APR - 2 2004

K032951

11. 510(k) Summary

Device: Chrono-log Whole Blood Aggregometer (WBA), Model 591A/592A

Date: September 5, 2003

Submitted by: Chrono-log Corp., 2 West Park Rd., Havertown, PA 19083

Contact: Nicholas J. Veriabo (610) 853-1130

Name of Device:

Trade/Proprietary Name - Chrono-log Whole Blood Aggregometer (WBA), Model 591A/592A

Common/Usual Name - Chrono-log Whole Blood Aggregometer

Classification Name - System, Automatic Platelet Aggregation

After examining the tests data included in this application, we have found the Chrono-log Whole Blood Aggregometer with Disposable Electrodes (WBA), Model 591A/592A to be substantially equivalent to Chrono-log Whole Blood Aggregometer (WBA) Model 591/592 (K962426).

11.1 Device Description:

The Chrono-log WBA, Model 591A/592A uses electrical impedance to measure platelet aggregation in a whole blood sample. The Impedance is measured using a Disposable electrode with two precious metal pins. A small voltage is applies across these two pins. When the electrode is placed into a diluted whole blood specimen and a monolayer is formed around the two pins. In the absence of an agonist, the platelet build-up stabilizes and a baseline is established. When an agonist is added to the specimen, the platelets begin to aggregate and collect on the electrode pins causing a change in impedance. The change of impedance is directly proportional to the amount of Aggregation in the specimen. This change of impedance is displayed on a front panel readout. The instrument has an analog output which produces an aggregation curve when connected to a strip chart recorder or AGGRO/LINK interface. Model 591A is a single channel version; Model 592A is the duel channel version.

11.2 Intended Use:

The Chrono-log WBA, Model 591A/592A is intended for determination of platelet function in a whole blood specimen, using ADP, Collagen and Ristocetin reagents.

11.3 Technical Description:

The Chrono-log Whole Blood Aggregometer with Disposable Electrodes (WBA), Model 591A/592A is the same device as the predicated device the Chrono-log Whole Blood Aggregometer (WBA) Model 591/592. Both devices use Impedance method of platelet

aggregation detection as described in Device Description. Both Devices have the same chassis design, automatic baseline setting, and front panel digital readout and the use the same internal circuit boards. The only new feature of the Model 591A/592A is the Disposable Electrode.

11.4 Performance:

The performance of the Chrono-log WBA Model 591A/592A was compared to the Chrono-log Whole Blood Aggregometer Model 591/592 using normal, healthy, drug free subjects. The samples were tested using Chrono-log Collagen, ADP, and Ristocetin Reagents. The following concentrations of reagents were run: Collagen 2μg/mL and 5μg/mL, ADP 1μM and 20μM and 1.0 mM; Ristocetin 0.15mg/mL, 0.15mg/mL and 1.0mg/mL. In all over 300 test were run on each type of electrodes. However, due to the fact that the Disposable Electrodes were sensitive to the high dose of Ristocetin, this reagent was eliminated from these calculations and are addressed separately. The results are expressed as aggregation in ohms obtained with the concentrations of agonist stated previously.

Table 11-1 shows the correlation between the Disposable and re-usable electrodes:

TABLE 11-1

No. of Samples	Pearson Correlation	Paired t test
250	R = 0.84	P < 0.0001

The Figure 11.1 is a scattergram showing the data distribution for the correlation Study.

