October 3, 2025

Tosoh Bioscience, Inc.
Corike Nuibe
Sr. Regulatory Affairs Specialist
3600 Gantz Road
Grove City, Ohio 43123

Re: K250073
Trade/Device Name: Tosoh Automated Glycohemoglobin Analyzer HLC-723GR01
Regulation Number: 21 CFR 862.1373
Regulation Name: Hemoglobin A1c Test System
Regulatory Class: Class II
Product Code: PDJ, LCP
Dated: December 30, 2024
Received: January 10, 2025

Dear Corike Nuibe:

We have reviewed your section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (the Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database available at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Additional information about changes that may require a new premarket notification are provided in the FDA guidance documents entitled "Deciding When to Submit a 510(k) for a Change to an Existing Device" (https://www.fda.gov/media/99812/download) and "Deciding When to Submit a 510(k) for a Software Change to an Existing Device" (https://www.fda.gov/media/99785/download).

Your device is also subject to, among other requirements, the Quality System (QS) regulation (21 CFR Part 820), which includes, but is not limited to, 21 CFR 820.30, Design controls; 21 CFR 820.90, Nonconforming product; and 21 CFR 820.100, Corrective and preventive action. Please note that regardless of whether a change requires premarket review, the QS regulation requires device manufacturers to review and approve changes to device design and production (21 CFR 820.30 and 21 CFR 820.70) and document changes and approvals in the device master record (21 CFR 820.181).

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801 and Part 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR Part 803) for devices or postmarketing safety reporting (21 CFR Part 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR Part 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR Parts 1000-1050.

All medical devices, including Class I and unclassified devices and combination product device constituent parts are required to be in compliance with the final Unique Device Identification System rule ("UDI Rule"). The UDI Rule requires, among other things, that a device bear a unique device identifier (UDI) on its label and package (21 CFR 801.20(a)) unless an exception or alternative applies (21 CFR 801.20(b)) and that the dates on the device label be formatted in accordance with 21 CFR 801.18. The UDI Rule (21 CFR 830.300(a) and 830.320(b)) also requires that certain information be submitted to the Global Unique Device Identification Database (GUDID) (21 CFR Part 830 Subpart E). For additional information on these requirements, please see the UDI System webpage at https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/unique-device-identification-system-udi-system.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-

assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Leslie Landree -S
2025.10.03 18:14:57 -04'00'

for Joshua M. Balsam, Ph.D.
Branch Chief
Division of Chemistry and
Toxicology Devices
OHT7: Office of In Vitro Diagnostics
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 07/31/2026
See PRA Statement below.

510(k) Number *(if known)*
K250073

Device Name
Tosoh Automated Glycohemoglobin Analyzer HLC-723GR01

Indications for Use *(Describe)*

The Tosoh Automated Glycohemoglobin Analyzer HLC-723GR01 is intended for in vitro diagnostic use for the quantitative measurement of % hemoglobin A1c (HbA1c) (DCCT/NGSP) and mmol/mol hemoglobin A1c (IFCC) in human venous whole blood and hemolysate specimens using ion-exchange high performance liquid chromatography (HPLC).

This test is to be used as an aid in diagnosis of diabetes and identifying patients who may be at risk for developing diabetes, and for monitoring of long-term blood glucose control in individuals with diabetes mellitus.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

This section applies only to requirements of the Paperwork Reduction Act of 1995.

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510k Summary (Summary of Safety and Effectiveness)

This 510(k) Summary is being submitted in accordance with requirements of Title 21 CFR 862.1373.

