



510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION DECISION SUMMARY

I Background Information:

A 510(k) Number

K251087

B Applicant

Daxor Corporation

C Proprietary and Established Names

Blood Volume Analyzer (200)

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
JWO	Class II	21 CFR 864.5950 - Blood Volume Measuring Device	HE - Hematology

II Submission/Device Overview:

A Purpose for Submission:

Clearance of New Device

B Measurand:

Red Cell Mass, Plasma Volume and Total Blood Volume

C Type of Test:

Quantitative

III Intended Use/Indications for Use:

A Intended Use(s):

See Indications for Use below.

B Indication(s) for Use:

The Daxor BVA-200® is an automated system that is used to measure/calculate the red cell mass (mL), plasma volume (mL) and total blood volume (mL), along with the related deviations from ideal values by amount (mL) and percentage (%) in adults. In addition, the Normalized Hematocrit (%) and Albumin Transudation Rate (%/min) are calculated. It is an in vitro medical device composed of a microprocessor, software, touchscreen, and gamma counter and accessory convenience kit.

The Daxor BVA-200 is intended to calculate human blood volumes by the method of tracer diffusion (Indicator dilution technique) with I-131 as the tracer after injection of I-131 Human Serum Albumin. The Daxor BVA-200 provides a Quantitative Assessment of total blood and plasma volumes using an automated system.

Data inputs to the software come from the measured characteristics of patient venous whole blood samples collected in K3EDTA vacutainer tubes (hematocrit and tracer concentration) and tracer calibration standards. The patient blood samples and the calibration standards are measured in a gamma counter, whose output is automatically input to this calculation program. The package also calculates the patient expected (or ideal) blood volume from physical parameters. Hyper- or hypovolemia, and associated red cell volumes are reported, with statistics showing the quality of the results.

For in vitro diagnostic use in a Clinical Laboratory setting and operated by laboratory technicians.

Rx use only.

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

D Special Instrument Requirements:

BVA-200

IV Device/System Characteristics:**A Device Description:**

The Daxor BVA-200 is an automated system that is used to calculate the red cell mass, plasma volume and total blood volume. It is an in vitro medical device composed of a microprocessor, software, touchscreen, and gamma counter. The accessory convenience kit includes single-use whole blood cartridges and protective sleeves. The Daxor BVA-200 is designed to calculate human blood volume, using the method of tracer dilution, utilizing tagged serum albumin (Volumex I-131, resulting in "I-HSA"). Data inputs to the software come from the measured characteristics of patient blood samples (hematocrit and tracer concentration) and tracer calibration standards. The package also calculates the patient expected (or ideal) blood volume from physical parameters. Hyper- or hypovolemia, and associated red cell volumes, are reported, with statistics showing the quality of the results. The patient blood samples and the

calibration standards are measured in a gamma counter, whose output is automatically input to this calculation program. The BVA-200 can be carried by hand or in a small case and may be used in proximity to the patient. It has a touchscreen for operator interaction and provides clear instructions and prompts for the steps necessary for performing the test.

B Principle of Operation:

BVA-200 device is capable of detecting I-131 concentrations quantitatively based on the known rate of gamma emissions from radioactive decay which is tightly concentration dependent. The source of I-131 in the original injectate is, after dilution, present in the quantities needed and thus will readily register against background for both detectors, with the number of counts scaling linearly with activity and the error scaling as the square root of activity. This is the counting statistical behavior required for the indicator dilution technique mathematics. If the time of blood draw differs from current, both devices will accommodate the extended time span by 'discounting' the gamma count rate by the known rate of decay from actual time of blood draw to actual time of gamma concentration measurement. The BVA-200 software will report the total blood volume with results that range from 1,700 mL to 14,500 mL as a function of the patient's true blood volume calculated by radio diffusion. The Daxor BVA-200 is used to measure/calculate the red cell volume (mL), plasma volume (mL), and total blood volume (mL), along with the related deviations from ideal values by amount (mL) and percentage (%) in adults. In addition, the Normalized Hematocrit (%) and Albumin Transudation Rate (%/min) are calculated.

C Instrument Description Information:

1. Instrument Name:

Blood Volume Analyzer (200)

2. Specimen Identification:

Manual Data Entry- Patient data entered into the BVA-200 includes administrative information (operator and facility), patient information (ID, height, weight, gender), injectate lot, and post-injection sampling times.

3. Specimen Sampling and Handling:

Remove the red cap from the clear sleeve and remove the cartridge from the sleeve. Attach an empty 3-mL purple topped vacutainer to the IV extension set check-valve. Allow the vacutainer to collect at a minimum 2.5 mL of blood. Remove the vacutainer from the check valve. Fill the 3-mL syringe with a minimum of 2-mL of blood.