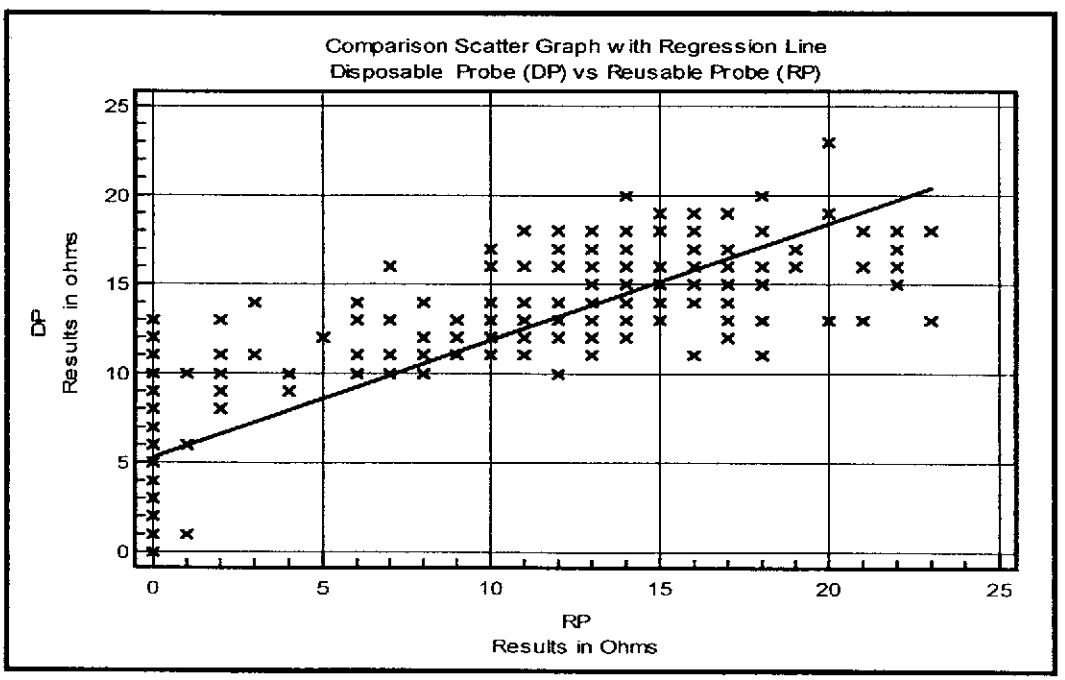


FIGURE 11.1

Test reproducibility, precision, and accuracy data was obtained to determine equivalence between the Disposable Electrode and the Reusable Electrode. Specimens were tested with several agonists, results are shown in Table 11-2 below. .

Agonist	Disposable Probe (Ω)	Re-usable Probe (Ω)	P value for paired t test	Pearson's R value
Collagen 2μg/mL	14.2 ± 2.2	13.9 ± 3.0	0.47	0.24
Collagen 5μg/mL	16.6 ± 2.3	17.7 ± 2.8	0.03	0.04
ADP 20μM	13.2 ± 2.5	9.94 ± 3.4	<0.01	0.61*

*p<0.05

Table 11-2. Whole Blood response to Various Agonists. Data are mean ± SD (n=50).

From our initial data using Ristocetin as the reagent, we determined that the disposable electrodes were more sensitive to Aggregation with Ristocetin than to the reusable electrodes. Further tests were run to determine if a lower concentration of reagent would yield a more comparable result to the reusable electrode using the standard Ristocetin concentration. These tests were run on normal donors and patients known to have von Willebrands Disease (vWD).

Two concentrations of Ristocetin, a low and high dose, were run with both the reusable and disposable electrodes. The low dose Ristocetin was 0.15 mg/mL for both types of electrodes. The higher dose of Ristocetin was 1mg/mL for reusable electrodes and 0.4 mg/mL for disposable electrodes. The Ristocetin dose was adjusted to 0.4 mg/mL to compensate for the high sensitivity seen with the disposable electrodes. The expectation was to see little or no Aggregation for the low dose Ristocetin in both the normal donors and the vWD Patients. With the high dose Ristocetin, we expected to see normal results (>5 Ω) with the normal patients and reduced (<6 Ω) or no aggregation with the vWD patients.

The results in Table 11.3 show that for normal patients, all results (N=12) were reduced or absent of Aggregation with the low dose Ristocetin. With the high dose Ristocetin, 11 of the 12 normal donors gave normal Aggregation with both methods. A different donor gave the reduced response for each type, leading us to believe that these were outliers.

Ristocetin Aggregation Normals		Ristocetin Aggregation Normals	
RP 0.15 mg/mL	**DP** 0.15 mg/mL	**RP** 1.0 mg/ml	**DP** 0.4 mg/ml
0	3	9	8
0	3	20	18
0	2	22	10
0	1	25	65
0	1	14	6
0	0	11	20
0	0	17	5
0	0	2	7
0	0	8	54
0	1	9	37
0	1	9	29
0	2	7	7

Table 11.3

The results in Table 11.4 are vWD patients. vWD Patients are known to give lower than normal aggregation with Ristocetin. The low dose Ristocetin gave reduced or absent results as expected for all patients. Six of the eight vWD patients gave reduced results with the reusable electrodes and seven of the eight vWD patients gave reduced results with the disposable electrodes.

