510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

A. 510(k) Number:

K172173

B. Purpose for Submission:

Clearance of new device

C. Measurand:

Hemoglobin

D. Type of Test:

Quantitative determination of hemoglobin

E. Applicant:

EKF-diagnostic GmbH

F. Proprietary and Established Names:

DiaSpect Tm system

G. Regulatory Information:

1. Regulation section:

   21 CFR 864.5620, Automated hemoglobin system

2. Classification:

   Class II

3. Product code:

   GKR, System, hemoglobin, automated

4. Panel:

   Hematology (81)

H. Intended Use:

1. Intended use(s):

   The DiaSpect Tm system is intended for the in vitro quantitative measurement of total hemoglobin in non-anticoagulated capillary whole blood and venous whole blood drawn in K_2EDTA or lithium heparin tubes. The DiaSpect Tm system consists of the DiaSpect Tm analyzer and specifically designed disposable cuvettes, the DiaSpect Tm Cuvettes. The device is intended for use in point-of-care settings. The DiaSpect Tm analyzer is only to be used with DiaSpect Tm Cuvettes.

2. Indication(s) for use:

   Same as intended use

3. Special conditions for use statement(s):

   For prescription use only

4. Special instrument requirements:

   DiaSpect Tm analyzer with DiaSpect Tm Cuvettes

I. Device Description:

The DiaSpect Tm System consists of an analyzer and cuvettes. The DiaSpect Tm analyzer is a spectrophotometric instrument for the measurement of total hemoglobin concentration in unaltered human blood. The DiaSpect Tm Cuvette is injection-molded of poly methyl methacrylate (PMMA) and contains a cavity of 10 µL volume. The distance between the walls of the optical window is approximately 0.13 mm, permitting photometric determination of hemoglobin in undiluted blood. The cuvette does not contain any reagents.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   HemoPoint® H2 Measurement System

2. Predicate 510(k) number(s):

   K081719

3. Comparison with predicate:

Similarities		
Item	Device DiaSpect Tm Analyzer K172173	Predicate HemoPoint H2 Measurment System K081719
Intended Use	The DiaSpect Tm system is intended for the in vitro quantitative measurement of total hemoglobin in non-anticoagulated capillary whole blood and venous whole blood drawn in K_2EDTA or lithium heparin tubes. The DiaSpect Tm system consists of the DiaSpect Tm analyzer and specifically designed disposable cuvettes, the DiaSpect Tm Cuvettes. The device is intended for use in point-of-care settings. The DiaSpect Tm analyzer is only to be used with DiaSpect Tm Cuvettes.	The HemoPoint H2 Hemoglobin Measurement System is indicated for the quantitative determination of hemoglobin in arterial, venous, or capillary whole blood of adults, infants, and children in a professional point-of-care setting. The microcuvettes part number 3010-100 is indicated for use in the Hemopoint® H2 Hemoglobin Measurement System and HemoCue® B Hemoglobin Photometer.
Analyte	Hemoglobin	Same
Sample Preparation (pre-treatment)	None	Same
Automation	Fully automated assay	Same
Calibration Procedure	Factory calibrated	Same
Built in Quality Control	Auto self-check between measurements	Same

Differences		
Item	Device DiaSpect Tm Analyzer	Predicate HemoPoint H2 Measurment System
Method of detection (Test methodology)	Optical absorbance	Azide methemoglobin
Sample Type	Capillary and Venous Whole Blood	Capillary, Venous, and Arterial Whole Blood
Sample Volume	10 µL	8 µL
Cuvette reagent components	None	Azide methemoglobin reagent
Cuvette storage	0 – 50°C	15 – 30°C
Control kit components	Three concentration levels of controls (1 vial of each)	Two concentration levels of controls (3 vials of each)
Quality Control	Requires three buffer-based controls to validate the calibration	Requires two buffer-based controls to validate the calibration

Differences		
Item	Device DiaSpect Tm Analyzer	Predicate HemoPoint H2 Measurment System
Measurement Range	1.2 – 25.5 g/dL	0.0 – 25.6 g/dL
Measuring Time	1 second	30–60 seconds