The assigned 510(k) Number is: K250073
Date of Preparation: October 1st, 2025

1. Applicant Information

Name: Tosoh Bioscience, Inc.
Address: 3600 Gantz Road
Grove City
OH 43123
USA
Contact: Corike Nuibe (Sr. Regulatory Affairs Specialist)
Email: corike.nuibe@tosoh.com
Phone: (385) 279-8114

2. Device Name/Trade Name

Device Trade Name: Tosoh Automated Glycohemoglobin Analyzer HLC-723GR01
Classification Name: Hemoglobin A1c test system
Product Code: PDJ, LCP
Regulation Number: 21 CFR Part 862.1373 and 21 CFR Part 864.7470
Regulation Name: Hemoglobin A1c test system, Glycosylated hemoglobin assay
Device Class: Class II
510(k) Review Panel: Clinical Chemistry
Regulation Medical Specialty: Clinical Chemistry

3. Predicate Device

Trade name: Tosoh Automated Glycohemoglobin Analyzer HLC-723G8
510(k) submitter/holder: Tosoh Bioscience, Inc.
510(k) Numbers: K200904

4. Description of the Device

The Tosoh Automated Glycohemoglobin Analyzer HLC-723GR01 is intended for in vitro diagnostic use for the quantitative measurement of % hemoglobin A1c (HbA1c)

(DCCT/NGSP) and mmol/mol hemoglobin A1c (IFCC) in human venous whole blood and hemolysate specimens using ion-exchange high performance liquid chromatography (HPLC). The Tosoh Automated Glycohemoglobin Analyzer HLC-723GR01 analyzer is to be used in the clinical laboratory setting. The analyzer hemolyzes and dilutes whole blood specimens and subsequently injects the diluted and hemolyzed sample into the injection valve and onto the TSKgel GR01 HbA1c Column. Manually hemolyzed and prediluted samples can be loaded in sample cups directly for analysis on the analyzer.
Separation of hemoglobin fractions is achieved by using differences in ionic interactions between the cation exchange group on the column resin surface and the hemoglobin components by a step gradient elution with three elution buffers of different ionic strengths. Changes in light absorbance at 415nm caused by hemoglobin fractions eluting from the column are monitored. The GR01 software has chromatographic peak retention time windows for the six expected hemoglobin fractions, A1a, A1b, HbF, LA1c+, SA1c, and A0. In addition, the software has retention time windows for the presumptive identification of the common hemoglobin variants, D, S, C, and E. An analysis requires 50 seconds per sample to complete. A printout of the results includes the sample ID, date, percentage, and retention time of each hemoglobin fraction, the SA1c percentage along with a chromatogram of the elution pattern of the hemoglobin fractions. The analyzer is equipped with external USB ports. These can be used to store assay results, to update and backup program versions, to attach an external device, for example an external printer or an optional handheld barcode scanner, and for software installation or backup of data. The last 150,000 assay results are automatically saved to the analyzer's internal memory and can be retrieved as list data in .CSV format and chromatograms in .PDF format.

The Tosoh Automated Glycohemoglobin Analyzer HLC-723GR01 system consists of the following components.

- GR01 HbA1c Elution Buffer No. 1, No. 2, No. 3
- TSKgel® GR01 HbA1c Column
- Hemoglobin A1c Controls Levels 1 and 2
  - 21 CFR 862.1660, Product Code JJX
- Hemoglobin A1c Calibrator Set
  - 21 CFR 862.1150, Product Code JIT
- Hemolysis and Wash Solution (L) and (LL)
  - 21 CFR 864.8540, Product Code GGK

5. Indications for Use

The Tosoh Automated Glycohemoglobin Analyzer HLC-723GR01 is intended for in vitro diagnostic use for the quantitative measurement of % hemoglobin A1c (HbA1c) (DCCT/NGSP) and mmol/mol hemoglobin A1c (IFCC) in human venous whole blood and hemolysate specimens using ion-exchange high performance liquid chromatography (HPLC).

This test is to be used as an aid in diagnosis of diabetes and identifying patients who may be at risk for developing diabetes, and for monitoring of long-term blood glucose control in individuals with diabetes mellitus.

6. Substantial Equivalence Information

The Tosoh Automated Glycohemoglobin Analyzer HLC-723GR01 is substantially equivalent to the claimed predicate device; the Tosoh Automated Glycohemoglobin Analyzer HLC-723G8 (k200904), based on comparisons of the intended use and technological characteristics.