Transfer blood from syringe into the cartridge until the cartridge is fully loaded. Hold the cartridge upright when filling. Inject until back-pressure is felt. The cartridges were field tested to ensure that the design allows for highly accurate volumes during the fill process. Inspect for bubbles to ensure that the cartridge is fully loaded.

The luer-lock on the cartridge has a bidirectional valve with a silicone actuator. Once activated by the syringe this valve allows the free flow of air or fluid. When the syringe is removed from the whole blood cartridge, the bidirectional valve in the cartridge luer-lock ensures that there will be no leakage. Place the filled cartridge back into the sleeve with the small luer-lock side facing up as shown on the label. Place the red cap back on the sleeve.

4. Calibration:

Calibration is automatically checked and, if necessary, adjusted at the beginning of each Daily QC test. User cannot proceed with the test until Daily QC has been performed and passed.

5. Quality Control:

Daily QC checks (a) background, (b) potential contamination of well, (c) the Volumex Standard, and (d) calibration, detector resolution, and constancy of the gamma counter. This test must be performed each day that patient samples are measured. The BVA-200 has a pop-up warning when Daily QC is due. Quarterly QC checks Efficiency and Linearity. Efficiency certifies the brightness of the detector by counting a source to verify that the received counts are within an acceptable range for the known strength of the source. Linearity measures energy calibration, detector resolution, and linearity of the gamma counter. The QC calibration sources, which vary in activity, span the measurement range of the gamma counter. The BVA-200 has a pop-up warning when Quarterly QC is due. The user cannot proceed with testing until appropriate QC testing has passed.

V Substantial Equivalence Information:

A Predicate Device Name(s):

Automated Multi-point Blood Volume Analyzer

B Predicate 510(k) Number(s):

K964406

C Comparison with Predicate(s):

Device & Predicate Device(s):	<u>Device</u> <u>K251087</u>	<u>Predicate</u> <u>K964406</u>
Device Trade Name	Blood Volume Analyzer (200)	Automated Multi-Point Blood Volume Analyzer
General Device Characteristic Similarities		
Intended Use/Indications For Use	The Daxor BVA-200® is an automated system that is used to measure/calculate the red cell mass (mL), plasma volume (mL) and total blood volume (mL), along with the related deviations from ideal values by amount (mL) and percentage (%)	The Daxor BVA-100 is a software package designed to calculate human blood volume, using the method of tracer dilution, utilizing tagged serum albumin (a commonly used tag is I-131, resulting in "I-HSA"). Data inputs to the software

Device & Predicate Device(s):	Device <u>K251087</u>	Predicate <u>K964406</u>
	in adults. In addition, the Normalized Hematocrit (%) and Albumin Transudation Rate (%/min) are calculated. It is an in vitro medical device composed of a microprocessor, software, touchscreen, and gamma counter and accessory convenience kit. The Daxor BVA-200 is intended to calculate human blood volumes by the method of tracer diffusion (Indicator dilution technique) with I-131 as the tracer after injection of I-131 Human Serum Albumin. The Daxor BVA-200 provides a Quantitative Assessment of total blood and plasma volumes using an automated system. Data inputs to the software come from the measured characteristics of patient venous whole blood samples collected in K3EDTA vacutainer tubes (hematocrit and tracer concentration) and tracer calibration standards. The patient blood samples and the calibration standards are measured in a gamma counter, whose output is automatically input to this calculation program. The package also calculates the patient expected (or ideal) blood volume from physical parameters. Hyper- or hypovolemia, and associated red cell volumes are reported, with statistics showing the quality of the results. For in vitro diagnostic use in a Clinical Laboratory setting and operated by laboratory technicians. Rx use only.	come from the measured characteristics of patient blood samples (hematocrit and tracer concentration) and tracer calibration standards. The package also calculates the patient expected (or ideal) blood volume from physical parameters. Hyper- or hypovolemia, and associated red cell volumes, are reported, with statistics showing the quality of the results. The patient blood samples and the calibration standards are measured in a gamma counter, whose output is automatically input to this calculation program.
Principle of Operation	Indicator Dilution method	Same
Operator	Nuclear Medical Technician (NucMed Tech)	Same
Tracer	I-131 labeled Human Serum Albumin	Same
Radiation emitted by device	None (for radiation emitted by disposable samples placed in device). Gamma ("Geiger") counters do not emit radiation but only detect	Same

