510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

I Background Information:

A 510(k) Number

K222635

B Applicant

Trinity Biotech (Primus Corporation, dba Trinity Biotech)

C Proprietary and Established Names

Premier Resolution System

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
GKA	Class II	21 CFR 864.7415 - Abnormal Hemoglobin Assay	HE - Hematology

II Submission/Device Overview:

A Purpose for Submission:

Clearance of a new instrument and assay

B Measurand:

Hemoglobin A, F, A2, S, C, E, D-Los Angeles

C Type of Test:

Quantitative, High Performance Liquid Chromatography

III Intended Use/Indications for Use:

A Intended Use(s):
See Indications for Use below.

B Indication(s) for Use:
The Premier Resolution System is an automated High Performance Liquid Chromatography (HPLC) system which performs the separation of hemoglobin species in venous whole blood samples for the quantitative analysis of normal hemoglobin (A, A2, and F), and the qualitative detection of major variant hemoglobin S, C, D-Los Angeles, and E in adult, adolescent, children and infant populations. The assays are performed on venous whole blood samples collected in tubes containing K2EDTA as anticoagulant.

The Premier Resolution System is intended for Professional Laboratory Use only.

The Premier Resolution System is intended for use with analytical components and reagents provided by Trinity Biotech.

The Premier Resolution System is intended to be used in conjuction with othe laboratory and clinical findings.

For In Vitro Diagnostic Use.

C Special Conditions for Use Statement(s):
Rx - For Prescription Use Only

D Special Instrument Requirements:

Premier Resolution Analyzer

IV Device/System Characteristics:

A Device Description:

The Premier Resolution System consists of a high-performance liquid chromatographic analyzer (Premier Resolution Analyzer), reagents, analytical column, and software. The system allows for the fractionation and quantitation of fetal hemoglobin (Hb F), hemoglobin A (HbA), and hemoglobin A2 (Hb A2), and the qualitative detection of major variant hemoglobin S, C, D-Los Angeles and E in adult, adolescent, children, and infant populations. This is accomplished using the principles of ion-exchange (IEX) high performance liquid chromatography (HPLC). The Analyzer consists of an integrated HPLC (Pumps, Injection, Valve and Detector), compact sample preparation system (Probe/Injection Port, Syringe Module and Sample Transport) and the workstation (CPU, Printer and Touch Screen Interface) with the Resolution Application Software.

The Premier Resolution Analyzer consists of four main components:

1. The HPLC system is comprised of a dual high pressure pump system, column, sample loop and fixed wavelength detector.
2. The autosampler, comprising of the Sample Probe, Syringe Module, and Injection Port, is paired with the Sample Transport system. Together these provide automated analysis for

batches of up to 210 samples (plus additional STAT samples are allowed throughout the run) and support continuous sample loading. The sample transport barcode reader ensures correct patient sample identification.

3. The integrated central processing unit (CPU) module provides system control and data storage capabilities, in addition to supporting LIS integration.
4. The Windows-based Premier Resolution Analyzer software provides real-time chromatography and system condition monitoring.

Components and Accessories:

- **Analyzer:** Premier Resolution Analyzer (10-00-0001)

- **Column:** Premier Resolution Analytical Column (10-06-0006)
  The Trinity Biotech Premier Resolution Analytical column is an ion-exchange column. Reagents and columns are for use with the Premier Resolution Analyzer only. The user is cautioned to not substitute columns or reagents from any other source/vendor. Information on reconstitution if applicable, handling and storage are provided in the individual package inserts for each component.

- **Reagents:**
  1) Premier Resolution Mobile Phase 1 Reagent, 940mL, (01-03-0082)
  2) Premier Resolution Mobile Phase 2 Reagent, 940mL, (01-03-0083)
  3) Premier Resolution Mobile Phase 1 Reagent, 3.8L, (01-03-0084)
  4) Premier Resolution Mobile Phase 2 Reagent, 3.8L, (01-03-0085)
  5) Premier Resolution Diluent Reagent (for Rinse Station), 3.8 L, (01-03-0087)
  6) Premier Resolution Diluent Reagent (for Syringe), 3.8 L, (01-03-0087)
  7) Premier Resolution Wash Reagent, 940 mL, (01-03-0088)
  8) Premier Resolution Piston Wash Reagent, 940mL (01-03-0093)

- A2+F Calibrator Kit, 300µL, (01-04-0044)
  The Premier Resolution Analyzer must be calibrated in order to report Hb F and Hb A2. It is also recommended to calibrate the system:
  - When the instrument is initially installed
  - When a column is changed
  - If control values are out of the acceptable range stated on the package insert
  - When reference material changes values or lot numbers

- A2+F Control Kit, 300µL, (01-04-0045)
  Controls in the normal and elevated ranges should be included in each batch run to monitor the performance of the system.

- FASC Position Marker Kit, 1000µL, (01-04-0046)
  The Trinity Biotech FASC Position Marker is lyophilized whole blood containing hemoglobins F, A, A2, S, and C. The material is used as a retention time marker for the known hemoglobins that it contains. It is mandatory to begin each batch with an FASC Position marker injection.

B Principle of Operation:

The Premier Resolution System employs the principles of ion exchange and high-performance liquid chromatography (HPLC). The instrument's pumps transfer reagents through the analytical column. The analytical column contains an ion-exchange resin bound to a silica gel support.

Hemolyzed samples are automatically injected onto the column during the flow of a mix of Premier Mobile Phase 1 and Mobile Phase 2. Hemoglobin species migrate through the column at rates determined by their individual physical properties. The charged proteins in the hemoglobin chains bind to the polyaspartic acid coating on the silica gel. As the assay continues, the gradient is increased to a higher percentage of Mobile Phase 2 to increase the ionic strength. The stronger ionic strength displaces the stronger bonded proteins from the polyaspartic acid coating. The weakest to strongest bonded hemoglobin fractions elute in the following sequence as the ionic strength of the mobile phase increases: HbF, HbA, HbE, HbA2, HbD, HbS and finally HbC. Once the hemoglobin has been displaced, it passes through the spectrophotometric detector, where it is detected at 413±2nm.

The compositions of Premier Resolution Mobile Phase 1 & 2 Reagents are designed to exhibit virtually identical absorption in the 413±2nm range to ensure a stable baseline. The detector signal is also referenced by the split-beam technique.

In the final stage of the assay, the column is re-equilibrated with Premier Resolution Mobile Phase 1 as the primary reagent. All reagent selection occurs in a timed sequence designed to allow complete elution of hemoglobin fractions.