Table 1. Comparison Table of Subject Device to Predicate Device

Feature	Candidate Device: Tosoh Automated Glycohemoglobin Analyzer HLC-723GR01	Predicate Device: Tosoh Automated Glycohemoglobin Analyzer HLC-723G8, v5.24F
Intended Use	The Tosoh Automated Glycohemoglobin Analyzer HLC-723GR01 is intended for in vitro diagnostic use for the quantitative measurement of % hemoglobin A1c (HbA1c) (DCCT/NGSP) and mmol/mol hemoglobin A1c (IFCC) in human venous whole blood and hemolysate specimens using ion-exchange high performance liquid chromatography (HPLC). This test is to be used as an aid in diagnosis of diabetes and identifying patients who may be at risk for developing diabetes, and for monitoring of long-term blood glucose control in individuals with diabetes mellitus.	Tosoh Automated Glycohemoglobin Analyzer HLC-723G8 is intended for in vitro diagnostic use for the measurement of % hemoglobin A1c (HbA1c) (DCCT/NGSP) and mmol/mol hemoglobin A1c (IFCC) in venous whole blood specimens using ion-exchange high-performance liquid chromatography (HPLC). This test is to be used as an aid in diagnosis of diabetes and identifying patients who may be at risk for developing diabetes, and for monitoring of long- term blood glucose control in individuals with diabetes mellitus.

Feature	Candidate Device: Tosoh Automated Glycohemoglobin Analyzer HLC-723GR01	Predicate Device: Tosoh Automated Glycohemoglobin Analyzer HLC-723G8, v5.24F
Assay Method	Ion-Exchange HPLC	Same
Detection Method	Analyte passes through a flow cell where changes in absorbance are measured at 415nm and recorded as a digital chromatogram. An additional filter at 500nm corrects for background absorbance.	Same
Applications/Test Time	50 Seconds	1.6 Minutes
Instrument Platform	Automated Glycohemoglobin Analyzer HLC-723GR01	Automated Glycohemoglobin Analyzer HLC-723G8
Sample Matrix	• Human Venous Whole Blood • Hemolysate	Human Venous Whole Blood
Sample Anticoagulants	K2 EDTA, K3 EDTA	Same
Traceability/ Standardization	Traceable to the Diabetes Control and Complications Trial (DCCT) reference method and IFCC. Certified via the National Glycohemoglobin Standardization Program (NGSP)	Same
Measuring Range	3.9 – 16.9 %HbA1c 19 – 161 mmol/mol HbA1c	4.0 – 16.9 %HbA1c
Hemoglobin Variant Interference	Accurate and reportable HbA1c% results in the presence of HbAC (38.8%), HbAD (42.7%), HbAE (31.4%), HbAS (42.7%). Non-clinically significant interference defined as ≤ ± 7% relative difference in the results from a comparative method at 6.5% or 8.0% HbA1c.	Accurate and reportable HbA1c% results in the presence of HbAC (39%), HbAD (39.5%), HbAE (26.0%), HbAS (39%). Non-clinically significant interference defined as ≤ ± 6% relative difference in the results from a comparative method at 6.5% or 8.0% HbA1c.
	Accurate HbA1c% in the presence of HbA2 up to 6.7%. Non-clinically significant interference is defined as ≤ ± 7% relative difference in the results from a comparative method at 6.5% or 8.0% HbA1c.	Accurate HbA1c% in the presence of HbA2 up to 5.5%. Non-clinically significant interference is defined as ≤ ± 6% relative difference in the results from a comparative method at 6.5% or 8.0% HbA1c.
	Accurate HbA1c% in the presence of HbF up to 32.2%.	Accurate HbA1c% in the presence of HbF up to 25%. Non-clinically significant interference is defined as ≤ ± 6% relative difference in the results from a comparative method at 6.5% or 8.0% HbA1c.