K. Standard/Guidance Document Referenced (if applicable):

- CLSI EP05-A3, Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline- Third Edition
- CLSI EP6-A, Evaluation 0f The Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline
- CLSI EP07-A2, Interference Testing in Clinical Chemistry; Approved Guideline - Second Edition
- CLSI EP09-A3, Measurement Procedure Comparison and Bias Estimation Using Patient Samples; Approved Guideline - Third Edition
- CLSI EP17-A2, Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline -- Second Edition
- CLSI EP25-A, Evaluation of Stability of In Vitro Diagnostic Reagents; Approved Guideline
- IEC 61010-1 Edition 3.0 2010-06, Safety requirements for electrical equipment for measurement, control, and laboratory use - part 1: general requirements [including: corrigendum 1 (2011)]
- IEC 61010-2-101 Ed. 2.0 b:2015 Safety requirements for electrical equipment for measurement, control and laboratory use - Part 2-101: Particular requirements for in vitro diagnostic (IVD) medical equipment
- EN 61326-1:2006, EN 61326-2-6:2006 Electromagnetic Compatibility (EMC) compliance test of the emissions and immunity

L. Test Principle:

The DiaSpect Tm utilizes a broad spectrum, multi-chromatic sensor which measures the absorbance over a wide spectral range in a clear plastic cuvette. The system uses a photometric approach to measure the concentration of hemoglobin per the Lambert-Beer Law, which states the relationship between the concentration of the material c (hemoglobin, in this case), the path length of the light travelling through the material l and the specific absorption coefficient at a distinct wavelength ε

$$A=\varepsilon lc$$

As the path length (which is the fixed cavity depth of the cuvettes) and the absorption coefficient are constant and known, the hemoglobin concentration is a linear function of the absorbance. With a mathematical model, a wavelength range was found where Hb and HbO2

have the same absorbance integral. Turbidity from the unhemolyzed blood, as well as the impact of possible interfering substances (such as bilirubin or white blood cells), are addressed by performane of reference measurements at infrared (600 nm to 750 nm) and blue (450 nm to 500 nm). During the measurement interval, a white LED is flashed. The light beam is sent through the sample to an optical sensor element and the sensor detects the absorbance of the blood sample at a broad wavelength range. A "light trap" prevents scattered light from arriving at the sensor.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

20-day Precision/Reproducibility

Reproducibility was conducted at three intended use sites over 20 operating days using three DiaSpect Cuvette lots (one lot per site), three DiaSpect Tm Analyzers (one instrument per site), and one lot of DiaSpect Controls (Levels 1, 2 and 3). Each control set was run in duplicate twice daily for 20 days, by two operators at each site. A total of 160 test results were generated for each control level at each site. SD and %CV for within-run, between-run, between-day, between-operator, and between-site were calculated for each site and all sites combined. Reproducibility results at all test sites were within the defined acceptance criteria.

Sample	N	Mean	Within-Run (SD, %CV)	Between-Run (SD, %CV)	Between-Day (SD, %CV)	Between-Operator (SD, %CV)	Between-Site (SD, %CV)	Total (SD, %CV)
Level 1	240	7.99	(0.085, 1.06%)	(0.05, 0.59%)	(0.04, 0.47%)	(0, 0%)	(0.04, 0.45%)	(0.11, 1.38%)
Level 2	240	12.58	(0.11, 0.88%)	(0.05, 0.38%)	(0.03, 0.22%)	(0, 0%)	(0.06, 0.47%)	(0.14, 1.09%)
Level 3	240	15.82	(0.15,0.92%)	(0.06, 0.36%)	(0.04, 0.27%)	(0, 0%)	(0.15, 0.97%)	(0.22, 1.41%)

Single-day Precision

Single-day precision was performed at a single site using K_2EDTA venous whole blood. Five donors provided five samples (one sample each), some of which were manipulated to increase or decrease hemoglobin levels. The study was performed at a single site using three instruments, three lots of cuvettes, and three operators. Each of three operators ran duplicate tests on all five levels, providing 54 measurements for each level. Single-day precision results were within the defined acceptance criteria.

Sample	N	Mean	Within-Run (SD, %CV)	Between-lot (SD, %CV)	Between-Operator (SD, %CV)	Between-Analyzer (SD, %CV)	Total (SD, %CV)
Level 1	54	4.87	(0.05, 0.97%)	(0.04, 0.82%)	(0.02, 0.42%)	(0.11, 2.19%)	(0.13, 2.57%)
Level 2	54	10.19	(0.19,1.87%)	(0, 0%)	(0.06, 0.6%)	(0.12, 1.17%)	(0.23, 2.29%)
Level 3	54	13.75	(0.38,2.77%)	(0.07, 0.48%)	(0.21, 1.5%)	(0, 0%)	(0.44, 3.19%)
Level 4	54	17.46	(0.69,3.93%)	(0, 0%)	(0.08, 0.48%)	(0.37, 2.14%)	(0.79, 4.5%)
Level 5	54	22.93	(1.45,6.33%)	(0, 0%)	(0.3, 1.32%)	(0, 0%)	(1.48, 6.47%)

b. Linearity/assay reportable range:

A linearity study was conducted using low and high-level hemoglobin concentrations prepared from a single, venous whole blood sample. A total of 11 hemoglobin concentrations (0.0, 0.2, 1.6, 3.7, 7.2, 10.4, 13.2, 16.5, 19.0, 23.7, 25.6 g/dL) spanning the claimed measuring range of the DiaSpect Tm Analyzer (0.3–25.5 g/dL) were tested in triplicate and analyzed using one DiaSpect Tm Analyzer and one lot of DiaSpect Tm Cuvettes. Average results were plotted against results obtained from a HemoPoint® H2 analyzer, which was used as the reference method. The data was analyzed using linear regression. The DiaSpect Tm demonstrated linearity over the claimed measuring range of 0.3–25.5 g/dL.

c. Traceability, Stability, Expected values (controls, calibrators, or methods):

<u>DiaSpect Tm Cuvette Stability</u>

DiaSpect Cuvette shelf-life was determined by using 12 different lots of DiaSpect Tm Cuvettes produced over a 2.5 year period. At the end of the 2.5 years, four cuvettes from each lot were tested by measuring the medium level of the DiaSpect Control HB, target value 12.6 g/dL, on the DiaSpect Tm Analyzer. The mean value of the measurements from all lots is 12.59 g/dL, with a total CV 0.75%. The data support a shelf-life stability claim of 2.5 years.

<u>Sample Stability</u>

Sample stability was assessed using one lot of DiaSpect Tm Cuvettes and one DiaSpect Tm analyzer. Five volunteers were used to donate two venous samples (one K_2EDTA and one lithium heparin). Samples were aliquoted into 500 µL aliquots for each time point of the study, labeled, and stored at refrigerated temperature (2–8 °C) and at room temperature (19–25 °C) for the duration of the study. Refrigerated

samples were tested at various time intervals (18, 23, 48, 72, 95, and 236 hours). Room temperature samples were also tested at various time intervals (4.5, 6.5, 19.25, 26, and 30.25 hours). The mean values of three replicates for each sample, storing temperature, anticoagulant, and measurement point were recorded. The study data support the recommended stability claim of 72 hours when stored at refrigerated temperatures (2–8°C). The study also demonstrates sample stability of up to 30 hours at room temperature (19–25 °C).

d. Detection limit:

Limit of Blank (LoB)

To determine Limit of Blank (LoB), plasma samples were obtained from five individual whole blood donors. The five plasma "blank" samples were tested for three days on one DiaSpect Tm meter in quadruplicate using two different lots of DiaSpect Tm Cuvettes for a total of 120 replicates. LoB was calculated by rank ordering the 60 samples per cuvette lot from low to high and averaging the 57th and 58th results (being the 95th percentile). LoB was determined to be 0.0 g/dL.

Limit of Detection (LoD)

To determine Limit of Detection (LoD), four K_2EDTA venous whole blood samples were collected from different donors. Four independent samples were prepared covering Hgb concentrations 0.1–0.4 g/dL. Each sample was tested 60 times on one DiaSpect Tm device using two different lots of DiaSpect Tm Cuvettes for 3 days. LoD was calculated by nonparametric analysis and was determined to be 0.3 g/dL.

Limit of Quantitation (LoQ)

To determine Limit of Quantitation (LoQ), nine unique donor venous whole blood samples were used to prepare concentrations from 0.7–1.5 g/dL. Each sample was tested 10 times per day using two lots of DiaSpect Tm Cuvettes on one DiaSpect Tm analyzer for 3 days to achieve variability. The mean and SD for each sample concentration for each cuvette lot was determined and the bias for each of the nine levels calculated. LoQ was determined from the specified Total Error to be 1.2 g/dL.

Detection Limits	Concentration
LoB	0.0 g/dL
LoD	0.3 g/dL
LoQ	1.2 g/dL

e. Analytical specificity:

A study was conducted to evaluate the effects of potential interferents on the DiaSpect Tm Analyzer. Venous whole blood collected in K_2EDTA tubes was

manipulated to create three hemoglobin concentrations of 11.0, 14.0, and 18.0 g/dL. Each hemoglobin concentration was spiked with a potential interferent at the test concentrations listed below. For disease conditions, K_2EDTA venous blood specimens from a minimum of five donors with the following conditions were collected: polycythemia, hypochromia, high WBC count and sickle cell. The predicate device HemoPoint(H2) was used as the reference method to obtain the Hgb concentration. Each sample was tested in duplicate on the Hemopoint (H2) and five times on the DiaSpect Tm Analyzer. The predicate HemoPoint (H2) average was used to calculate the bias against each individual DiaSpect Tm result. All potential interferents tested showed no significant interference up to the concentrations listed in the table below.