Device & Predicate Device(s):	Device <u>K251087</u>	Predicate <u>K964406</u>
	radiation. Further, the shielding around the detector itself is designed to isolate the gamma counter from ambient or external radiation to permit counting samples of low activity (improve signal to noise ratio).	
Values Reported	Total Blood Volume (TBV), Red Cell Volume (RCV), Plasma Volume (PV), along with patient-specific norms and deviations	Same
Scintillation Counter	Scintillates on bombardment with gamma rays	Same
Patient exposure to radiation	I-131 dose is limited to maximum activity of 25 microcuries (μCi). The EDE from a $25\mu\text{Ci}$ dose is 101 rem, which is roughly the same as the annual exposure from naturally occurring sources of radiation (excluding radon) at sea level.	Same
Operator exposure to radiation	Operator (Nuclear Medical technician) is exposed to very small fraction (approximately 1/1000) of patient radiation during procedure, based on time handling dose and in proximity to patient. Nuclear Medical technicians are monitored for exposure to radiation.	Same
Quality Control	Integrated Procedures	Same
Report Available	Onscreen Printed via attached printer Downloaded as file via thumb drive	Same
Total Blood Volume	The BVA-200 software will report the total blood volume with results that range from 1,700 mL to 14,500 mL as a function of the patient's true blood volume calculated by radio diffusion.	Same
General Device Characteristic Differences		
Sample Type	Whole Blood	Plasma
Phlebotomy volume required	3 mL blood	6 mL blood
Sample size	1.8 mL	1 mL
Shielding	Tungsten	Lead
Gamma Detection	Smaller Crystal size and material - counts fewer emissions, linearly corrected mathematically	Larger Crystal size and material - counts more emissions
Crystal Material	CsI advantages increased moisture	NaI

Device & Predicate Device(s):	<u>Device</u> <u>K251087</u>	<u>Predicate</u> <u>K964406</u>
	resistance and plastic deformation rather than cracking	
Photomultiplier	Photomultiplier silicon	Photomultiplier tube
Mitigation of Radiation Contamination	Samples are introduced into detector well inside disposable plastic sleeves.	Samples are placed in plastic drop tubes of sample changer. If drop tubes become contaminated, they can be cleaned or swapped out.
Samples Introduced to gamma counter	Directly by operator, in response to software prompts.	Aliquots are placed in a carousel according to designated pattern indicated on device, and carousel sequentially delivers them to the gamma counter well.
User Interaction	Integrated Touchscreen (6" diagonal)	Attached Windows based computer & keyboard

VI Standards/Guidance Documents Referenced:

CLSI EP05-A3, Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline —3rd Edition

CLSI EP06, Evaluation of Linearity of Quantitative Measurement Procedures —2nd Edition

CLSI EP07, Interference Testing in Clinical Chemistry —3rd Edition

CLSI EP09c, Measurement Procedure Comparison and Bias Estimation Using Patient Samples—3rd Edition

CLSI EP25, Evaluation of Stability of In Vitro Diagnostic Reagents —2nd Edition

CLSI EP28-A3c, Defining Establishing and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline —3rd Edition

CLSI EP37, Supplement Tables for Interference Testing in Clinical Chemistry—1st Edition

IEC 62304, Edition 1.1 2015-06 CONSOLIDATED VERSION Medical Device Software – Software life cycle processes

IEC 61010-1, Edition 3.1 2017-01 CONSOLIDATED VERSION Safety requirements for electrical equipment for measurement, control, and laboratory use – Part 1 General requirements.

IEC 60601-1-2, Edition 4.1 2020-09 CONSOLIDATED VERSION Medical electrical equipment – Part 1-2: General requirements for basic safety and essential performance – Collateral Standard: Electromagnetic disturbances.

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

Repeatability/Reproducibility

This study validated the precision of the BVA-200 compared to the predicate BVA-100 device. This test compared the values for Total Blood Volume (TBV), Red Cell Volume (RCV), Plasma Volume (PV), Gamma Counts, and Normalized Hematocrit (nHct). The study was conducted with 10 tracer-spiked concentrations. The study included two operators, two calibrator lots (standards), and two instruments across two days per site (between-instrument nested between-site), two runs per day, and two replicates per run for a total of 64 data points per sample set (one whole blood sample separated into plasma + red cell concentrate). Low Hct and High Hct blood to set baseline from the same subject. Volumex chosen was the highest activity level for this study at 30 μ Ci. All total precision percentage coefficient of variation results were below 3.6% CV.