Both the subject device (Tosoh Automated Glycohemoglobin Analyzer HLC-723GR01 and the Predicate device (Tosoh Automated Glycohemoglobin Analyzer HLC-723G8, v5.24F) have the same intended use, principle of operation, intended user, use environment and similar

technological characteristics. The analytical performance data does not raise any new questions of safety or effectiveness for the subject device. Therefore, the subject device is substantially equivalent to the predicate device.

7. Summary of Non-Clinical Performance Testing

a. Precision/Reproducibility

Precision of the Tosoh Automated Glycohemoglobin Analyzer HLC-723GR01 (GR01 analyzer) was evaluated based on CLSI EP05-A3: Evaluation of Precision of Quantitative Measurement Procedures, 3rd Edition. Repeatability (within-run precision) and reproducibility (inter-run precision) of the GR01 analyzer was determined measuring %HbA1c in both K2 EDTA venous whole blood samples and corresponding hemolysates. HbA1c concentrations of approximately 5.0% (31 mmol/mol), 6.5% (48 mmol/mol), 8.0% (64 mmol/mol), and 12.0% (108 mmol/mol) were tested over two (2) runs per day, with two (2) replicates per run, at three (3) sites/instruments, with three (3) reagent lots, for 20 non-consecutive days per reagent lot, for a total of 60 days on three (3) GR01 analyzers. Following are the results shown for each sample type (whole blood and hemolysate), per analyzer and for the three GR01 analyzers combined, for NGSP units (%). A summary for the Precision data is shown for IFCC units (mmol/mol) for both Whole Blood and Hemolysate samples.

Results of Precision Study for Whole Blood Samples (NGSP %)

Table 2. Summary of Precision Analysis for all Analyzers Combined (Whole Blood/NGSP (%))

%HbA1c Target [Actual Mean]	Repeatability		Between Run		Between Day		Between Lot		Between Site/Instrument		Total Variation / Reproducibility	
	SD	CV	SD	CV	SD	CV	SD	CV	SD	CV	SD	CV
5.0% [4.91%]	0.024	0.48%	0.000	0.00%	0.024	0.48%	0.028	0.57%	0.025	0.52%	0.051	1.03%
6.5% [6.88%]	0.026	0.38%	0.015	0.22%	0.043	0.62%	0.050	0.73%	0.011	0.17%	0.074	1.07%
8.0% [8.24%]	0.025	0.31%	0.016	0.20%	0.049	0.59%	0.058	0.71%	0.017	0.21%	0.084	1.01%
12.0% [11.79%]	0.031	0.26%	0.023	0.19%	0.063	0.53%	0.078	0.66%	0.032	0.27%	0.112	0.95%
Abbreviations: 'SD': Standard Deviation | 'CV': Coefficient of Variation												

Results of Precision Study for Hemolysate Samples (NGSP %)

Table 3. Summary of Precision Analysis for all Analyzers Combined (Hemolysate/NGSP (%))

%HbA1c Target [Actual Mean]	Repeatability		Between Run		Between Day		Between Lot		Between Site/Instrument		Total Variation / Reproducibility	
	SD	CV	SD	CV	SD	CV	SD	CV	SD	CV	SD	CV
5.0% [4.90%]	0.017	0.35%	0.012	0.25%	0.024	0.50%	0.029	0.60%	0.027	0.56%	0.052	1.05%
6.5% [6.87%]	0.028	0.40%	0.011	0.15%	0.042	0.61%	0.057	0.83%	0.005	0.07%	0.077	1.12%
8.0% [8.25%]	0.025	0.30%	0.012	0.14%	0.050	0.61%	0.057	0.69%	0.016	0.20%	0.082	1.00%
12.0% [11.82%]	0.032	0.27%	0.021	0.18%	0.065	0.55%	0.073	0.62%	0.043	0.37%	0.114	0.96%
Abbreviations: 'SD': Standard Deviation | 'CV': Coefficient of Variation												

Results of Precision Study for Whole Blood Samples (IFCC mmol/mol)

Table 4. Summary of Precision Analysis for all Analyzers Combined (Whole Blood/IFCC (mmol/mol))