Ristocetin Aggregation vW Patients		Ristocetin Aggregation vW Patients	
RP 0.15 mg/mL	**DP** 0.15 mg/mL	**RP** 1.0 mg/ml	**DP** 0.4 mg/ml
0	0	3	0
0	0	12	4
0	1	25	19
0	1	1	0
0	2	2	2
0	0	4	0
2	0	0	0
0	0	0	0

Table 11.4

In this study, the disposable electrodes performed better than the reusable electrodes for identifying donors with von Willebrands Disease using high and low dose Ristocetin.

Another way to demonstrate substantial equivalency is to show that the new device can detect increasing and decreasing amount of aggregation similar to the predicate device. With the Impedance Method of platelet aggregation, when aggregation takes place in the sample, the platelets stick to the electrode wires or pins on the disposable electrodes causing an increase in impedance as measured by the Aggregometer. Increased amounts of platelet build-up (aggregation) produce a greater impedance result; a reduced amount of aggregation produces a lower impedance result. One of the factors that influence platelet aggregation in whole blood is platelet count. Specifically, a significant reduction in aggregation is seen with platelet counts below 50,000/uL. [1] Because there is only a small number of platelets in the sample (platelet count), the total amount of aggregation will be less than a sample with a normal amount of platelets. This has been demonstrated in prior studies using impedance aggregation.[2]

We demonstrate that both the Model 591A/592A with the disposable electrodes and the Model 591/592 with the reusable electrodes were able to detect the changes in Aggregation in relation to platelet count. This was done in both Whole Blood and PRP. Platelet counts below 50,000/uL gave results below the normal range. Table 11.4 shows the values at various platelet counts with disposable and reusable electrodes in Whole Blood. Table 11.5 shows the values at various platelet counts with disposable and reusable electrodes in PRP.

Whole Blood		
Platelet Count*	DP	RP
300	30	18
294	25	14
164	15	21
144	19	21
73	15	18
64	13	19
34	7	6
32	7	8
21	5	3
18	9	8
10	4	3
1	1	0
0	2	0

Table 11.4 * X 10^3/uL

PRP		
Platelet Count*	DP	RP
181	19	22
104	13	17
104	17	16
58	8	9
31	7	3
27	10	9
15	5	4
15	3	1
4	1	0

Table 11.5

Figures 11.2, 11.3, 11.4 and 11.5 are scatter graphs with liner regression lines showing the relationship between the results and platelet count.