BVA-200 TBV

Sample	N	Mean	Repeatability (Within-Run)		Between-Run		Between-Day		Between-Operator		Between-Instrument		Between-Calibrator		Reproducibility Total Precision	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Sample (HIGH_Vol_1000)	64	989	16.7	1.69	0.1	0.01	14.3	1.45	2.0	0.20	4.2	0.42	3.3	0.33	22.71	2.30
Sample (HIGH_Vol_15000)	64	14,322	379.6	2.65	14.2	0.10	186.6	1.30	42.7	0.30	93.7	0.65	101.2	0.71	447.17	3.12
Sample (HIGH_Vol_2500)	64	2,443	51.6	2.11	4.6	0.19	36.6	1.50	6.9	0.28	12.3	0.50	20.1	0.82	68.02	2.78
Sample (HIGH_Vol_5000)	64	4,967	120.6	2.43	6.6	0.13	101.1	2.04	42.4	0.85	40.0	0.81	10.5	0.21	168.28	3.39
Sample (HIGH_Vol_7500)	64	7,392	173.3	2.34	1.7	0.02	106.0	1.43	23.8	0.32	52.6	0.71	60.6	0.82	219.72	2.97
Sample (LOW_Vol_1000)	64	1,108	13.8	1.25	1.3	0.12	14.1	1.27	4.3	0.39	2.8	0.25	3.7	0.33	20.76	1.87
Sample (LOW_Vol_15000)	64	16,133	353.9	2.19	50.1	0.31	79.9	0.50	107.9	0.67	115.2	0.71	81.9	0.51	407.14	2.52
Sample (LOW_Vol_2500)	64	2,747	68.6	2.50	2.1	0.08	31.3	1.14	15.5	0.56	1.7	0.06	22.4	0.82	80.22	2.92
Sample (LOW_Vol_5000)	64	5,419	104.6	1.93	8.0	0.15	84.1	1.55	17.7	0.33	33.8	0.62	26.2	0.48	142.20	2.62
Sample (LOW_Vol_7500)	64	6,925	151.0	2.18	1.0	0.01	84.1	1.21	63.7	0.92	7.3	0.11	47.6	0.69	190.40	2.75

BVA-200 RCV

Sample	N	Mean	Repeatability (Within-Run)		Between-Run		Between-Day		Between-Operator		Between-Instrument		Between-Calibrator		Reproducibility Total Precision	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Sample (HIGH_Vol_1000)	64	536	9.0	1.68	0.0	0.00	7.8	1.46	1.1	0.21	2.3	0.43	1.9	0.35	12.33	2.30
Sample (HIGH_Vol_15000)	64	7,984	211.6	2.65	7.9	0.10	104.0	1.30	23.8	0.30	52.2	0.65	56.4	0.71	249.25	3.12
Sample (HIGH_Vol_2500)	64	1,343	28.4	2.11	2.6	0.19	20.1	1.50	3.8	0.28	6.7	0.50	11.2	0.83	37.44	2.79
Sample (HIGH_Vol_5000)	64	2,763	67.1	2.43	3.7	0.13	56.3	2.04	23.7	0.86	22.2	0.80	5.8	0.21	93.67	3.39
Sample (HIGH_Vol_7500)	64	4,121	96.6	2.34	0.9	0.02	59.1	1.43	13.2	0.32	29.3	0.71	33.8	0.82	122.48	2.97
Sample (LOW_Vol_1000)	64	186	2.3	1.24	0.2	0.11	2.4	1.29	0.7	0.38	0.4	0.22	0.6	0.32	3.48	1.87
Sample (LOW_Vol_15000)	64	2,834	62.2	2.19	8.8	0.31	14.0	0.49	19.0	0.67	20.2	0.71	14.5	0.51	71.57	2.53
Sample (LOW_Vol_2500)	64	464	11.6	2.50	0.3	0.06	5.3	1.14	2.6	0.56	0.3	0.06	3.8	0.82	13.57	2.92
Sample (LOW_Vol_5000)	64	928	17.9	1.93	1.4	0.15	14.4	1.55	3.0	0.32	5.8	0.62	4.4	0.47	24.33	2.62

Sample	N	Mean	Repeatability (Within-Run)		Between-Run		Between-Day		Between-Operator		Between-Instrument		Between-Calibrator		Reproducibility Total Precision	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Sample (LOW_Vol_7500)	64	1,146	25.0	2.18	0.2	0.02	13.9	1.21	10.5	0.92	1.2	0.10	7.9	0.69	31.50	2.75

