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

A. 510(k) Number:

K050053

B. Purpose for Submission:

To obtain clearance for the HemoRAM System with the AggRAM Aggregation (Remote Analyzer Module) System.

C. Manufacturer and Instrument Name:

Helena Laboratories, Inc.

HemoRAM/AggRAM Analyzer System

D. Type of Test or Tests Performed:

Platelet Aggregation and Ristocetin Cofactor testing

E. System Descriptions:

1. Device Description:

   The HemoRAM/AggRAM Analyzer System consists of a software program (HemoRAM) and a remote analyzer module (AggRAM) for platelet aggregation testing. The HemoRAM system consists of a CPU, monitor, keyboard and printer. The software program calculates slope and maximum percent aggregation, displays and prints log phase, calculates and automatically smoothes curves, evaluates and charts quality control for ristocetin cofactor based on Westgard rules, generates Levey-Jennings charts with an intergral action log and produces customized reports. The AggRAM module is a 4-channel analyzer capable of performing several agonist tests such as platelet aggregation.

2. Principles of Operation:

   The AggRAM is a platelet aggregation recorder. It measures human platelet aggregation by the absorbance method using up to four channels per module simultaneously. All components of the AggRAM system are controlled and monitored by a computer. Software and memory are provided via a hard disk and one CD drive. All user input is through the keyboard and mouse. The entries are used to select the type of test, start or stop the automatic sequence of operations, enter patient data, select instrument parameters, and to change displays.

The optical section of each of the four channels consists of a photo detector and a laser diode. The sample inside the cuvette is flooded with laser light (650 nm) emitted by the laser. Platelets suspended in the mixture cause reduced transmission, so that the amount of light reaching the photo detector is proportional to the number of platelets in solution. The photo detector converts the light intensity into an analog signal, which is digitized and sent to the CPU for processing.

Platelet Aggregation:

A number of substances (aggregation reagents) will induce platelet aggregation. These reagents include ADP, collagen epinephrine, serotonin, arachidonic acid and ristocetin. The clinician selects the aggregation reagent(s), which will generate the most significant clinical information.

The aggregation capacity of platelets is determined by the amount of aggregation induced when a known amount of regent is added to the platelet rich plasma (PRP). The absorbance of the unreacted PRP mixed with the aggregation reagent represents 0% aggregation, and the absorbance of a platelet poor plasma control represents 100% aggregation. As platelets aggregate, the number of floating platelets decreases, reducing the light absorbed by the PRP. Various parameters related to the aggregation curve, or the maximum aggregation rate, are used as data.

Ristocetin Cofactor:

A diluted suspension of lyophilized platelets is prepared and used to set 100% activity. Ristocetin is added to undiluted platelet suspensions and allowed to incubate at 37° C. Upon addition of a diluted plasmas specimen, the AggRAM makes an immediate absorbance measurement of the mixture (platelets, ristocetin and plasma). This reading establishes the 0% agglutination baseline. The slope of the reaction (agglutination vs. time) is compared to a standard curve to determine % activity.

3. Modes of Operation:

   Semi-automated

4. Specimen Identification:

   Patient information can either be entered by the operator through the Patient Demographics Entry window or imported via the LIS.

5. Specimen Sampling and Handling:

   Specimens are manually prepared according to the procedure for the assay being performed.

6. Calibration:

   Daily, or each time turned on, and prior to the instrument's first run; an Optical Calibration Check must be performed. Acceptable values are shown with a gray background color. Unacceptable values are shown with different background colors, each representing a type of failure and a message displays attributing the background color to a specific failure.

7. Quality Control:

   The instrument automatically performs a self test any time the power is turned on. Each laboratory should establish its own normal range of expected value for the procedures in use. Each laboratory should also establish a quality control program that includes normal and abnormal controls to evaluate the instrument, reagent and the technologist performance. Control data should be compared to the assay ranges printed on the assay sheet provided with the control.

   The software automatically keeps a record of control values from each run. At the end of every month, the software determines the mean ± SD for each lot of control. Five Westgard Rules are included in the software to allow the laboratory to automatically monitor trends in QC data and to determine when QC data will no longer be accepted unless corrective action is taken.