HbA1c Target (mmol/mol) [Actual Mean]	Repeatability		Between Run		Between Day		Between Lot		Between Site/Instrument		Total Variation / Reproducibility	
	SD	CV	SD	CV	SD	CV	SD	CV	SD	CV	SD	CV
31 [30]	0.188	0.62%	0.000	0.00%	0.280	0.93%	0.365	1.21%	0.252	0.84%	0.557	1.85%
48 [52]	0.155	0.30%	0.070	0.14%	0.402	0.78%	0.551	1.07%	0.169	0.33%	0.723	1.40%
64 [67]	0.153	0.23%	0.127	0.19%	0.514	0.77%	0.542	0.81%	0.138	0.21%	0.785	1.18%
108 [105]	0.166	0.16%	0.186	0.18%	0.696	0.66%	0.862	0.82%	0.387	0.37%	1.200	1.14%
Abbreviations: 'SD': Standard Deviation | 'CV': Coefficient of Variation												

Results of Precision Study for Hemolysate Samples (IFCC mmol/mol)

Table 5. Summary of Precision Analysis for all Analyzers Combined (Hemolysate/IFCC (mmol/mol))

HbA1c Target (mmol/mol) [Actual Mean]	Repeatability		Between Run		Between Day		Between Lot		Between Site/Instrument		Total Variation / Reproducibility	
	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)
31 [30]	0.125	0.42%	0.140	0.47%	0.279	0.93%	0.378	1.26%	0.246	0.82%	0.562	1.87%
48 [52]	0.141	0.27%	0.076	0.15%	0.401	0.78%	0.598	1.16%	0.145	0.28%	0.752	1.46%
64 [67]	0.137	0.20%	0.131	0.20%	0.520	0.78%	0.559	0.84%	0.154	0.23%	0.801	1.20%
108 [106]	0.191	0.18%	0.194	0.18%	0.693	0.66%	0.860	0.81%	0.504	0.48%	1.244	1.18%
Abbreviations: 'SD': Standard Deviation | 'CV': Coefficient of Variation												

b. Method Comparison

The method comparison study was designed in accordance with CLSI EP 21: Evaluation of Total Analytical Error for Quantitative Medical Laboratory Measurement Procedures - Second Edition, and parts of CLSI EP09c: Measurement Procedure Comparison and Bias Estimation Using Patient Samples - Third Edition. Hemoglobin A1c (HbA1c) test results of the Tosoh Automated Glycohemoglobin Analyzer HLC 723GR01 (GR01 analyzer) in an Intended Use setting were compared with results obtained with comparator testing run on the Tosoh Automated Glycohemoglobin Analyzer HLC-723G8 (G8 analyzer); comparator testing was performed in a National Glycohemoglobin Standardization Program (NGSP) Secondary Reference Laboratory (SRL). One Hundred and thirty-five (135) K2EDTA venous whole blood with HbA1c concentrations that spanned the GR01 measuring range (3.9% HbA1c to 16.9% NGSP units) were evaluated. Each sample was measured in triplicate with the G8 comparator device, and the mean value was defined as the "true" HbA1c value. Each sample was also measured in singlicate on one of three investigational GR01 analyzers placed at three (3) separate Moderate to High Complexity Clinical Laboratories. Sample distribution was as follows:

Table 6. Method Comparison Study - Sample Distribution

%HbA1c Level	Whole Blood		Hemolysate	
	N	% of Samples	N	% of Samples
≤ 5.0%	5	3.7	5	3.7
>5.0 – 6.0%	16	11.9	15	11.1
>6.0 – 6.5%	31	23.0	32	23.7
> 6.5 – 7.0%	31	23.0	32	23.7
>7.0 – 8.0%	21	15.6	20	14.8
>8.0 – 9.0%	9	6.7	10	7.4
>9.0	22	16.3	21	15.6
Total	135	100	135	100

Bias between the Candidate and NGSP method was calculated using Passing-Bablok regression analysis for both NGSP. The regression parameters, slope and intercept, were the following:

