Monitoring vs Conventional Therapy for Glycemic Control in Adults with Type 1 Diabetes Treated with Multiple Daily Injections, The GOLD Randomized Clinical Trial. JAMA 2017;317:379-387. doi:10.1001/jama.2016.19976

14. Shah VN, Kanapka LG, Akturk HK, et al. Time in Range Is Associated with Incident Diabetic Retinopathy in Adults with Type 1 Diabetes: A Longitudinal Study. *DTT* 2024;26(4):246-251. doi: 10.1089/dia.2023.0486

15. Battelino T, Danne T, Bergenstal RM, et al. Clinical targets for continuous glucose monitoring data interpretation: recommendations from the international consensus on time in range. *Diabetes Care* 2019;pii:dc190028, [epub ahead of print]. doi:10.2337/dci19-0028

16. Kerr M, Roberts G, Souto D et al. *DTT* 2020;22(Supp 1):Abstract 334. doi: 10.1089/dia.2020.2525.abstracts

17. Bergenstal RM, Kerr MSD, Roberts GJ, et al. Flash CGM Is Associated With Reduced Diabetes Events and Hospitalizations in Insulin-Treated Type 2 Diabetes. *J Endo Society* 2021;5(4):1-9. doi:10.1210/jendso/bvab013

18. Roussel R, Riveline JP, Vicaut E, de Pouvourville G, Detournay B et al. (2021) Important Drop in Rate of Acute Diabetes Complications in People With Type 1 or Type 2 Diabetes After Initiation of Flash Glucose Monitoring in France: The RELIEF Study. Diabetes Care 44 (6): 1368-1376.

19. Hirsch I, Burugapalli BS, Brandner L et al. Impact of Continuous Glucose Monitoringon Healthcare Resource Utilization Among Medicaid Beneficiaries with Type 2diabetes Treated with Basal Insulin. *DTT* 2024;26(Supp 2):Abstract #633. doi: 10.1089/dia.2024.2525.abstracts

20. Hirsch I, Burugapalli BS, Brandner L et al. Impact of Continuous Glucose Monitoringon Healthcare Resource Utilization Among Medicaid Beneficiaries with Type 2diabetes Treated with Multiple Daily Injection Therapy. *DTT* 2024;26(Supp 2):Abstract #789. doi:10.1089/dia.2024.2525.abstracts

21. Deshmukh H, Wilmot EG, Gregory R, et al. Effect of Flash Glucose Monitoring on Glycemic Control, Hypoglycemia, Diabetes-Related Distress, and Resource Utilization in the Association of British Clinical Diabetologists (ABCD) Nationwide Audit. *Diabetes Care* 2020;43(9):2153-2160. doi:10.2337/dc20-0738

22. Fokkert M, van Dijk P, Edens M, et al. Improved well-being and decreased disease burden after 1-year use of flash glucose monitoring (FLARE-NL4). BMJ Open Diabetes Res Care. 2019;7(1):e000809. doi: 10.1136/bmjdrc-2019-000809

23. Charleer S, De Block C, Van Huffel L, et al. Quality of Life and Glucose Control After 1 Year of Nationwide Reimbursement of Intermittently Scanned Continuous Glucose Monitoring in Adults Living With Type 1 Diabetes (FUTURE): A Prospective Observational Real-World Cohort Study. Diabetes Care. 2020;43(2):389-97. doi: 10.2337/dc19-1610

24. Kelso IG, Tadi P. Cognitive Assessment. StatPearls. https://www.ncbi.nlm.nih.gov/books/NBK556049. Accessed 9 April 2024.

25. Chávez-Reyes J, Escárcega-González CE, Chavira-Suárez E, et al. Susceptibility for Some Infectious Diseases in Patients With Diabetes: The Key Role of Glycemia. *Front Public Health* 2021; epub Feb 16;9:559595. doi: 10.3389/fpubh.2021.559595

26. Kaplan, R. M. and R. D. Hays (2022). "Health-Related Quality of Life Measurement in Public Health." Annual Review of Public Health 43(Volume 43, 2022): 355-373.

27. Luscombe, F. A. (2000). "Health-Related Quality of Life Measurement in Type 2 Diabetes." Value in Health 3: S15-S28.

28. Yaron M, Roitman E, Aharon-Hananel G, Landau Z, Ganz T et al. (2019) Effect of Flash Glucose Monitoring Technology on Glycemic Control and Treatment Satisfaction in Patients With Type 2 Diabetes. Diabetes Care 42 (7): 1178-1184.