BVA-200 PV

Sample	N	Mean	Repeatability (Within-Run)		Between-Run		Between-Day		Between-Operator		Between-Instrument		Between-Calibrator		Reproducibility Total Precision	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Sample (HIGH_Vol_1000)	64	453	7.6	1.68	0.0	0.00	6.6	1.46	0.9	0.20	1.9	0.42	1.5	0.33	10.39	2.29
Sample (HIGH_Vol_15000)	64	6,339	168.0	2.65	6.3	0.10	82.5	1.30	18.9	0.30	41.4	0.65	44.8	0.71	197.86	3.12
Sample (HIGH_Vol_2500)	64	1,101	23.2	2.11	2.0	0.18	16.5	1.50	3.1	0.28	5.5	0.50	9.1	0.83	30.61	2.78
Sample (HIGH_Vol_5000)	64	2,204	53.5	2.43	3.0	0.14	44.9	2.04	18.9	0.86	17.7	0.80	4.7	0.21	74.70	3.39
Sample (HIGH_Vol_7500)	64	3,271	76.7	2.34	0.8	0.02	47.0	1.44	10.5	0.32	23.3	0.71	26.8	0.82	97.28	2.97
Sample (LOW_Vol_1000)	64	922	11.5	1.25	1.1	0.12	11.7	1.27	3.6	0.39	2.3	0.25	3.0	0.33	17.25	1.87
Sample (LOW_Vol_15000)	64	13,299	291.7	2.19	41.3	0.31	65.8	0.49	89.0	0.67	95.0	0.71	67.6	0.51	335.62	2.52
Sample (LOW_Vol_2500)	64	2,283	57.1	2.50	1.7	0.07	26.0	1.14	12.8	0.56	1.4	0.06	18.6	0.81	66.72	2.92
Sample (LOW_Vol_5000)	64	4,492	86.6	1.93	6.7	0.15	69.7	1.55	14.7	0.33	28.1	0.63	21.6	0.48	117.79	2.62
Sample (LOW_Vol_7500)	64	5,778	126.0	2.18	0.8	0.01	70.2	1.21	53.2	0.92	6.1	0.11	39.8	0.69	158.92	2.75

BVA-200 nHct

Sample	N	Mean	Repeatability (Within-Run)		Between-Run		Between-Day		Between-Operator		Between-Instrument		Between-Calibrator		Reproducibility Total Precision	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Sample (HIGH_Vol 1000)	64	12	0.2	1.67	0.0	0.00	0.2	1.67	0.0	0.00	0.1	0.83	0.0	0.00	0.30	2.50
Sample (HIGH_Vol 15000)	64	175	4.7	2.69	0.2	0.11	2.3	1.31	0.5	0.29	1.2	0.69	1.2	0.69	5.53	3.16
Sample (HIGH_Vol 2500)	64	29	0.6	2.07	0.1	0.34	0.4	1.38	0.1	0.34	0.2	0.69	0.2	0.69	0.79	2.72
Sample (HIGH_Vol 5000)	64	61	1.5	2.46	0.1	0.16	1.2	1.97	0.5	0.82	0.5	0.82	0.1	0.16	2.05	3.36
Sample (HIGH_Vol 7500)	64	90	2.1	2.33	0.0	0.00	1.3	1.44	0.3	0.33	0.6	0.67	0.7	0.78	2.65	2.95
Sample (LOW_Vol 1000)	64	4	0.1	2.50	0.0	0.00	0.1	2.50	0.0	0.00	0.0	0.00	0.0	0.00	0.14	3.54
Sample (LOW_Vol 15000)	64	62	1.4	2.26	0.2	0.32	0.3	0.48	0.4	0.65	0.4	0.65	0.3	0.48	1.58	2.55
Sample (LOW_Vol 2500)	64	10	0.3	3.00	0.0	0.00	0.1	1.00	0.1	1.00	0.0	0.00	0.1	1.00	0.35	3.46
Sample (LOW_Vol 5000)	64	20	0.4	2.00	0.0	0.00	0.3	1.50	0.1	0.50	0.1	0.50	0.1	0.50	0.53	2.65
Sample (LOW_Vol 7500)	64	25	0.6	2.40	0.0	0.00	0.3	1.20	0.2	0.80	0.0	0.00	0.2	0.80	0.73	2.91

2. Linearity:

This study validated the linearity of the analytical measurement range of the BVA-200 compared to the predicate BVA-100 device. This test measured the linearity of values for Total Blood Volume (TBV), Red Cell Volume (RCV), Plasma Volume (PV), Gamma Counts, and Normalized Hematocrit (nHct). Multiple samples were measured n=319 in both the BVA-100 and BVA-200 to assess both linearity and bias at the high and low measurements. The following results were obtained from the data in the method comparison study:

	N	Mean Expected	Mean Observed	SD	CV Percent	Global Slope	Mean Bias Percent	CI Lower	CI Upper
TBV	319	5323	5348	170	3.24	1.02	0.41	5088	5608
RCV	319	1905	1912	56	3.00	1.01	0.38	1828	1996
PV	319	3417	3433	105	3.11	1.02	0.37	3275	3590