Table 7. Summary of Method Comparison – Passing-Bablok Parameter Estimates

Specimen Type	N	Slope (95% CI)	Intercept (95% CI)
Whole Blood	135	1.0045 (1.0000 to 1.0135)	–0.0222 (–0.0743 to 0.0000)
Hemolysate	135	1.0125 (1.0039 to 1.0189)	–0.0788 (–0.1226 to –0.0241)

Bias was estimated based on the Passing-Bablok regression parameters and was as follows:

Table 8. Bias Estimation based on Passing-Bablok

Specimen Type	Decision Level	Bias	% Bias
Whole Blood	5.0%	0.000	0.006
	6.5%	0.007	0.108
	8.0%	0.014	0.172
	12.0%	0.032	0.265
Hemolysate	5.0%	-0.016	-0.326
	6.5%	0.002	0.038
	8.0%	0.021	0.265
	12.0%	0.071	0.593

- Total Error near Medical Decision Points

Using the results of bias estimation (%Bias) in the method comparison study and precision estimates in the precision study (%CV), Total Error (TE) at four HbA1c concentrations (5.0%, 6.5%, 8.0% and 12.0%) was calculated as follows: %TE =|%Bias| + 1.96*%CV*(1+%Bias/100).

The results are presented below.

Table 9. Total Error near Medical Decision Points

	HbA1c Level	%Bias	%CV	%Total Error
Whole Blood	Sample 1 [5.0%]	0.006	1.03	2.02
	Sample 2 [6.5%]	0.108	1.07	2.21
	Sample 3 [8.0%]	0.172	1.01	2.16
	Sample 4 [12.0%]	0.265	0.95	2.13
Hemolysate	Sample 1 [5.0%]	-0.326	1.05	2.38
	Sample 2 [6.5%]	0.038	1.12	2.23
	Sample 3 [8.0%]	0.265	1.00	2.23
	Sample 4 [12.0%]	0.593	0.96	2.49

c. Matrix Comparison

The data of the Matrix Comparison Evaluation support the use of K2-EDTA and K3-EDTA blood collection tubes. There was no clinical or statistical difference as the total bias between the two collection tubes met the acceptance criteria of ≤±6%, thus they may be used interchangeably for testing HbA1c on the GR01 HPLC Analyzer.

d. Traceability, Stability, Expected values (Calibrators)

The assigned HbA1c values of the Tosoh Automated Glycohemoglobin Analyzer are certified with The National Glycohemoglobin Standardization Program (NGSP). See NGSP website for current certification at http://www.ngsp.org.

The final reportable result is traceable to both the International Federation of Clinical Chemistry (IFCC) and the Diabetes Control and Complications Trial (DCCT). The International Federation of Clinical Chemistry (IFCC) units of mmol/mol are calculated using the Master Equation NGSP (%) = [0.09148 x IFCC (mmol/mol)] + 2.152]. HbA1c results are provided to the customers using two different units: NGSP equivalent units (%) and IFCC equivalent units (mmol/mol).

Calibrators (Tosoh A1c Calibrator Set) and Controls (Tosoh A1c Control Set) were used in the performance studies for use with this device. The calibrators and controls are both 510(k) exempt.

e. Linearity

The results of the linearity study support the claimed measuring range of 3.9% to 16.9% HbA1c (NGSP units), and 19 to 161 mmol/mol (IFCC units).

f. Analytical Specificity

i. Endogenous Interference

The endogenous interference study was performed in compliance with CLSI EP07-A3, Interference Testing in Clinical Chemistry; Third Edition. Interference studies were conducted at known concentrations of HbA1c samples from both diabetic and non-diabetic donors. Specimens were spiked with increasing amounts of the interfering substance and then assayed ten (10) times. The mean result of each sample was then compared to the mean result of the untreated, reference sample. Significant interference was defined as an observed difference in HbA1c concentration greater than ± 5% from the untreated reference sample.

