

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
INSTRUMENT ONLY TEMPLATE**

A. 510(k) Number:

K050421

B. Purpose for Submission:

New Device

C. Manufacturer and Instrument Name:

MS 4/5 Hematology Analyzer, Melet Schloesing Laboratories USA

D. Type of Test or Tests Performed:

Quantitative, White Blood Cells (WBC), Red Blood Cells (RBC), Platelets, Hemoglobin, White Blood Cell Differential, Hematocrit

E. System Descriptions:

1. Device Description:

The MS 4/5 is a quantitative, automated hematology analyzer that provides a leukocyte differential count for in-vitro diagnostic use in clinical laboratories. The analyzer utilizes the Coulter principle to enumerate white blood cells, red blood cells and platelets. The system consists of a single stand-alone analyzer unit and five reagents which are utilized during its measurement and cleaning cycle. The system also includes on-board software that controls all internal moving parts of the instrument, processes the information, reports results and stores data related to each run (time, date, patient ID, comments patients or control results).

2. Principles of Operation:

The MS 4/5 hematology analyzer utilizes the Coulter principle to enumerate white blood cells, red blood cells and platelets based on their impedance of an electrical field as the cell is aspirated through a calibrated orifice. Hemoglobin is determined by the ICSH recommendation standard Drabkin's method of measurement of reduced hemoglobin in a photometric chamber at 540nm. White blood cells types are differentiated by volume based on the lobulation of their nucleus into three different subpopulations: Lymphocytes, Monocytes and Granulocytes. The basophils and eosinophils are further differentiated based on their granulation.

3. Modes of Operation:

The blood sampling system is a manual placement of single tube followed by automatic sampling and analysis.

4. Specimen Identification:

The specimen identification number is generated automatically.

5. Specimen Sampling and Handling:

The MS 4/5 system requires whole blood anticoagulated with K₂EDTA in plastic or glass tubes. Blood collection should be free of trauma. Blood tubes should be mixed by hand gently with the anticoagulant immediately after drawing the sample and mixed gently by hand or mechanical mixer immediately prior to analysis. Blood should be assayed within four hours if stored at room temperature and 24 hours if stored between 0 and 4°C.

6. Calibration:

The MS 4/5 analyzer is calibrated at setup. Changing reagent does not require recalibration unless indicated by unacceptable quality control results according to the laboratory's procedures. Calibration verification must be performed in accordance with the laboratory's regulatory requirements. Calibration material is supplied by an independent vendor.

7. Quality Control:

A minimum of two levels of quality control material should be run a minimum of every day of testing and with each change of reagent lot. Quality control materials are obtained from an independent vendor.

8. Software:

The software for the MS 4/5 allows the user to: (1) Analyze a sample or a control, to display and print the results, (2) Recall an analysis from the memory and print it, (3) Modify the parameters of the banks (i.e. reference values), (4) Modify the system parameters (i.e. time, date, etc.), (5) Make the device perform maintenance actions (i.e. priming of reagent). The software can interface with an external keyboard, mouse, printer and computer.

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

Yes X or No _____

F. Regulatory Information:

1. Regulation section:

21 CFR 864.5220, Automated Differential Cell Counter

2. Classification:

Class II

3. Product code:

GKZ, Counter, Differential Cell

4. Panel:

(81) Hematology

G. Intended Use:

1. Indication(s) for Use:

The MS 4/5 is a quantitative, automated hematology analyzer that provides a leukocyte differential count for in-vitro diagnostic use in clinical laboratories.

2. Special Conditions for Use Statement(s):

Not applicable.