Potential Interferent	Test Concentration	Potential Interferent	Test Concentration
Bilirubin	20.0 mg/dL	Ferrous Fumarate	30 mg/dL
Cholesterol	500 mg/dL	Iron Dextran	284 mg/dL
Creatinine	5 mg/dL	Folic Acid	1000 ng/dL
Protein	12 mg/dL	Vitamin B12	2500 ng/dL
Triglyceride	1000 mg/dL	Lithium Carbonate	23 mg/dL
Urea	258 mg/dL	Immunoglobin	500 mg/dL
Uric Acid	24 mg/dL	Methyldopa	1.7 mg/dL
Acetaminophen	2 mg/dL	Salicylic Acid	100 mg/dL
Ascorbic Acid	6 mg/dL	5x EDTA	Tube filled to 1/5 volume
Dopamine	0.1 mg/dL	Ferrous Sulfate	22 mg/dL
Ibuprofen	55 mg/dL	Ammonium Ferric Citrate	30 mg/dL
Tetracycline	1.5 mg/dL		

f. Assay cut-off:

Not applicable

2. Comparison studies:

a. Method comparison with predicate device:

Method comparison studies were performed across four sites to support the substantial equivalence of the DiaSpect Tm Hemoglobin System with the predicate device. Capillary (fingerstick), K_2EDTA, and lithium heparin venous whole blood specimens from a total of 399 subjects across four point-of-care clinical sites were tested on-site with both the DiaSpect Tm system (in singlicate) and in the HemoPoint H2 Hemoglobin Analyzer (comparative method, in duplicate).

A total of 364 male and female subjects, ranging from 9 months to 89 years of age, provided 363 capillary samples ranging from 8.5 to 20.1 g/dL, 349 K_2EDTA venous samples ranging from 6.5 to 19.9 g/dL and 120 heparin venous samples ranging from 10.4 to 20.0 g/dL when tested on the DiaSpect Tm system. An additional 35 contrived K_2EDTA venous samples were divided between three sites and tested to challenge the full measuring range of the DiaSpect Tm system. Of the 349 K_2EDTA venous samples, five samples with hemoglobin values of 6–7 g/dL were tested in comparison with the predicate at one additional internal site to demonstrate the performance of the device around these levels.

Testing was performed by nine operators using four DiaSpect Tm analyzers and three lots of DiaSpect Tm Cuvettes. Capillary whole blood and K_2EDTA venous whole blood were tested at all four sites by nine operators. Lithium heparin was tested at one site by two operators. The results for all natural and contrived samples combined are summarized in the table below. Linear regression analyses demonstrate comparable performance between the DiaSpect Tm and HemoPoint (H2) across the analytical measuring range.

Overall Results Summary, Natural and Contrived, Samples All Sites

Site #	Blood Type	N (Natural)	N (Contrived)	Slope (95% CI)	Intercept (95% CI)	r
1	EDTA Venous	100	12	0.9805 (0.947, 1.014)	0.5607 (0.099, 1.022)	0.984
	Capillary	101	N/A	0.9628 (0.928, 1.008)	0.3985 (-0.167, 0.964)	0.977
2	EDTA Venous	120	11	1.0067 (0.980, 1.032)	-0.1795 (-0.558, 0.199)	0.989
	Heparin Venous	120	11	1.0229 (1.004, 1.042)	-0.3606 (-0.643, 0.079)	0.994
	Capillary	119	N/A	1.0129 (0.951, 1.075)	0.0958 (-0.989, 0.798)	0.943
3	EDTA Venous	119	12	0.9944 (0.963, 1.011)	-0.0547 (-0.295, 0.382)	0.992
	Capillary	120	N/A	0.9889 (0.952, 1.026)	0.0772 (-0.454, 0.698)	0.978
4	EDTA Venous	5	N/A	0.9487 (0.642, 1.255)	0.7755 (-3.518, 5.069)	0.985
	Capillary	23	N/A	1.0145 (0.743, 1.286)	-0.3496 (-4.109, 3.410)	0.861
TOTAL	EDTA Venous	349*	35	0.9858 (0.969, 1.002)	0.2130 (-0-029, 0.455)	0.986
	Capillary	363	N/A	0.9903 (0.963, 1.018)	0.1164 (-0.276, 0.509)	0.963

*See introductory study description.