All functions are controlled by the computer. The computer processes the signal from the spectrophotometric detector and calculates the concentration of hemoglobin fractions as a percentage of the total detected. Integration is by peak area in Absorbance Units (AU)-seconds. The computer software also calculates the retention time.

As the sample is processed, the chromatogram is displayed at the top right of the main assay screen in real time. The computer produces printed reports with the sample identification information, date, and time, followed by the chromatogram with peaks either numbered or with retention times indicated at the apex of each peak. A peak summary report is printed after the chromatogram with the retention time, relative retention time, % area and comments for each peak in the chromatogram.

The software, specially designed for Variant analysis, controls the four basic analyzer operation functions of sample identification, analyzer operation, calculation of results, as well as printing and storing complete reports. Based on computer hard disc capacity, chromatograms and batch summary reports can be automatically archived.

C Instrument Description Information:

1. Instrument Name:
   Premier Resolution Analyzer

2. Specimen Identification:
   Automatically read by the barcode reader or manually entered by operator

3. Specimen Sampling and Handling:
   Whole blood samples should be collected by venipuncture in K2EDTA anticoagulant. The use of other anticoagulants on the Premier Resolution Analyzer is not supported.

4. Calibration:
   The Premier Resolution Analyzer must be calibrated in order to report Hb F and Hb A2. It is also recommended to calibrate the system:
   - When the instrument is initially installed
   - When a column is changed
   - If control values are out of the acceptable range stated on the package insert
   - When reference material changes values or lot numbers

   The Trinity Biotech A2+F Calibrator Kit is intended for use with the Trinity Biotech Premier Resolution analyzer to monitor the performance of the assay. No substitutions are permitted or authorized.

5. Quality Control:
   Controls in the normal and elevated ranges should be included in each batch run to monitor the performance of the system. The Trinity Biotech A2+F Calibrator Kit is intended for use with the Trinity Biotech Premier Resolution analyzer to monitor the performance of the assay. No substitutions are permitted, registered, or authorized and no other uses are intended, registered, or authorized.

V Substantial Equivalence Information:

A Predicate Device Name(s):
Variant II B-thalassemia

B Predicate 510(k) Number(s):
K991127

C Comparison with Predicate(s):

Device & Predicate Device(s):	K222635	K991127
Device Trade Name	Premier Resolution System	Bio-Rad Variant II β - thalassemia
General Device Characteristic Similarities		
Intended Use/Indications For Use	The Premier Resolution System is an automated High Performance Liquid Chromatography (HPLC)	The Variant™ II B-thalassemia Program is intended for the separation and area percent

	system which performs the separation of hemoglobin species in venous whole blood samples for the quantitative analysis of normal hemoglobin (A, A2, and F), and the qualitative detection of major variant hemoglobin S, C, D-Los Angeles, and E in adult, adolescent, children and infant populations. The assays are performed on venous whole blood samples collected in tubes containing K2EDTA as anticoagulant. The Premier Resolution System is intended for Professional Laboratory Use only. The Premier Resolution System is intended for use with analytical components and reagents provided by Trinity Biotech. The Premier Resolution System is intended to be used in conjunction with other laboratory and clinical findings. For In Vitro Diagnostic Use.	determinations of hemoglobins A2 and F and as an aid in the identification of abnormal hemoglobins in whole blood using ion-exchange high performance liquid chromatography (HPLC). The Variant™ II B-thalassemia Program is intended for use only with the Bio-Rad Variant™ II Hemoglobin Testing System. For in vitro diagnostic use only.
Chemistry	Ion Exchange HPLC	Same
Sample Tube Processing	Aspiration of whole blood from closed tube	Same
Sample Hemolysis	Performed automatically by the system	Same
Automated Sample Introduction	Continuous loading with sample racks	Same
Separation System	Ion-exchange high performance liquid chromatography (HPLC) protein separation on analytical column based on ionic interaction with the column material and elution by buffer gradient with increasing ionic strength.	Same

Separation Unit	Analytical Column	Analytical Column
Calibration	A2+F Calibrator	A2+F Calibrator
Control	A2+F Control	A2+F Control
Position Marker	FASC Position Marker	FASC Position Marker
General Device Characteristic Differences		
Analysis Throughput	4 Minutes – Quick Scan 8 Minutes – High Resolution	6 Minutes
Absorbance Wavelength	413 nm	415 nm
Collection Tubes	K2EDTA	K2EDTA, K3EDTA
Hemoglobin	HbA, HbA2, HbF HbS, HbC, HbD-LA, HbE	HbA2, HbF

VI Standards/Guidance Documents Referenced:

CLSI EP05-A3, Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline - Third Edition;
CLSI EP06, Evaluation of the Linearity of Quantitative Measurement Procedures; Approved Guideline, Second Edition;
CLSI EP07-A2, Interference Testing in Clinical Chemistry; Approved Guideline, Third Edition;
CLSI EP14-A3, Evaluation of Commutability of Processed Samples; Approved Guideline, Third Edition;
CLSI EP17-A2 Evaluation of Detection Capability for Clinical Measurement Procedures, Second Edition;
CLSI EP25-A, Evaluation of Stability of In Vitro Diagnostic Reagents; Approved Guideline;
IEC 61010-1 Edition 3.1 2017-01, Safety requirements for electrical equipment for measurement, control, & laboratory use - Part 1;
IEC 60601-1-2 Edition 4.1 2020-09, Medical electrical equipment - Part 1-2: General requirements;
IEC 62304 Edition 1.1 2015-06, Medical device software - Software life-cycle processes;
IEC 62366-1:2015+A1:2020, Medical devices Part 1: Application of usability engineering to medical devices;
ISO 14971:2019, Medical Devices – Application of Risk Management to Medical Devices;

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

Single Site Precision

A single-site precision study was conducted to evaluate the repeatability and within-laboratory precision of the Premier Resolution System. Fourteen (14) whole blood samples of varying concentrations of HbA, HbA2, HbF, HbS, HbC, HbD-LA, and HbE were analyzed on the Premier Resolution System using the Quick Scan and High-Resolution assay modes for the quantitation hemoglobin fractions. The 20x2x2 study design was conducted over 20 days, with two runs per day and two replicates per run, in accordance with CLSI EP05-A3. The study yielded 80 data points for each analyte to establish a balanced dataset. Overall, repeatability and within-laboratory precision study performed met the specification of the acceptance criteria..