H. Substantial Equivalence Information:

1. Predicate Device Name(s) and 510(k) numbers:

Bayer Advia 120 Hematology System, K971998

2. Comparison with Predicate Device:

Similarities		
Item	Device	Predicate
	<i>MS 4/5</i>	<i>Bayer Advia 120</i>
Directly measured parameters	Directly measures Whit Blood Cells, Red Blood Cells, Platelets, Hemoglobin, MCV, MPV, Neutrophils, Lymphocytes, Monocytes, Eosinophils and Basophils	Same
WBC measurement principle	Red cells are hemolyzed by reagent and WBCs analyzed by laser light scatter signals.	Same
RBC measurement principle	Analyzed by a single optical cytometer after dilutions.	Same
Platelet measurement principle	Platelets counted with RBCs from a common detector with 2 different gain settings.	Same
RBC/ Platelet Size	Simultaneous measurement of laser light scatter	Same
Hemoglobin measurement principle	ICSH cyanmethemoglobin method	Same
Eosinophil and Basophil measurement principle	Cytochemical	Same
Red Cell indices (MCH, MCHC)	Mathematically calculated from RBC count, hemoglobin and MCV determination	Same
Determination of Hematocrit	Mathematically calculated from RBC count and MCV	Same
RDW and PDW	Calculated by cell-by-cell measurement of cell volume and hemoglobin concentration	Same
Patient abnormal flags	Can be chosen and set by the individual use facility	Same
Quality Control Analysis and Data Storage	On-board software module	Same
Sample Type	Whole blood collected in EDTA	Same
Precision (except platelets)	All parameters less than 3%	Same
Probe Cleaning	Automated, Self-Cleaning	Same
Power Supply	Completely contained within instrument	Same

Differences		
Item	Device	Predicate
	<i>MS 4/5</i>	<i>Bayer Advia 120</i>
Differentiation of Granulocytes, Monocytes and Lymphocytes	Nucleus to Plasma Density/Volume	Reaction to cytochemical staining and analysis (Peroxidase Method)
Blood sampling system	Manual placement of single tube followed by automatic sampling and analysis for both open and closed tube.	Automatic sampling of closed tubes from multiple tube racks or single tube port. Manual open tube mode option available.
Sample Volume	30 μ L	157 μ L
Throughput	20 per hour	120 per hour
Measurement of Reticulocytes and CHr	The MS 4/5 does not perform measurement of reticulocytes of CHr.	Performs reticulocytes measurements
Method of Calibration	Requires moderate amount of manual input	Requires minimal manual input
Calibrator and Quality Control Material	Available from Independent Distributor	Available from Bayer
Analytical Ranges (Linearity)	Limits of Linearity are less than the Advia 120 due to limitation of sample tested	Linearity ranges exceed those of the MS 4/5
Platelet Precision	4.3%	2.93%
Sample Stability	6 hours at room temperature and 24 hours at 4 ° C	Depends on parameter. Stable from 8 to 72 hours at room temperature, and 8 to 72 hours refrigerated
Features controlled by Software	Software features and changes significantly less than the Advia 120	Greater flexibility of options due to increased software capacity
Software Upgrade	User exchanges processor chip	Software upgraded by CD
Operator Manual	Printed Version	On-Line
Waste Disposal	Manual	Closed System through pneumatic option
Fluidics and mechanical system	Uses computer controlled, motor-driven peristaltic pumps and syringes for the fluidics and mechanical systems	Computer controlled pneumatically driven system for fluidics and mechanical systems

I. Special Control/Guidance Document Referenced (if applicable):

Class II Special Control Guidance Document: Premarket Notification for Automated Differential Cell Counters for Immature or Abnormal Blood Cells Final Guidance for Industry and FDA, December 4, 2001

J. Performance Characteristics:

1. Analytical Performance:

a. *Accuracy:*

120 whole blood samples were assayed in duplicate on the MS 4/5 and the predicate device using three reagent lots for each component on each instrument. The results are as follows:

Analyte	Slope	Intercept	r	r ²
WBC (10 ³ /uL)	1.01	-0.12	0.99	0.98
RBC (10 ⁶ /uL)	1.03	-0.04	0.99	0.97
Hemoglobin (g/dL)	1.00	+0.19	0.99	0.97
Hematocrit (%)	1.02	+0.16	0.98	0.96
Platelet (10 ³ /uL)	1.02	-5.2	0.98	0.96

White Blood Cell Differential Correlation: Manual differentials (300 cells) were performed and the cells were classified as positive or negative based on the criteria defined in the Reference Leukocyte Differential Count (Proportional) and Evaluation Methods, Approved Standard, NCCLS, H20-A. The false positive and false negative ratios of the MS 4/5 are shown below. Additionally, a t-test to detect systematic error and a f-test to detect random error were applied to compare the MS 4/5 data with the predicate device.