	N	Mean Expected	Mean Observed	SD	CV Percent	Global Slope	Mean Bias Percent	CI Lower	CI Upper
nHCT	319	40.14	40.27	1.22	3.00	1.00	0.37	38.43	42.11

An additional study using contrived samples (from one subject whole blood) was performed to verify linearity and absence of bias at very high and low volume measurements (2000 ml to 18000 ml). Analysis was performed at nine analyte concentration levels, which were known relative to one another by dilution ratios or by formulation. Two replicates were performed at each concentration level. The concentration levels exceeded the minimum and maximum concentration levels claimed in the analytical measurement range. This test compared the linearity of values from TBV, RCV, PV, gamma counts and normalized HCT, between BVA-100 and BVA-200. Performed by three operators on three instruments (two BVA-200 and one BVA-100) for a total of n=54 samples tested. A chosen dose above 30 μ Ci was used as this dose was not injected into anyone. The coefficient of variation (CV) for repeatability was $\leq 5\%$ for all measured parameters across the tested concentration range. The maximum deviation from linearity was $\leq 8\%$ for all measured parameters across the tested concentration range, as determined by comparison to a linear regression model.

Also, this study was also used to validate the albumin transudation rate (ATR) linearity of the BVA-200 compared to the predicate BVA-100 device. Analysis was performed at five analyte concentration levels (from one subject whole blood), which were known relative to one another by dilution ratios or by formulation. Two replicates were performed at each concentration level (n=25 samples per replicate) tested on each device. A chosen dose above 30 μ Ci was used as this dose was not injected into anyone. The coefficient of variation (CV) for repeatability was $\leq 0.05\%$ for all measured parameters across the tested concentration range. In conclusion, there is no clinically meaningful deviation from linearity.

3. Analytical Specificity/Interference:

A hemolysis interference study was performed. Hemolysis is a common interferant in medical diagnostic tests involving measuring analytes in blood. A study was performed with contrived samples to compare the BVA-200 reported parameters across three hemolysis levels. Baseline samples were verified to have no hemolysis. Partial hemolysis was induced by subjecting blood samples to a partial freezing cycle at -20C. Gross hemolysis was induced by subjecting the partially hemolyzed blood samples to an additional complete freezing cycle (until completely frozen) at -20C. Level of hemolysis was verified by three independent methods (colorimetric matching, quantification of fluorescent absorption at 540 nm, and Hct measurement). Ten independent samples were used, with volume values measured after partial hemolysis and gross hemolysis compared to the baseline (no hemolysis). Results for all parameters (TBV, PV, RCV, and nHct) were not affected by hemolysis: the difference between the partial hemolysis values and the no hemolysis values were - 0.72% $\pm$ 0.77%, expressed as a percentage of the baseline no hemolysis values; and gross hemolysis values were - 0.14% $\pm$ 2.16%, expressed as a percentage of the baseline no hemolysis values.

4. Assay Reportable Range:

Not Applicable.

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

Sample Stability

Analysis was performed on 10 samples in whole blood collection cartridges. Testing was conducted under well mixed, 18-hour, 24-hour, 48-hour, and 120-hour settling conditions. The study performed validates the measurement of cartridges up to four days of stability at refrigerated (4°C/ 40°F) and room temperature (22°C/ 72°F).

6. Detection Limit:

Not Applicable.

7. Assay Cut-Off:

Not Applicable.

8. Accuracy (Instrument):

Method Comparison Study

The method comparison study was conducted at three sites (one laboratory and two hospitals) including 319 independent blood volume measurements from patients 18 years old or older. There were nine operators that tested samples on the BVA-200. Each subject received an injection of radioactive tracer, and then 5 separate blood samples were taken at subsequent times, each to be used to calculate an independent single-point blood volume measurement. The Volumex tracer required for BVA testing was supplied by Daxor. BVA-200 personnel were blinded as to the results of the BVA-100 measurement. The subjects included patients with heart disease (including congestive heart failure), hypertension, hypercholesterolemia, anemia, diabetes, thyroid disease, renal disease, clotting disorders, trauma, and a variety of related concomitant medications; an amputee was included among the subjects.