Premier Resolution Quick Scan

Description	N	Mean (%)	Repeatability		Between-Run		Between-Day		Within-Laboratory	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
A High	80	83.56	0.25	0.30%	0.37	0.44%	2.98	3.57%	3.01	3.61%
A Mid	80	51.24	0.35	0.68%	0.15	0.30%	0.25	0.50%	0.46	0.89%
A2 Mid	80	2.57	0.04	1.63%	0.03	1.07%	0.03	1.08%	0.06	2.23%
A2 Low	80	1.75	0.04	2.02%	0.02	0.90%	0.10	5.57%	0.10	5.99%
F High	80	11.38	0.05	0.43%	0.03	0.26%	0.10	0.92%	0.12	1.05%
F Mid	80	1.67	0.04	2.42%	0.00	0.00%	0.04	2.18%	0.05	3.26%
S High	80	74.63	0.33	0.44%	0.18	0.24%	0.55	0.74%	0.67	0.89%
S Mid	80	30.61	0.14	0.47%	0.14	0.45%	0.22	0.73%	0.30	0.98%
C High	80	81.22	0.41	0.50%	0.43	0.53%	0.23	0.28%	0.63	0.78%
C Mid	80	31.91	0.46	1.43%	0.26	0.81%	0.20	0.61%	0.56	1.75%
D High	80	69.98	0.70	1.00%	0.71	1.01%	0.86	1.23%	1.32	1.88%
D Mid	80	38.14	0.30	0.79%	0.37	0.97%	0.61	1.61%	0.78	2.04%
E High	80	81.22	1.38	1.70%	0.00	0.00%	1.85	2.28%	2.31	2.84%
E Mid	80	22.30	0.14	0.62%	0.17	0.75%	0.65	2.90%	0.68	3.06%

Premier Resolution High Resolution

Description	N	Mean (%)	Repeatability		Between-Run		Between-Day		Within-Laboratory	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
A High	80	83.64	0.43	0.52%	0.38	0.45%	2.98	3.56%	3.03	3.63%
A Mid	80	50.60	0.41	0.81%	0.48	0.94%	0.30	0.59%	0.69	1.37%
A2 Mid	80	2.48	0.10	4.13%	0.15	5.92%	0.00	0.00%	0.18	7.22%
A2 Low	80	1.59	0.06	3.92%	0.09	5.98%	0.00	0.00%	0.11	7.15%
F High	80	11.11	0.12	1.07%	0.03	0.27%	0.37	3.31%	0.39	3.49%
F Mid	80	1.34	0.08	5.78%	0.04	3.23%	0.08	6.24%	0.12	9.10%
S High	80	76.89	0.57	0.74%	0.42	0.54%	0.74	0.96%	1.02	1.33%
S Mid	80	32.01	0.30	0.92%	0.23	0.73%	0.39	1.22%	0.54	1.69%
C High	80	81.07	0.51	0.63%	0.49	0.61%	0.61	0.75%	0.94	1.15%
C Mid	80	32.84	0.44	1.34%	0.00	0.00%	0.50	1.52%	0.67	2.03%
D High	80	73.83	1.07	1.45%	0.89	1.21%	0.84	1.14%	1.62	2.20%
D Mid	80	39.80	0.34	0.84%	0.23	0.58%	0.33	0.84%	0.53	1.32%
E High	80	77.26	0.93	1.20%	0.94	1.21%	3.33	4.31%	3.58	4.63%
E Mid	80	22.46	0.13	0.57%	0.22	0.98%	0.66	2.93%	0.70	3.14%

Between-Lot and Between-Instrument Precision

Between-Lot and Between-Instrument Precision studies were conducted to evaluate the variation characteristics of consumable reagent lots for the Premier Resolution System. These

studies were conducted to complement the single-site and multisite precision studies to evaluate the imprecision of the consumable reagent lots. A 3x5x5 study design was performed at a single site with one run per day on three (3) different lots of consumable reagents (3 lots of Premier Resolution analytical columns, 3 lots of Mobile Phase 1, 3 lots of Mobile Phase 2, 3 lots of Diluent) or three (3) different instruments, over five (5) days, and with five (5) replicates per run. Five (5) whole blood samples with varying levels of hemoglobin A, A2, F, S, C, D-Los Angeles, and E were tested on the Premier Resolution using the Quick Scan and High-Resolution assay modes.

The following testing were performed each day over the course of five (5) days (not necessarily consecutive days):

- Three (3) different lots of Premier Resolution analytical columns were tested using only one (1) dedicated instrument, one (1) lot of Mobile Phase 1 and 2, and one (1) lot of Diluent to generate the column-to-column precision data.
- Three (3) different lots of Mobile Phase 1 were tested using only one (1) dedicated instrument, one (1) lot of analytical column, one (1) lot of Mobile Phase 2 and one (1) lot of Diluent to generate the Mobile Phase-to-Mobile Phase precision data.
- Three (3) different lots of Mobile Phase 2 were tested using only one (1) dedicated instrument, one (1) lot of analytical column, one (1) lot of Mobile Phase 1 and one (1) lot of Diluent to generate the Mobile Phase-to-Mobile Phase precision data.
- Three (3) different lots of Diluent were tested using only one (1) dedicated instrument, one (1) lot of analytical column, and one (1) lot of Mobile Phase 1 and 2 to generate the Diluent-to-Diluent precision data.
- Three (3) Premier Resolution systems were tested using only one (1) lot of analytical columns, one (1) lot of Mobile Phase 1 and 2, and one (1) lot of Diluent. The instrument-to-instrument data were collected from the first run of each day consumable lot studies.

Overall, the performance of the Premier Resolution System met the predetermined specifications. The results are summarized below.

Quick Scan Assay Mode – Mobile Phase 1

Description	Mean	N	Repeatability		Between-Lot		Within-Day		Between-Day		Within-Lab	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
A Normal	87.85	75	0.18	0.2%	0.26	0.3%	0.32	0.4%	0.57	0.7%	0.65	0.7%
A2 Normal	2.74	75	0.03	1.0%	0.01	0.2%	0.03	1.0%	0.06	2.2%	0.07	2.5%
A SF	33.39	75	0.24	0.7%	0.03	0.1%	0.24	0.7%	0.15	0.5%	0.29	0.9%
A2 SF	4.20	75	0.19	4.6%	0.00	0.0%	0.19	4.6%	0.05	1.3%	0.20	4.8%
F SF	5.91	75	0.05	0.9%	0.00	0.0%	0.05	0.9%	0.00	0.0%	0.07	1.3%
S SF	43.25	75	0.27	0.6%	0.00	0.0%	0.27	0.6%	0.00	0.0%	0.36	0.8%
C	32.07	75	0.20	0.6%	0.16	0.5%	0.25	0.8%	0.00	0.0%	0.33	1.0%
D_LA	32.97	75	0.41	1.3%	0.31	0.9%	0.51	1.6%	0.00	0.0%	0.62	1.9%
E	24.77	75	0.14	0.6%	0.11	0.5%	0.18	0.7%	0.00	0.0%	0.44	1.8%