Cell Type	Manual Differential		Automated Differential	
	False Positive Ratio (%)	False Negative Ratio (%)	t test at p=0.05	f test at p=0.05
Granulocytes	1.2	1.6	No systematic error	No random error
Lymphocytes	2.6	1.9	No systematic error	No random error
Monocytes	2.4	1.3	No systematic error	No random error
Basophils	0.5	1.0	No systematic error	No random error
Eosinophils	2.4	2.7	No systematic error	No random error
Morphology Classification	1.8	2.2	No systematic error	No random error

b. *Precision/Reproducibility:*

A single lot number of whole blood control material was pooled and divided into four portions, each sufficient for 5 day testing. Each portion was assayed in duplicate twice a day for 5 days, for a total of 20 test days. The results are as follows:

		Within-Run		Between-Day		Total	
Analyte	Mean	SD	CV	SD	CV	SD	CV
WBC ($10^3/\mu\text{L}$)	8.76	0.159	1.8	0.030	0.3	0.165	1.9
RBC ($10^6/\mu\text{L}$)	3.89	0.058	1.5	0.031	0.8	0.066	1.7
MCV (fL)	89.8	0.59	0.7	0.41	0.5	1.05	1.2
Hemoglobin (g/dL)	13.3	0.159	1.2	0.294	2.2	0.353	2.6
Platelets (%)	234	9.4	4.0	2.3	1.0	10.2	4.3
MPV (fL)	8.96	0.15	1.7	0.12	1.4	0.19	2.2
RDW (%)	8.97	0.14	1.6	0.11	1.3	0.18	2.0

c. *Linearity:*

Linearity was determined by assaying normal and abnormal specimens (in triplicate) for the parameters below. For each determination, duplicate assays were performed for each of five dilutions within the stated range.

Linear Range	Low Limit Tested	High Limit Tested	Slope	r^2
WBC ($\times 10^3 \mu\text{L}$)	1.8	52.0	1.02	0.98
RBC ($\times 10^6 \mu\text{L}$)	0.84	7.85	0.96	0.99
Hemoglobin (g/dL)	2.5	24.1	0.97	0.97
Platelets ($\times 10^3 \mu\text{L}$)	24	785	1.03	0.96
Hematocrit (%) Used to determine MCV	10	78	1.04	0.99

d. *Carryover:*

A sample with a high concentration of the analyte was assayed three consecutive times, followed by the analysis of a low sample three consecutive times. The results are as follows:

Parameter	High Sample Concentration	Low Sample Concentration	% Carryover
WBC	48.6	2.3	1.2
RBC	7.29	1.26	1.6
Hemoglobin	18.8	6.3	1.8
Platelets	678	37	2.3

e. *Interfering Substances:*

Samples with extreme lipemia, chylomicrons, or extremely high bilirubin concentrations might produce falsely elevated hemoglobin values. In-house studies show that accurate hemoglobin values are produced in samples with bilirubin values up to 20 mg/dL.

2. Other Supportive Instrument Performance Data Not Covered Above:

An in-house comparison study was performed with the predicate device on 100

samples, assayed within two hours of collection, using at least three reagent lots. The results are as follows:

Analyte	Slope	Intercept	r	r ²
WBC (10 ³ /uL)	0.96	+0.31	0.99	0.98
RBC (10 ⁶ /uL)	1.02	-0.04	0.98	0.96
Hemoglobin (g/dL)	0.95	+0.68	0.98	0.96
Hematocrit (%)	1.04	-0.6	0.96	0.92
Platelet (10 ³ /uL)	1.02	+1.8	0.95	0.90

Clinical Sensitivity and Specificity were assessed against the predicate device. See results below:

Parameter	Sensitivity (%)	False Negative (%)	Specificity (%)	False Positive (%)
WBC	96.3	3.7	95.4	4.6
RBC	95.8	4.2	96.1	3.9
Hemoglobin	97.2	2.8	96.1	3.9
MCV	95.7	4.3	95.3	4.7
Platelets	95.3	4.7	95.6	4.4
White Cell Differential	Refer to 1.(a) White Blood Cell Differential Correlation			
Cell Morphology	Refer to 1.(a) White Blood Cell Differential Correlation			

K. Proposed Labeling:

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

L. Conclusion:

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