Table 10. Endogenous Interfering Substances Tested

Potential Interfering Substance	Concentration with No Interference
Albumin	20 g/dL
Ascorbic Acid	300 mg/dL
Bilirubin - Conjugated	100 mg/dL
Bilirubin - Unconjugated	100 mg/dL
Rheumatoid Factor	750 IU/mL
Triglycerides	6,000 mg/dL

Albumin, ascorbic acid, conjugated and unconjugated bilirubin, triglyceride and rheumatoid factor do not interfere with the Tosoh Automated Glycohemoglobin Analyzer HLC-723GR01 assay up to the stated concentrations.

ii. Drug Interference

The exogenous interference study was performed in compliance with CLSI EP07-A3, Interference Testing in Clinical Chemistry -Third Edition. Interference studies were conducted at known concentrations of HbA1c samples from both diabetic and non-diabetic donors. Specimens were spiked with increasing amounts of the interfering substance and then assayed ten (10) times. The mean result of each sample was then compared to the mean result of the untreated, reference sample. Significant interference was defined as an observed difference in HbA1c concentration greater than ± 5% from the untreated reference sample.

Table 11. Exogenous Interfering Substances Tested

Potential Interfering Substance	Concentration with No Interference
Acetaminophen	20 mg/dL
Acetylcysteine	330 mg/dL
Ampicillin	1,000 mg/dL
Cefoxitin	2,500 mg/dL
Cyclosporine	0.7 mg/dL
Doxycycline	50 mg/dL
Heparin	5.000 U/L
Ibuprofen	50 mg/dL
Levodopa	20 mg/dL
Metformin	5 mg/dL
Methyldopa	30 mg/dL
Metronidazole	200 mg/dL
Phenylbutazone	400 mg/dL
Rifampicin	6.4 mg/dL
Salicylic Acid	60 mg/dL
Theophylline	10 mg/dL

The exogenous substances evaluated do not interfere with the Tosoh Automated Glycohemoglobin Analyzer HLC-723GR01 assay at therapeutic doses.

iii. Cross Reactivity with Hemoglobin Derivatives

A cross-reactivity study was performed to assess potential interferences from Acetylated hemoglobin (Hb), Carbamylated Hb, Aldehyde Hb, and Labile HbA1c with samples from both diabetic and non-diabetic donors. Specimens were spiked with increasing amounts of the interfering substance and then assayed ten (10) times. The mean result of each sample was then compared to the mean result of the untreated, reference sample. Significant interference was defined as an observed difference in HbA1c concentration

greater than ± 5% from the untreated reference sample. The following results were concluded as not interfering with the assay.

- Acetylated Hb up to 50 mg/dL
- Carbamylated Hb up to 25 mg/dL
- Aldehyde Hb up to 25 mg/dL
- Labile HbA1c up to 2000 mg/dL

In conclusion, Acetylated hemoglobin (Hb), Carbamylated Hb, Aldehyde Hb, and Labile HbA1c with HbA1c do not cross-react with the assay up to the concentrations shown above.

iv. Hemoglobin Variant Interference

The hemoglobin variant interference study was performed by comparing HbA1c results of samples with the presence of common Hb variants measured with both the GR01 analyzer and the reference method, Tosoh Automated Glycohemoglobin Analyzer HLC-723G8, Ver. 5.24F ("G8 v5.24F"), which is which has been demonstrated to be free from interference by these hemoglobin variants in compliance to CLSI EP07: Interference Testing in Clinical Chemistry; Approved Guideline – Third Edition.
Interference due to the presence of certain levels of common Hb variants (HbAC, HbAD, HbAE, and HbAS) and hemoglobinopathy, elevated HbA2 and elevated Fetal Hemoglobin (HbF) is well-known when measuring %HbA1c in clinical specimens.

Interference studies were performed to identify the level of (1) Hb variants and HbA2, and (2) HbF likely to cause interference with HbA1c measurements.