Quick Scan Assay Mode – Mobile Phase 2

Description	Mean	N	Repeatability		Between-Lot		Within-Day		Between-Day		Within-Lab	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
A Normal	87.72	75	0.22	0.3%	0.25	0.3%	0.33	0.4%	0.61	0.7%	0.70	0.8%
A2 Normal	2.74	75	0.05	1.8%	0.00	0.0%	0.05	1.8%	0.02	0.9%	0.06	2.0%
A SF	34.34	75	0.34	1.0%	0.18	0.5%	0.39	1.1%	0.00	0.0%	0.39	1.1%

Description	Mean	N	Repeatability		Between-Lot		Within-Day		Between-Day		Within-Lab	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
A2 SF	4.18	75	0.12	2.8%	0.00	0.0%	0.12	2.8%	0.02	0.6%	0.12	2.8%
F SF	5.75	75	0.06	1.1%	0.02	0.3%	0.06	1.1%	0.00	0.0%	0.06	1.1%
S SF	42.59	75	0.41	1.0%	0.35	0.8%	0.54	1.3%	0.00	0.0%	0.54	1.3%
C	30.58	75	0.17	0.6%	0.24	0.8%	0.30	1.0%	0.00	0.0%	0.30	1.0%
D_LA	32.18	75	0.38	1.2%	0.00	0.0%	0.38	1.2%	0.00	0.0%	0.52	1.6%
E	23.44	75	0.09	0.4%	0.19	0.8%	0.21	0.9%	0.00	0.0%	0.41	1.7%

Quick Scan Assay Mode – Diluent

Description	Mean	N	Repeatability		Between-Lot		Within-Day		Between-Day		Within-Lab	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
A Normal	88.08	75	0.24	0.3%	0.38	0.4%	0.45	0.5%	0.17	0.2%	0.48	0.5%
A2 Normal	2.83	75	0.03	1.2%	0.02	0.8%	0.04	1.5%	0.03	1.1%	0.05	1.9%
A SF	34.42	75	0.16	0.5%	0.03	0.1%	0.17	0.5%	0.06	0.2%	0.18	0.5%
A2 SF	4.26	75	0.06	1.4%	0.01	0.3%	0.06	1.4%	0.03	0.8%	0.07	1.6%
F SF	5.88	75	0.04	0.6%	0.04	0.6%	0.05	0.9%	0.00	0.0%	0.06	1.0%
S SF	41.78	75	0.15	0.4%	0.21	0.5%	0.26	0.6%	0.00	0.0%	0.31	0.7%
C	30.39	75	0.14	0.4%	0.24	0.8%	0.27	0.9%	0.00	0.0%	0.27	0.9%
D_LA	31.59	75	0.38	1.2%	0.30	1.0%	0.49	1.5%	0.00	0.0%	0.59	1.9%
E	23.84	75	0.18	0.7%	0.25	1.1%	0.31	1.3%	0.00	0.0%	0.46	1.9%

Quick Scan Assay Mode – Columns

Description	Mean	N	Repeatability		Between-Lot		Within-Day		Between-Day		Within-Lab	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
A Normal	87.61	75	0.16	0.2%	0.46	0.5%	0.49	0.6%	0.56	0.6%	0.74	0.8%
A2 Normal	2.81	75	0.04	1.4%	0.03	1.2%	0.05	1.8%	0.00	0.0%	0.05	1.8%
A SF	34.51	75	0.32	0.9%	0.28	0.8%	0.42	1.2%	0.05	0.1%	0.43	1.2%
A2 SF	4.30	75	0.09	2.1%	0.05	1.1%	0.10	2.4%	0.01	0.3%	0.10	2.4%
F SF	6.03	75	0.06	1.0%	0.10	1.7%	0.12	2.0%	0.00	0.0%	0.14	2.2%
S SF	42.72	75	0.36	0.8%	0.32	0.7%	0.48	1.1%	0.00	0.0%	0.58	1.3%
C	30.25	75	0.14	0.5%	0.39	1.3%	0.41	1.4%	0.00	0.0%	0.41	1.4%
D_LA	32.30	75	0.29	0.9%	0.28	0.9%	0.40	1.2%	0.00	0.0%	0.53	1.6%
E	23.56	75	0.18	0.8%	0.40	1.7%	0.44	1.9%	0.00	0.0%	0.68	2.9%

Quick Scan Assay Mode – Instruments

Description	Mean	N	Repeatability		Between-Instrument		Within-Day		Between-Day		Within-Lab	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
A Normal	87.90	75	0.22	0.3%	0.35	0.4%	0.42	0.5%	0.43	0.5%	0.60	0.7%
A2 Normal	2.76	75	0.03	1.3%	0.05	1.9%	0.06	2.3%	0.02	0.8%	0.07	2.4%
A SF	34.07	75	0.22	0.7%	0.58	1.7%	0.62	1.8%	0.00	0.0%	0.62	1.8%
A2 SF	4.21	75	0.13	3.1%	0.03	0.8%	0.13	3.2%	0.01	0.2%	0.13	3.2%
F SF	5.84	75	0.05	0.9%	0.10	1.7%	0.11	2.0%	0.00	0.0%	0.11	2.0%
S SF	42.56	75	0.24	0.6%	0.78	1.8%	0.82	1.9%	0.00	0.0%	0.82	1.9%
C	30.98	75	0.15	0.5%	0.96	3.1%	0.97	3.1%	0.00	0.0%	0.97	3.1%
D_LA	32.33	75	0.44	1.4%	0.65	2.0%	0.78	2.4%	0.00	0.0%	0.78	2.4%
E	24.13	75	0.17	0.7%	0.70	2.9%	0.72	3.0%	0.00	0.0%	0.72	3.0%

High-Resolution Assay Mode – Mobile Phase 1

Description	Mean	N	Repeatability		Between-Lot		Within-Day		Between-Day		Within-Lab	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
A Normal	89.31	75	0.21	0.2%	0.45	0.5%	0.50	0.6%	0.53	0.6%	0.72	0.8%
A2 Normal	2.63	75	0.05	1.8%	0.05	2.0%	0.07	2.7%	0.01	0.4%	0.07	2.7%
A SF	35.18	75	0.23	0.6%	0.13	0.4%	0.26	0.7%	0.18	0.5%	0.32	0.9%
A2 SF	4.16	75	0.09	2.1%	0.04	1.0%	0.10	2.3%	0.01	0.2%	0.10	2.3%
F SF	5.95	75	0.06	1.0%	0.02	0.3%	0.07	1.1%	0.00	0.0%	0.07	1.2%