29. Talbo MK, Katz A, Hill L, Peters TM, Yale JF et al. (2023) Effect of diabetes technologies on the fear of hypoglycaemia among people living with type 1 diabetes: a systematic review and meta-analysis. EClinicalMedicine 62 102119.

30. Deshmukh H, Wilmot EG, Gregory R, Barnes D, Narendran P et al. (2021) Predictors of diabetes-related distress before and after FreeStyle Libre-1 use: Lessons from the Association of British Clinical Diabetologists nationwide study. Diabetes Obes Metab 23 (10): 2261-2268.

31. Oluchi SE, Manaf RA, Ismail S, Kadir Shahar H, Mahmud A, Udeani TK. Health Related Quality of Life Measurements for Diabetes: A Systematic Review. Int J Environ Res Public Health. 2021 Sep 1;18(17):9245. doi: 10.3390/ijerph18179245. PMID: 34501838; PMCID: PMC8431362.

32. Poovazhagi V. Risk factors for mortality in children with diabetic keto acidosis from developing countries. World J Diabetes. 2014;5(6):932-8.

33. Cox DJ, Irvine A, Gonder-Frederick L, Nowacek G, Butterfield J. Fear of hypoglycemia: quantification, validation, and utilization. Diabetes Care. 1987;10(5):617-21.

34. Wild D, von Maltzahn R, Brohan E, Christensen T, Clauson P, Gonder-Frederick L. A critical review of the literature on fear of hypoglycemia in diabetes: Implications for diabetes management and patient education. Patient education and counseling. 2007;68:10-5.

35. Clinical investigation of medical devices for human subjects — Good clinical practice (ISO 14155:2020). https://www.iso.org/standard/71690.html. Accessed 11 April 2024.

36. Sec 862.1355 Integrated Continuous Glucose Monitoring System. https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/cfrsearch.cfm?fr=862.1355. Accessed 16 April 2024.

37. Select Updates for the Premarket Cybersecurity Guidance: Section 524B of the FD&C Act (Published 13 March 2024). https://www.fda.gov/media/176944/download. Accessed 18 April 2024.

Appendix

iCGM Performance Requirements (21CFR862.1355)

(A) For all iCGM measurements less than 70 mg/dL, the percentage of iCGM measurements within +/-15 mg/dL of the corresponding blood glucose value must be calculated, and the lower one-sided 95% confidence bound must exceed 85%.

(B) For all iCGM measurements from 70-180 mg/dL, the percentage of iCGM measurements within +/- 15% of the corresponding blood glucose value must be calculated, and the lower one-sided 95% confidence bound must exceed 70%.

(C) For all iCGM measurements greater than 180 mg/dL, the percentage of iCGM measurements within +/- 15% of the corresponding blood glucose value must be calculated, and the lower one-sided 95% confidence bound must exceed 80%.

(D) For all iCGM measurements less than 70 mg/dL, the percentage of iCGM measurements within +/-40 mg/dL of the corresponding blood glucose value must be calculated, and the lower one-sided 95% confidence bound must exceed 98%.

(E) For all iCGM measurements from 70-180 mg/dL, the percentage of iCGM measurements within +/- 40% of the corresponding blood glucose value must be calculated, and the lower one-sided 95% confidence bound must exceed 99%.

(F) For all iCGM measurements greater than180 mg/dL, the percentage of iCGM measurements within +/- 40% of the corresponding blood glucose value must be calculated, and the lower one-sided 95% confidence bound must exceed 99%.

(G) Throughout the device measuring range, the percentage of iCGM measurements within +/- 20 % of the corresponding blood glucose value must be calculated, and the lower one-sided 95% confidence bound must exceed 87%.

(H) When iCGM values are less than 70 mg/dL, no corresponding blood glucose value shall read above 180 mg/dL.

(I) When iCGM values are greater than 180 mg/dL, no corresponding blood glucose value shall read less than 70 mg/dL.

(J) There shall be no more than 1% of iCGM measurements that indicate a positive glucose rate of change greater than 1 mg/dL/min when the corresponding true negative glucose rate of change is less than -2 mg/dL/min as determined by the corresponding blood glucose measurements.

(K) There shall be no more than 1% of iCGM measurements that indicate a negative glucose rate of change less than -1 mg/dL/min when the corresponding true positive glucose rate of change is greater than 2 mg/dL/min as determined by the corresponding blood glucose measurements.