(1) Common Hemoglobin Variants and Elevated HbA2
The hemoglobin variant study was performed using K2 EDTA venous whole blood samples known to contain hemoglobin variants HbS, HbC, HbE, HbD and elevated HbA2. The samples containing the hemoglobin variants were tested using the GR01 and using the comparator method (G8 v5.24F), which has been demonstrated to be free from interference by these hemoglobin variants. Non-clinically significant interference was defined as ≤ ±7% relative difference in the results from the comparative method at 6.5% or 8.0% HbA1c. The following table summarizes the test results.

(2) Fetal Hemoglobin (HbF)
No clinically significant interference with HbA1c results was observed up to 32.2% HbF.

Test results for the Hemoglobin Variance Interference evaluations are as follows:

Table 12. Hemoglobin Variant Interference Study – Relative Difference at Medical Decision Points

Variant	n	HbA1c Range	Variant Range	Mean (Range) of Relative Bias from Reference Method at Approximately 6.5% and 8.0% HbA1c	
				~6.5 % HbA1c	~8.0 % HbA1c
HbC	25	4.6% to 14.3%	30.0% to 38.8%	2.79 (0.74 to 4.65)	1.80 (-0.61 to 3.85)
HbD	22	5.7% to 10.9%	24.3% to 42.7%	0.50 (-3.08 to 5.26)	-1.16 (-4.71 to 1.27)
HbE	34	5.0% to 12.8%	19.5% to 31.4%	1.54 (-3.57 to 4.92)	2.08 (0.00 to 7.19)
HbS	29	4.7% to 14.4%	26.6% to 42.7%	2.49 (1.57 to 3.91)	2.71 (1.99 to 4.43)
HbA2	33	4.7% to 14.3%	3.5% to 6.7%	2.51 (0.77 to 4.65)	1.26 (-0.61 to 2.99)
HbF	33	5.5% to 11.7%	3.8% to 32.2%	-1.2 (-3.0 to 1.5)	-2.6 (-4.2 to 0.8)

In conclusion, no clinically significant interference with HbA1c results was observed for the common hemoglobin variants HbAC, HbAD, HbAE or HbAS at the levels stated in the table above.
No clinically significant interference with HbA1c results was observed up to 6.7% HbA2. No clinically significant interference with HbA1c results was observed up to 32.2% HbF.

Expected Values/Reference Range

The sponsor provided the following information in labeling regarding expected values:

The “Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes - 2021”, American Diabetes Association gives the following criteria for the diagnosis of diabetes and categories of increased risk for diabetes.

Table 13. Reference Ranges

	In NGSP units	In IFCC units	Comment
HbA1c	≥ 6.5 %	(≥ 48 mmol/mol)	Cutoff point to diagnose diabetes
HbA1c	5.7 - 6.4 %	(39 – 47 mmol/mol)	Increased risk for diabetes (prediabetes)

The HbA1c reference range (non-diabetic) is reported as below
HbA1c: 4.0 - 6.0 % (mean 5.0 %, SD 0.5 %)

This range can be converted into IFCC units as:
HbA1c: 20 - 42 mmol/mol,

using the following Master Equation:
IFCC (mmol/mol) = 10.93 x NGSP(%) – 23.50

8. Proposed Labeling

The labeling is sufficient and satisfies the requirements of 21 CFR Part 809.10.

9. Conclusion

The information and data contained in this 510(k) document demonstrate that the Tosoh Automated Glycohemoglobin Analyzer HLC-723GR01 is an accurate, reliable, precise test that correlates well with current cleared methods and NGSP standardized testing for the quantitation of HbA1c. Furthermore, the performance criteria as stipulated by the Special Control requirements for HbA1c systems that diagnose diabetes have been met.

Overall, the contents of this submission demonstrate that the Tosoh Automated Glycohemoglobin Analyzer HLC-723GR01 is substantially equivalent in intended use and technological characteristics to the Tosoh Automated Glycohemoglobin Analyzer HLC-723G8 v5.24F (k200904). Therefore, the Tosoh Automated Glycohemoglobin Analyzer HLC-723GR01 is safe and effective for its intended use, and meets the Federal Food, Drug and Cosmetic Act criteria for 510(k) clearance of this device.