Description	Mean	N	Repeatability		Between-Lot		Within-Day		Between-Day		Within-Lab	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
S SF	44.17	75	0.23	0.5%	0.11	0.3%	0.26	0.6%	0.00	0.0%	0.31	0.7%
C	30.67	75	0.24	0.8%	0.17	0.6%	0.29	1.0%	0.00	0.0%	0.29	1.0%
D_LA	32.26	75	0.17	0.5%	0.30	0.9%	0.35	1.1%	0.00	0.0%	0.49	1.5%
E	23.57	75	0.27	1.2%	0.27	1.2%	0.38	1.6%	0.00	0.0%	0.57	2.4%

High-Resolution Assay Mode – Mobile Phase 2

Description	Mean	N	Repeatability		Between-Lot		Within-Day		Between-Day		Within-Lab	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
A Normal	89.16	75	0.19	0.2%	0.74	0.8%	0.76	0.9%	0.00	0.0%	0.76	0.9%
A2 Normal	2.71	75	0.05	1.9%	0.07	2.7%	0.09	3.3%	0.00	0.0%	0.09	3.3%
A SF	34.86	75	0.21	0.6%	0.08	0.2%	0.22	0.6%	0.00	0.0%	0.22	0.6%
A2 SF	4.11	75	0.06	1.5%	0.04	0.9%	0.07	1.8%	0.04	1.0%	0.08	2.0%
F SF	5.90	75	0.06	1.0%	0.02	0.4%	0.06	1.1%	0.00	0.0%	0.07	1.2%
S SF	44.07	75	0.23	0.5%	0.06	0.1%	0.23	0.5%	0.00	0.0%	0.29	0.7%
C	30.73	75	0.18	0.6%	0.17	0.5%	0.25	0.8%	0.00	0.0%	0.25	0.8%
D_LA	32.45	75	0.13	0.4%	0.28	0.9%	0.31	1.0%	0.00	0.0%	0.43	1.3%
E	23.41	75	0.31	1.3%	0.11	0.5%	0.33	1.4%	0.00	0.0%	0.47	2.0%

High-Resolution Assay Mode – Diluent

Description	Mean	N	Repeatability		Between-Lot		Within-Day		Between-Day		Within-Lab	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
A Normal	88.60	75	0.15	0.2%	0.41	0.5%	0.44	0.5%	0.30	0.3%	0.53	0.6%
A2 Normal	2.75	75	0.06	2.2%	0.06	2.1%	0.08	3.0%	0.21	7.7%	0.23	8.2%
A SF	34.96	75	0.19	0.5%	0.26	0.8%	0.32	0.9%	0.32	0.9%	0.45	1.3%
A2 SF	4.17	75	0.08	2.0%	0.04	0.9%	0.09	2.2%	0.24	5.7%	0.25	6.1%
F SF	6.00	75	0.05	0.9%	0.04	0.7%	0.07	1.1%	0.00	0.0%	0.14	2.3%
S SF	43.93	75	0.53	1.2%	0.45	1.0%	0.69	1.6%	0.00	0.0%	0.69	1.6%
C	30.33	75	0.16	0.5%	0.31	1.0%	0.35	1.2%	0.00	0.0%	0.36	1.2%
D_LA	32.38	75	0.20	0.6%	0.50	1.6%	0.54	1.7%	0.00	0.0%	0.84	2.6%
E	23.39	75	0.22	0.9%	0.31	1.3%	0.38	1.6%	0.00	0.0%	0.56	2.4%

High-Resolution Assay Mode – Columns

Description	Mean	N	Repeatability		Between-Lot		Within-Day		Between-Day		Within-Lab	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
A Normal	88.81	75	0.25	0.3%	0.40	0.4%	0.47	0.5%	0.56	0.6%	0.73	0.8%
A2 Normal	2.61	75	0.06	2.2%	0.19	7.3%	0.20	7.6%	0.00	0.0%	0.20	7.6%
A SF	34.54	75	0.22	0.7%	0.27	0.8%	0.35	1.0%	0.00	0.0%	0.35	1.0%
A2 SF	3.98	75	0.08	2.0%	0.18	4.4%	0.19	4.9%	0.00	0.0%	0.19	4.9%
F SF	5.81	75	0.05	0.9%	0.14	2.5%	0.15	2.6%	0.00	0.0%	0.15	2.6%
S SF	43.37	75	0.30	0.7%	0.48	1.1%	0.56	1.3%	0.00	0.0%	0.56	1.3%
C	30.29	75	0.25	0.8%	0.17	0.6%	0.30	1.0%	0.00	0.0%	0.30	1.0%
D_LA	32.23	75	0.16	0.5%	0.27	0.8%	0.31	1.0%	0.00	0.0%	0.42	1.3%
E	23.19	75	0.14	0.6%	0.34	1.5%	0.36	1.6%	0.00	0.0%	0.44	1.9%

High-Resolution Assay Mode – Instruments

Description	Mean	N	Repeatability		Between-Instrument		Within-Day		Between-Day		Within-Lab	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
A Normal	89.03	75	0.13	0.1%	0.67	0.7%	0.68	0.8%	0.41	0.5%	0.79	0.9%
A2 Normal	2.71	75	0.04	1.7%	0.14	5.2%	0.15	5.4%	0.00	0.0%	0.15	5.4%
A SF	34.95	75	0.20	0.6%	0.27	0.8%	0.34	1.0%	0.00	0.0%	0.34	1.0%
A2 SF	4.17	75	0.08	1.9%	0.13	3.2%	0.15	3.7%	0.00	0.0%	0.15	3.7%
F SF	5.95	75	0.05	0.9%	0.08	1.3%	0.09	1.6%	0.00	0.0%	0.10	1.7%
S SF	44.01	75	0.24	0.5%	0.33	0.7%	0.40	0.9%	0.00	0.0%	0.40	0.9%
C	30.55	75	0.19	0.6%	0.33	1.1%	0.38	1.3%	0.00	0.0%	0.38	1.3%

Description	Mean	N	Repeatability		Between-Instrument		Within-Day		Between-Day		Within-Lab	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
D_LA	32.43	75	0.21	0.7%	0.58	1.8%	0.61	1.9%	0.00	0.0%	0.76	2.3%
E	23.43	75	0.20	0.9%	0.36	1.5%	0.41	1.7%	0.00	0.0%	0.55	2.3%

Multisite Precision (Reproducibility)

A multisite precision study was conducted using a 3x5x5 study design across three (3) sites over five (5) days with five (5) replicates per day. Three (3) Premier Resolution Systems (one per site) and Mobile Phase 1, 2, and Diluent Reagents (one lot of each), analytical column, and precision samples for the study were provided to the sites. The study assessed instrument-to-instrument, operator-to-operator, and site-to-site precision. Seven (7) whole blood samples with varying levels of hemoglobin A, A2, F, S, C, D-Los Angeles, and E were tested on the Premier Resolution using the Quick Scan and High-Resolution assay modes.