Comparison of a sufficient number of full 5-point time-zero blood volume measurements between BVA-100 and BVA-200 devices, to establish substantial equivalence, including measurement of:

- Total Blood Volume (TBV)
- Red Cell Volume (RCV)
- Plasma Volume (PV)
- Albumin transudation rate (ATR)

The following table shows the results for Passing-Bablok and Deming Regressions for the Instrument vs Comparator (BVA-200 vs. BVA-100):

Measure	Regression	N	Slope (95% CI)	Intercept (95% CI)	Pearson correlation coefficient
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TBV	Passing-Bablok	319	1.031 (1.014 to 1.049)	-138 (-235 to -59)	0.99
TBV	Deming	319	1.033 (1.017 to 1.050)	-153 (-241 to -69)	0.99
RCV	Passing-Bablok	319	1.016 (1.002 to 1.030)	-25 (-50 to 2)	0.99
RCV	Deming	319	1.024 (1.008 to 1.040)	-37 (-68 to -10)	0.99
PV	Passing-Bablok	319	1.033 (1.016 to 1.051)	-99 (-155 to -46)	0.99
PV	Deming	319	1.029 (1.014 to 1.046)	-83 (-138 to -32)	0.99
nHct	Passing-Bablok	319	1.007 (0.982 to 1.032)	-0.19 (-1.18 to 0.77)	0.98
nHct	Deming	319	1.022 (0.999 to 1.047)	-0.76 (-1.71 to 0.21)	0.98

9. Carry-Over:

This protocol established the test procedure to validate that the BVA-200 met the carry-over effect standards. Since the BVA-200 device utilized an Iodinated-Human Serum Albumin (I-131) which can lead to sample carry-over from one specimen reaction into the subsequent specimen reactions, the carry-over study was performed to determine if any of the amount of I-131 sample was carried over from one specimen to next such that a high I-131 sample could impact the results of other parameters for a subsequent low-level sample (desired volume 2000, 18000). Analysis was performed on four separate samples in whole blood collection cartridges. Testing follows a series of high samples followed by a series of low samples in addition to alternating high and low samples. A chosen dose above 30 μ Ci was used as this would not be injected into anyone. Sufficient high-level samples immediately followed by low-level samples by the same operator and with the same equipment were utilized to assess the potential for carryover. In conclusion, there is no carryover observed.

B Comparison Studies:

1. Method Comparison with Predicate Device:

Discussed under Instrument Accuracy.

2. Matrix Comparison:

Not Applicable.

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:

BVA-200 Verification of Reference Ranges

The reference ranges for the BVA-200 (n=22 healthy subjects) confirmed the reference range of the ideal (patient normal) values for the calculated volumes (which are based on calculations).

Reference Status	Normal	Has Medical Condition
N	22	41
Age	36.7 ± 16.5	53.8 ± 16.8
Sex	Female = 59% Male = 41%	Female = 24% Male = 76%
Inpatient / Outpatient	Outpatient Subject = 100%	Outpatient Subject = 54% Inpatient Subject = 46%
Hct	41.3 ± 3.1	39.5 ± 5.91
Deviation from Ideal Weight (%)	26.9% ± 33.7%	40.2% ± 30.5%
Ideal TBV	4860 ± 655	5430 ± 848
Ideal RCV	1850 ± 328	2150 ± 397
Ideal PV	3010 ± 352	3280 ± 466
BVA200_TBV	4950 ± 808	5770 ± 1420
BVA200_RCV	1850 ± 357	2030 ± 507
BVA200_PV	3110 ± 497	3730 ± 1070
BVA200_SD	0.0196 ± 0.0107	0.0154 ± 0.00641
BVA200_Slope (%/min)	0.205% ± 0.070%	0.197% ± 0.076%
BVA200_TBV Deviation from patient Ideal (%)	+1.75% ± 7.77%	+5.72% ± 15.8%
BVA200_RCV Deviation from patient Ideal (%)	-0.13% ± 8.29%	-5.40% ± 15.3%
BVA200_PV Deviation from patient Ideal (%)	+3.07% ± 10.5%	+13.1% ± 23.2%

Value	Normal Range	Normal Females (N=13)	Normal Males (N=9)
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TBV	-8 to +8	0.529 ± 0.09		3.52 ± 5.58		
RCV	-10 to +10	0.95 ± 8.39		-1.69 ± 8.39		
PV	-8 to +8	0.291 ± 11.9		7.07 ± 6.78		
ATR	0 to 0.25	0.179 ± 0.0608		0.242 ± 0.0692		
nHct	37 - 41 (females) 40 - 46 (males)	39.0 ± 4.53		44.2 ± 3.74		
Value		Normal	Mild	Moderate	Severe	Extreme
TBV (absolute dev %)		0 to 8	>8 to 16	>16 to 24	>24 to 32	>32
RCV (absolute dev %)		0 to 10	>10 to 20	>20 to 30	>30 to 40	>40
PV (absolute dev %)		0 to 8	>8 to 16	>16 to 24	>24 to 32	>32
Value		Normal	Elevated		High	Very High
ATR (%/min)		0 to 0.25	0.25 to 0.40		0.40 to 0.50	> 0.50

F Other Supportive Instrument Performance Characteristics Data:

Validation Studies

A study on container suitability was performed to determine impact of settling or non-uniformity of blood components, cartridge drop testing, incline testing, isotope emission characteristics over time and temperature stress, and device and sample shipping impact on gamma count measurement accuracy, along with an explanation of radiation stability.