8. Software:

   The system consists of a PC and one or more AggRAM modules. The PC acts as the operator interface and runs the Windows 2000 operating system. The PC handles most of the calculations and all data storage except temperature adjustment offset and the serial number of the module. An external LIS may also be attached to the serial port for import and export of information. Test results are saved to the hard drive and shown in reports on the monitor and printer.

   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 864.5425

2. Classification:

    Class II

3   Product code:

    JPA

4. Panel:

    81 Hematology

G. Intended Use:

1. Indication(s) for Use:

    The AggRAM Analyzer is a 4-channel aggregometer designed to perform platelet aggregation and Ristocetin cofactor testing on patients for hemostasis abnormalities. Platelet aggregation studies are performed to quantitate platelet response and identify abnormal platelet function. The agonist, Ristocetin, can be used in the diagnosis of von Willebrand's disease. Ristocetin Cofactor reagents are used to quantitate the von Willebrand factor activity.

2. Special Conditions for Use Statement(s):

    Not applicable

H. Substantial Equivalence Information:

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

    Platelet Aggregation Chromogenic Kinetic System-4 (PACKS-4)

    K912201 & K921465

2. Comparison with Predicate Device:

Similarities		
Item	Device	Predicate
Sample matrix - aggregation	Platelet rich plasma (PRP)	Same
Ristocetin Cofactor	Yes	Same
Assay procedures	Software driven	Same

4

Differences		
Item	Device	Predicate
Pattern interpretation	Computer notes	Manual on printout
Chromogenic measurements	Yes	No
Platelet aggregation & Ristocetin Cofactor run simultaneously	Yes	No
Expandable test menu	Yes	No

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

Not applicable

J. Performance Characteristics*:*

1. <u>Analytical Performance</u>:

   a. Accuracy:

   Platelet Aggregation

   Studies performed at Helena Laboratories were done on each of five agonists (ADP, Collagen, Epinephrine, Arachidonic Acid, Ristocetin). 50 normal donors and donors taking aspirin and other medications which might affect platelet aggregation were used for correlation studies. Additional abnormal samples were created by treating normal specimens with platelet receptor blocking agents. The abnormal samples for Ristocetin testing were created by depleting the von Willebrand factor and then mixing with normal platelets, to create specimens similar to those seen in patients with von Willebrand's Disease. All samples were tested on the PACKS-4 and the AggRAM analyzers. Linear regression data and one way analysis of variance (ANOVA) were generated on each agonist.

   Additional comparison data were generated by Indiana University Division of Thrombosis, South Bend, IN, where >20 samples were tested for each of the five agonists on the PACKS-4 and AggRAM instruments.

Agonist	N	R value
ADP	104	0.982
Collagen	107	0.978
Epinephrine	104	0.967
Arachidonic Acid	103	0.969
Ristocetin	105	0.979

Ristocetin Cofactor

Comparison studies were performed with normal plasma donors, patients with von Willebrand Disease and other abnormal plasmas created by dilution or immunodepletion of von Willebrand Factor. All samples were tested on the PACKS-4 and the AggRAM analyzers. Linear regression data and ANOVA were generated on each agonist.

Additional comparison data were generated by Indiana University Division of Thrombosis, South Bend, IN, where 59 samples were tested for Ristocetin Cofactor on the PACKS-4 and AggRAM instruments.

A total of 114 samples were tested with an r value of 0.981.

b. *Precision/Reproducibility*:

The NCCLS EP-5 guideline was used to establish precision studies protocol on normal and abnormal control plasma. The study consisted of one run of duplicate Ristocetin Cofactor determinations per day for 20 days duration. The data were then analyzed according to the guidelines. Within run and between run studies were done with one (4 channels) and two (8 channels) analyzers.

Normal: Total within-run standard deviation = 7.5

                Total precision standard deviation = 7.38

Abnormal/low: Total within-run standard deviation = 3.5

                Total precision standard deviation = 4.33

c. *Linearity*:

NCCLS EP-6 guidelines were used to evaluate the linearity of the AggRAM with the Ristocetin Cofactor Kit system. Assayed normal plasma was used to make five pools. Tris Buffered Saline was used to make the dilutions. The assayed value of normal plasma Ristocetin Cofactor was 114%. The study showed system linearity of 11% to 80%.

    d. *Carryover*:

       Not applicable

    e. *Interfering Substances*:

       Not applicable

2. Other Supportive Instrument Performance Data Not Covered Above:

K. Proposed Labeling:

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

L. Conclusion:

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