The performance of the Premier Resolution System in the Multisite Precision Study of the Quick Scan and High Resolution Assay Repeatability and Reproducibility Precision study performed met the predetermined acceptance criteria.

Multisite Precision – Quick Scan

Description	Mean	N	Repeatability		Between-Day		Between-Site		Reproducibility	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
FASC F	17.16	75	0.09	0.52%	0.27	1.55%	0.82	4.80%	0.87	5.07%
FASC A	42.89	75	0.22	0.52%	0.33	0.78%	0.34	0.78%	0.52	1.22%
FASC S	12.87	75	0.07	0.51%	0.06	0.50%	0.09	0.69%	0.13	0.99%
FASC C	14.14	75	0.11	0.78%	0.08	0.57%	0.26	1.87%	0.30	2.11%
A2+F I F	2.94	75	0.04	1.33%	0.04	1.39%	0.12	4.17%	0.14	4.59%
A2+F I A	82.75	75	0.31	0.38%	1.00	1.21%	1.16	1.40%	1.57	1.89%
A2+F I A2	3.11	75	0.04	1.17%	0.06	2.04%	0.06	2.08%	0.10	3.15%
A2+F II F	7.23	75	0.10	1.36%	0.12	1.70%	0.27	3.69%	0.31	4.28%
A2+F II A	45.53	75	0.24	0.52%	0.24	0.53%	0.27	0.60%	0.44	0.96%
A2+F II S	27.63	75	0.18	0.65%	0.21	0.77%	0.19	0.69%	0.34	1.22%
A2 A2	1.63	75	0.03	2.12%	0.03	1.80%	0.05	2.92%	0.07	4.04%
C-Trait C	30.51	75	0.26	0.85%	0.36	1.17%	0.86	2.82%	0.97	3.17%
D-Trait D	35.03	75	0.20	0.57%	0.34	0.96%	0.58	1.64%	0.70	1.99%
E-Trait E	23.08	75	0.34	1.47%	0.31	1.36%	0.73	3.17%	0.87	3.75%

Multisite Precision – High-Resolution

Description	Mean	N	Repeatability		Between-Day		Between-Site		Reproducibility	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
FASC F	17.31	75	0.11	0.64%	0.06	0.35%	1.43	8.28%	1.44	8.31%
FASC A	43.97	75	0.26	0.60%	0.04	0.08%	0.30	0.68%	0.40	0.91%
FASC S	13.46	75	0.10	0.72%	0.06	0.45%	0.07	0.50%	0.13	0.98%

Description	Mean	N	Repeatability		Between-Day		Between-Site		Reproducibility	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
FASC C	14.30	75	0.17	1.17%	0.07	0.47%	0.15	1.05%	0.24	1.65%
A2+F I F	2.89	75	0.07	2.47%	0.04	1.30%	0.07	2.30%	0.10	3.62%
A2+F I A	85.21	75	0.32	0.37%	0.97	1.14%	0.62	0.73%	1.20	1.40%
A2+F I A2	3.03	75	0.06	1.90%	0.05	1.52%	0.02	0.50%	0.08	2.49%
A2+F II F	7.29	75	0.08	1.11%	0.09	1.27%	0.29	3.93%	0.31	4.27%
A2+F II A	46.13	75	0.31	0.67%	0.50	1.09%	0.30	0.65%	0.66	1.44%
A2+F II S	28.99	75	0.19	0.66%	0.32	1.09%	0.37	1.28%	0.52	1.81%
A2 A2	1.59	75	0.05	3.33%	0.03	1.73%	0.03	1.85%	0.07	4.18%
C-Trait C	30.53	75	0.22	0.71%	0.26	0.86%	0.31	1.03%	0.46	1.51%
D-Trait D	36.65	75	0.38	1.03%	0.22	0.59%	0.39	1.07%	0.59	1.60%
E-Trait E	22.25	75	0.27	1.23%	0.30	1.35%	0.46	2.06%	0.61	2.76%

2. Linearity:

A linearity study was conducted to establish the linear range of quantitative measurements of normal hemoglobin A, A2 and F and major variants S, C, D-Los Angeles, and E on the Premier Resolution. The study was performed at a single site. Linearity was determined for HbF, HbA, HbA2, HbS, HbC, HbD-LA, and HbE for both Quick Scan and High Resolution modes. Hemoglobin species of HbF, HbA, HbA2, HbS, HbC, HbD-LA, and HbE were each prepared with 13 equally spaced concentration levels with 4 replicates per level. Quick Scan and High Resolution data were evaluated separately for each hemoglobin A, A2, F, S, C, D-Los Angeles, and E.

The linearity ranges for individual hemoglobin fractions are summarized below.

Hemoglobin	Quick Scan Range	High Resolution Range
HbF	0.4 – 71.6%	0.4 – 72.3%
HbA	0.0 – 89.7%	0.0 – 90.5%
HbA2	1.5 – 6.1%	1.6 – 6.1%
HbS	0.0 – 68.9%	0.3 – 71.3%
HbC	0.0 – 86.6%	0.0 – 85.9%
HbD-LA	0.0 – 85.7%	0.0 – 87.6%
HbE	0.0 – 81.3%	0.0 – 77.1%

3. Analytical Specificity/Interference:

An interference study was conducted to evaluate the susceptibility of the Premier Resolution system to the following interfering substances: D-Glucose, acetaldehyde, lipemia (triglycerides), icterus (bilirubin), acetylsalicylic acid, sodium heparin, lithium heparin, K2EDTA, and K3EDTA. Human blood samples containing HbA, HbA2, HbF, HbS, HbC, HbD-LA and HbE were tested with interfering substances. Each hemoglobin species was evaluated at two different levels. Spiked experimental samples and a control sample were

prepared from the same source of blood for each interferent. From this testing, the maximum amount of the interferent that does not cause analytical interference was determined.