Passing-Bablok Regression All Sites

		Passing-Bablok regression	r
All results	Capillary	y = -0.1198 + 1.011x	0.965
	EDTA Venous	Y = 0.4867 + 0.9637x	0.986

b. Matrix comparison:

A comparison between K_2EDTA and lithium heparin venous blood was performed on the overall data comparing results for matched natural specimens from the same subjects tested with the DiaSpect Tm system. Paired natural K_2EDTA and heparin samples (n=120), ranging from 10.4 – 19.9 (K_2EDTA) or 10.4 – 20.0 (heparin) g/dL Hgb, agreed closely and can be used interchangeably in the DiaSpect Tm system. A comparison between K_2EDTA and capillary blood was also performed on the overall data comparing results for matched natural specimens from the same subjects tested with the DiaSpect Tm system. Agreement between capillary and K_2EDTA samples in the DiaSpect was comparable to that of the predicate system as summarized in the table below.

Comparison	Slope	Intercept	R
DiaSpect K_2EDTA vs Heparin	0.9981	0.0644	0.9812
DiaSpect, Venous vs Capillary	0.9702	0.4634	0.8839
HemoPoint (predicate), Venous vs Capillary	0.8964	1.4695	0.8926

3. Clinical studies:

a. Clinical Sensitivity:

Not applicable

b. Clinical specificity:

Not applicable

c. Other clinical supportive data (when a. and b. are not applicable):

4. Clinical cut-off:

Not applicable

5. Expected values/Reference range:

   Reference ranges were verified by testing whole blood specimens from healthy donors using the DiaSpect Tm system. The reference ranges were based on the existing medically accepted published reference ranges[1].

Population	Age Range	Cited Reference Range
Adult Male	≥ 22 years	13.0 – 17.0 g/dL
Adult Female	≥ 22 years	12.0 – 15.0 g/dL
Child/Adolescent	> 2 years to 21 years	11.0 – 15.5 g/dL
Infant	1 month to 2 years	9.4 – 16.5 g/dL

[1] Dacie and Lewis, Practical Haematology, 12th Edition, 2017.

N. Instrument Name:

DiaSpect Tm analyzer

O. System Descriptions:

1. Modes of Operation:

   Does the applicant's device contain the ability to transmit data to a computer, webserver, or mobile device?

   Yes _____ or No _____X___

   Does the applicant's device transmit data to a computer, webserver, or mobile device using wireless transmission?

   Yes _____ or No ____X____

2. Software:

   In accordance with FDA Guidance "*Content of Premarket Submissions for Management of Cybersecurity in Medical Devices*", the risk to a patient in the event of the occurrence of harm and severity of harm if there was a cybersecurity threat or some level of vulnerability was considered. The DiaSpect Tm design and associated controls ensure that the software employed does not pose a cybersecurity threat to the device functionality and safety.

   FDA has reviewed applicant's Hazard Analysis and software development processes for this line of product types:

   Yes ____X____ or No _____

3. Specimen Identification:

   There is no sample identification function for the DiaSpect Tm.

4. Specimen Sampling and Handling:

   The DiaSpect Hemoglobin cuvette draws a small amount (approximately 10μL) of venous or capillary blood by capillary effect. The cuvette is then inserted into the meter.

5. Calibration:

   The DiaSpect Tm analyzer is factory calibrated and is not user adjustable.

6. Quality Control:

   The DiaSpect Tm system includes 3 levels of control solutions with known hemoglobin concentration. The DiaSpect Control HBT is produced in three concentrations that correspond to three levels of human hemoglobin. Each vial contains 1.9 mL of a solution of a red dye (Rhodamine) in purified water. The reagent does not contain any material of human or animal origin. Users are directed to perform control testing on each day of testing, when a new canister of test cartridge is opened, or when test results seem inaccurate. The DiaSpect Control HBT is exempt from premarket notification.

P. Other Supportive Instrument Performance Characteristics Data Not Covered In The "Performance Characteristics" Section above:

Cleaning and Disinfection Validation Study

A cleaning and disinfection validation study was conducted to validate virucidal efficacy using the selected disinfectant with the recommended disinfection protocol. In the presence of a 100% duck serum organic load, PDI Super Sani-Cloth® Germicidal Disposable Wipes (EPA Registration No. 9480-4), a ready to use pre-saturated towelette, demonstrated complete inactivation of Duck Hepatitis B virus (surrogate for Human Hepatitis B virus) for all tested materials, following two-minute exposure at 20°C. Results of the study also demonstrate no significant change in appearance and function of the DiaSpect Tm analyzer after 5000 disinfection and cleaning cycles designed to simulate a 5-year life span of the meter.

Q. Proposed Labeling:

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

R. Conclusion:

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