Validate the process for manufacturing the Whole blood Cartridge

The study was performed to validate the process for manufacturing the Whole Blood Cartridge. A total of n=109 cartridge sets (body and lid) were included in the assessment. Three lots were included in the study. A 30-psi liquid pressure test limit was determined by sampling people's maximum applicable force using a 3 mL syringe and by surveying nuclear medicine technician's maximal perceived force in a clinical setting (maximum pressure a reasonably trained individual would likely apply). Distilled water (3mL syringe) was used to press the plunger until the analog pressure gauge reads 30 psi for 3 seconds. The same cartridge was tested twice (n=218 measurements). Visual inspections of cartridge for leaks were performed. If there were leaks this would be marked as failure. The weight range of the filled cartridges were within the required range of 1.8660g to 1.9241 g for both rounds of testing. There were no failures noted.

Operational Use on an Incline

The study was provided to determine the quantitative effect of tilting the BVA-200 unit during use. The BVA-200 unit was placed on a non-level surface during use and four different tilt positions were evaluated by positioning the instrument at two longitudinal (fore and aft) and two latitude (left and right) at 15-degree angles. The blood volume analysis was performed on normal and abnormal samples using 20 cartridges, sleeves and caps. All parameters were less than 5% average percent difference (nHct, TBV, RCV, PV) and average absolute difference ATR less than 0.05%, tests passed.

Cartridge Drop Test

The study was provided to test for vulnerability to performance changes in the BVA-200 cartridge after experiencing mechanical shock such as drop from benchtop height (48 inches) on its largest face and one of its edges (ATM D5276 standing height for plasticware). The cartridge does not have corners; therefore corner drops will not be performed. Blood volume analysis was performed before and after testing on normal and abnormal samples using 20 cartridges, sleeves and caps. All parameters were less than 5% average percent difference (nHct, TBV, RCV, PV) and average absolute difference ATR less than 0.05%, tests passed.

BVA-200 Device and Sample Shipping

The study was provided to establish a qualified method of packaging for shipping the BVA-200 unit and whole blood samples as recommended by ISTA 3A standard, performed by contract vendor. Blood volume analysis was performed before and after testing on normal and abnormal samples using 40 cartridges, sleeves and caps. Initial condition BVA-200 rugged plastic shipping container, and refrigerated shipper tested in temperature and humidity (21°C 32% 12 hours), controlled temperature and humidity (100°F, 85% RH 72 hours), shock 9 drops, vibration random with and without top load, random vibration under low pressure, shock 8 drops, rotational edge drop 200 mm (8 in), full rotational flat drop, and bridge impact 400 mm (16 in). All parameters were less than 5% average percent difference (nHct, TBV, RCV, PV) and average absolute difference ATR less than 0.05%, tests passed.

Preliminary thermal testing of the cartridges was performed during the engineering / design phase, subjecting the cartridges to -14°C and 40°C for extended periods. Even though membranes of some cartridges ruptured on freezing, this testing showed that radiation counts were stable after exposure to either temperature extreme. This would be expected based on the insensitivity of gamma emission from I-131 (the analyte) to temperature above zero degrees Kelvin, so long as the rupture is not accompanied by loss of contents. It is not recommended to ship filled WBC if there is any possibility of encountering freezing temperatures during transit and the packaging is not temperature stabilized.

Sample Stability

BVA-200 Settling Effect Study

The spiked venous whole blood stability, settling, FEDEX shipping study, and non-level positioning demonstrate that the gamma emission from a fixed amount of blood is impervious to temperature and humidity; that the decrease in radiation emission over time corresponds to the known decrease in radiation from the isotope in question (I-131); that the WBCC can withstand shipping; that the BVA-200 operates in a non-level position up to 15 degrees in any direction; and that settling does not affect gamma emissions read by the gamma counter scintillator inside the BVA-200. Stability testing was performed on whole blood cartridges that were first measured, then allowed to settle in either refrigerated or room temperature conditions for a period up to four days. Samples were recounted at 18, 24, 48, and 120 hours in both agitated and settled states. Contrived samples were used that covered a wide range of possible Hct and volume values. No significant differences were observed, nor was there any significant drift of measurements observed. The study performed validates the measurement of cartridges up to four days of stability at refrigerated (4°C/ 40°F) and room temperature (22°C/ 72°F).

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.