Each substance with the potential to cause interference was tested at a concentration level that is at least three times the highest expected concentration or at least five times the recommended additive concentration for anticoagulants and preservatives.

Overall, it was established that there is no interference with the quantitation of hemoglobin fractions HbF, HbA, HbA2, HbS, HbC, HbD-LA, and HbE from the following interferents up to the concentrations stated in the table below:

Interferent	Concentration	Hemoglobin
D-Glucose (HbF Only)	5000mg/dL	HbF Only
Acetaldehyde	20mg/dL	HbF, HbA, HbA2, HbS, HbC, HbD, HbE
Triglyceride	4500mg/dL	
Unconjugated Bilirubin	20mg/dL	
Conjugated Bilirubin	10mg/dL	
Acetylsalicylic Acid	90mg/dL	
Sodium Heparin	85 IU	
Lithium Heparin	85 IU	
K2EDTA	9 mg/mL	
K3EDTA	9 mg/mL	

4. Assay Reportable Range:

The assay reportable ranges established based on the LoQ and Linearity studies are summarized in the table below.

Hemoglobin	Quick Scan Range	High Resolution Range
HbF	1.1 – 71.6%	1.1 – 72.3%
HbA	2.3 – 89.7%	2.2 – 90.5%
HbA2	1.5 – 6.1%	1.6 – 6.1%
HbS	1.0 – 68.9%	0.9 – 71.3%
HbC	1.0 – 86.6%	1.7 – 85.9%
HbD-LA	1.5 – 85.7%	1.4 – 87.6%
HbE	1.5 – 81.3%	2.7 – 77.1%

5. Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):

Sample Stability

To establish the sample stability claim for patient whole blood samples on the Premier Resolution system, a study was conducted for the Premier Resolution system using samples of normal and abnormal hemoglobins. The stability of the samples when stored at room

temperature (20–25°C), refrigerated (2–8°C), frozen (-18 to -22°C) and frozen (-70°C) was evaluated. Also, after each time point of the study, the hemolysate samples were kept on board and evaluated 24 hours later for on-board stability.

The freeze-thaw effects on patient samples were also evaluated. The freeze-thaw stability testing requires fresh, never frozen samples to be tested initially. The sample then underwent 24 hours of storage in a -65 to -75°C environment. The sample was taken out, thawed, and retested on the same instrument and consumables. This process was repeated for a total of 10 freeze-thaw data points. Each freezing event was required to be stored at -65 to -75°C for at least 24 hours before thawing. This study determined the number of freeze-thaw cycles a sample can go through before degrading.

Whole blood samples of normal, HbF, HbS, HbC, HbD-Los Angeles and HbE were used. Human whole blood samples, free of known interferences, were used for this study. The samples were tested on the Premier Resolution using the Quick Scan and High-Resolution assay modes. Sample stability was assessed in terms of measurand drift for each test sample.

Overall, the sample stability study data support the following claims:

- The recommended storage stability for blood collected as samples in K2EDTA anticoagulant tubes is:
    - 48 hours at 20 to 25ºC (RT)
    - 7 days at 2 to 8ºC (Refrigerated)
    - 168 days at -75 to -65°C (Frozen)
- The on-board stability is 24 hours.
- The recommended number of allowable freeze-thaw cycles is one (1).

Reagent Stability

The stability of the Premier Resolution Mobile Phase 1 (940mL), Premier Resolution Mobile Phase 1 (3.8L), Premier Resolution Mobile Phase 2 (940mL), Premier Resolution Mobile Phase 2 (3.8L), Premier Resolution Diluent (3.8L), Premier Resolution Wash, (940mL), and Premier Resolution Piston Wash (940mL), which are reagents used with the Premier Resolution System, was evaluated. Three lots of these reagents were aged in standard packaging for performance testing at the following timepoints:

- Initial
- 12 Month
- 24 Month
- 26 Month.

At each interval, the in-use (open container) stability claim of 60 day was performance validated as well, including at 30, 60, and 66 days to provide an additional safety margin.

Overall, the Premier Resolution Mobile Phase 1 (940mL), Premier Resolution Mobile Phase 1 (3.8L), Premier Resolution Mobile Phase 2 (940mL), Premier Resolution Mobile Phase 2 (3.8L), Premier Resolution Diluent (3.8L), Premier Resolution Wash (940mL), and Premier

Resolution Piston Wash (940mL) are stable when stored at the specified temperature ranges of 2–28°C/36–82°F for up to two years from the date of production based on successfully completed stability studies.

6. Detection Limit:

A study was conducted to determine the limit of quantitation (LoQ), limit of blank (LoB), and limits of detection (LoD), for hemoglobin A, A2, F, S, C, D-Los Angeles, and E on the Premier Resolution System. The LoB/LoD/LoQ study was performed using one (1) instrument, two (2) different reagent lots over the course of five (5) days with four (4) levels for each phenotype, three (3) replicates per day. Two instruments were allocated to the study to perform the Quick Scan and High-Resolution runs simultaneously. The Quick Scan and High-Resolution data statistics were calculated independent of one another.

For the LoB evaluation, Diluent Reagent, as used for onboard sample dilutions, was utilized as the blank sample determinations. Each run was QC verified with FASC and A2+F controls bracketing for the 60 Limit of Blank data points generated over two days.

For the LoD and LoQ evaluation, human whole blood samples collected in K2EDTA tubes containing 4 different levels of HbA, HbA2, HbF, HbS, HbC, HbD-Los Angeles and HbE were tested in the Quick Scan and High Resolution modes. One Premier Resolution instrument was used for Quick Scan, the second Premier Resolution instrument was used for High-Resolution. Four (4) samples with concentrations between 0.1–5.0% of the analytes, HbF, HbA2, HbS, HbC, HbD-Los Angeles, and HbE, were analyzed daily on each instrument in replicates of three (3) for five (5) days, providing 60 data points per reagent lot of each phenotype in the Quick Scan and High Resolution mode.

The derived LoB, LoD, and LoQ are summarized below.

Hb Phenotype	Quick Scan			High Resolution		
	LoB	LoD	LoQ	LoB	LoD	LoQ
F	0.0%	0.2%	1.1%	0.0%	0.1%	1.1%
A	0.0%	0.1%	2.3%	0.0%	0.7%	2.2%
A2	0.0%	0.1%	1.5%	0.0%	0.2%	1.5%
S	0.0%	0.1%	1.0%	0.0%	0.3%	0.9%
C	0.0%	0.1%	1.0%	0.0%	0.3%	1.7%
D-Los Angeles	0.0%	0.1%	1.5%	0.0%	0.1%	1.4%
E	0.0%	0.1%	1.5%	0.0%	0.6%	2.7%

7. Assay Cut-Off:

Not applicable

8. Accuracy (Instrument):

Not applicable

9. Carry-Over:

A study was conducted to evaluate the carryover effects for hemoglobins A, A2, and F on the Premier Resolution Quick Scan (QS) and High Resolution (HR) assay modes.

In the evaluation of HbA carryover, a variant trait sample (HbS) was used as the low-level concentration sample and normal patient blood was used as the high-level concentration sample. In the evaluation of HbA2 carryover, A2+F Control level I were used as the low-level concentration sample and A2+F Control Level II were used as the high-level concentration sample. In the evaluation of HbF carryover, a high HbF(>14%) patient sample was used as the high-level concentration sample and a normal patient sample was used as the low-level concentration sample.

Overall, the Premier Resolution Quick Scan and High Resolution assays for HbA, HbA2, and HbF passed the pre-defined acceptance criteria and therefore demonstrated no significant carryover in using the Quick Scan or the High Resolution assay mode for the quantitation of HbA, HbA2, and HbF.

B Comparison Studies:

1. Method Comparison with Predicate Device:

A method comparison study was conducted to compare the performance of the Premier Resolution system to that of the predicate, Bio-Rad Variant II system, to demonstrate substantial equivalence between the test method and the comparator method with respect to quantitation of Hb A, A2 and F, and detection of hemoglobins S, C, D and E in patient whole blood samples. The study was performed at three external sites. The test samples at each testing site included normal and abnormal samples.

Each site tested patient samples on the Premier Resolution using both the Quick Scan assay and the High Resolution Assay and on the Variant II instrument. All patient samples were tested on the Premier Resolution within two days of the comparative method or within sample storage stability, whichever was shorter.

Data was analyzed per site and was combined from all sites for analysis. Data analysis consisted of a linear comparison by Passing-Bablok method of Hb A, A2, F, S, C, D and E concentrations between the Premier Resolution and the Bio-Rad Variant II. The standard error of the regression slope and intercept was computed.

Results – All Sites Combined

Quick Scan Mode Vs. Bio-Rad Variant II

Phenotype	N	Interval (%)	Correlation	Slope (95% CI)	Intercept (95% CI)
HbA	682	2.5 to 89.7	0.994	1.1 (1.1, 1.1)	-8.5 (-10.2, -7.0)

Phenotype	N	Interval (%)	Correlation	Slope (95% CI)	Intercept (95% CI)
HbA2	602	1.6 to 6.1	0.972	1.0 (1.0, 1.0)	0.1 (0.1, 0.1)
HbF	160	1.1 to 48.9	0.993	0.9 (0.9, 1.0)	0.1 (0.1, 0.2)
HbS	106	7.5 to 67.1	0.989	0.9 (0.9, 1.0)	2.4 (1.4, 3.6)
HbC	49	9.5 to 82.8	0.996	0.9 (0.9, 0.9)	2.6 (1.3, 4.4)
HbD-LA	17	11.6 to 82.7	0.994	0.9 (0.8, 1.0)	6.9 (2.2, 11.3)
HbE	25	5.5 to 70.4	0.972	1.0 (0.8, 1.2)	-2.3 (-8.5, 2.8)

High Resolution Mode Vs. Bio-Rad Variant II

Phenotype	N	Interval (%)	Correlation	Slope (95% CI)	Intercept (95% CI)
HbA	586	3.5 to 90.5	0.994	1.1 (1.1, 1.1)	-6.9 (-8.2, -5.6)
HbA2	598	1.6 to 6.0	0.971	1.0 (1.0, 1.0)	0.0 (0.0, 0.2)
HbF	158	1.1 to 46.6	0.992	1.0 (1.0, 1.0)	0.0 (0.0, 0.1)
HbS	110	1.9 to 67.9	0.990	1.0 (0.9, 1.0)	2.2 (1.2, 3.5)
HbC	49	10.2 to 82.5	0.993	0.9 (0.8, 0.9)	3.7 (2.3, 6.5)
HbD-LA	17	11.7 to 84.1	0.994	0.9 (0.8, 1.1)	6.1 (1.2, 10.7)
HbE	25	5.3 to 66.7	0.978	0.9 (0.7, 1.1)	-0.4 (-6.7, 3.3)

2. Matrix Comparison:

Whole Blood vs. Hemolysate

An evaluation of matrix effects was conducted in accordance with *CLSI EP14-A2: Evaluation of Matrix Effects; Approved Guideline – Second Edition*. Whole blood collected was used as the reference comparative method against prepared hemolysates. The instrument performed an automated dilution on whole blood samples, prepared hemolysate samples were used to test if there were matrix effects on manual preparation of the hemolysate against the reference, whole blood. Test venous whole blood samples consisted of each hemoglobin, HbA, HbA2, HbF, HbS, HbC, HbD-Los Angeles, and HbE.

Bland-Altman analysis and Passing-Bablok regression analysis were performed on samples of each phenotype. All phenotypes were found to fall within the acceptable criteria.

C Clinical Studies:

1. Clinical Sensitivity:

Not applicable

2. Clinical Specificity:

   Not applicable

3. Other Clinical Supportive Data (When 1. and 2. Are Not Applicable):

   Not applicable

D Clinical Cut-Off:

Not applicable

E Expected Values/Reference Range:

An analysis was conducted to establish the reference range claim for HbA and HbA2 for the Premier Resolution system. This analysis excludes results with reported HbF, HbS, HbC, HbD-LA, HbE and/or an abnormal level of HbA2. Data from human whole blood patient samples collected at three external sites were grouped and analyzed to determine reference range for HbA and HbA2.

Trinity Biotech Premier Resolution assays measured hemoglobins A and A2 on the listed number (N) of apparently healthy females and males, aged 1 to 97. Using the nonparametric technique, the resulting mean with reference range includes the remaining 95% of samples (the 95th percentile), as shown in the tables below:

N	Assay	Hb	Mean (%)	Lower Reference Range Limit (%)	Upper Reference Range Limit (%)
470	Quick Scan	A	87.2	83.0	89.6
485	Quick Scan	A2	3.0	2.4	3.5
374	High-Resolution	A	88.9	85.1	90.5
481	High-Resolution	A2	2.9	2.3	3.3

F Other Supportive Instrument Performance Characteristics Data:
None

VIII Proposed Labeling:

The labeling supports the finding of substantial equivalence for this device.

IX Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.