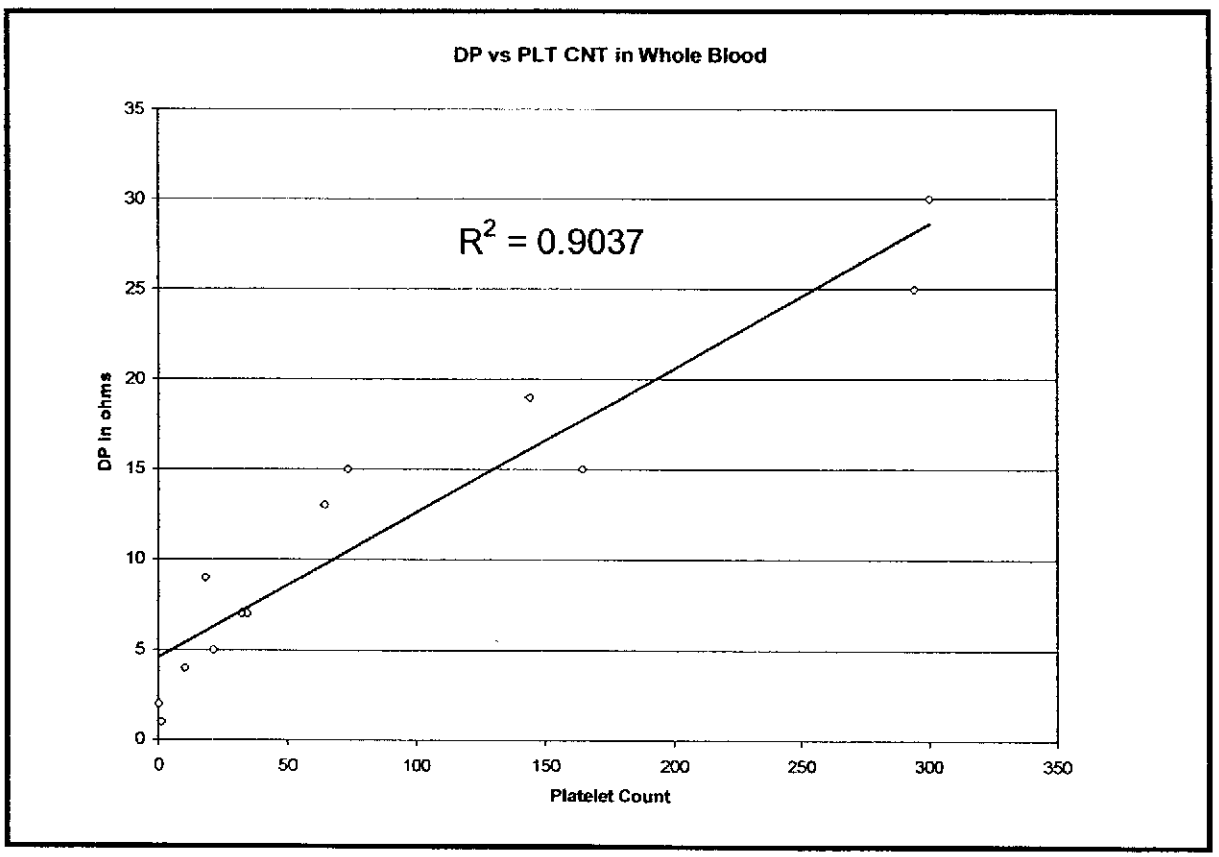


FIGURE 11.2

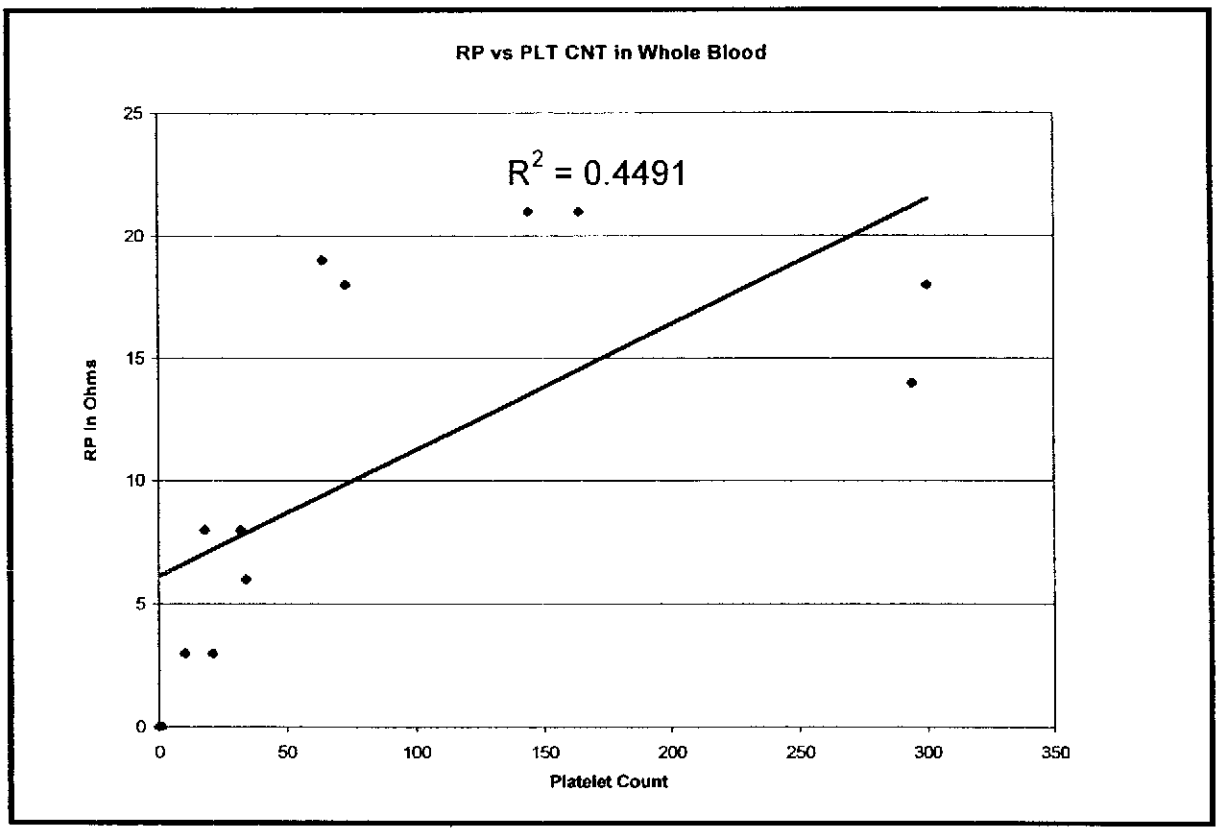


FIGURE 11.3

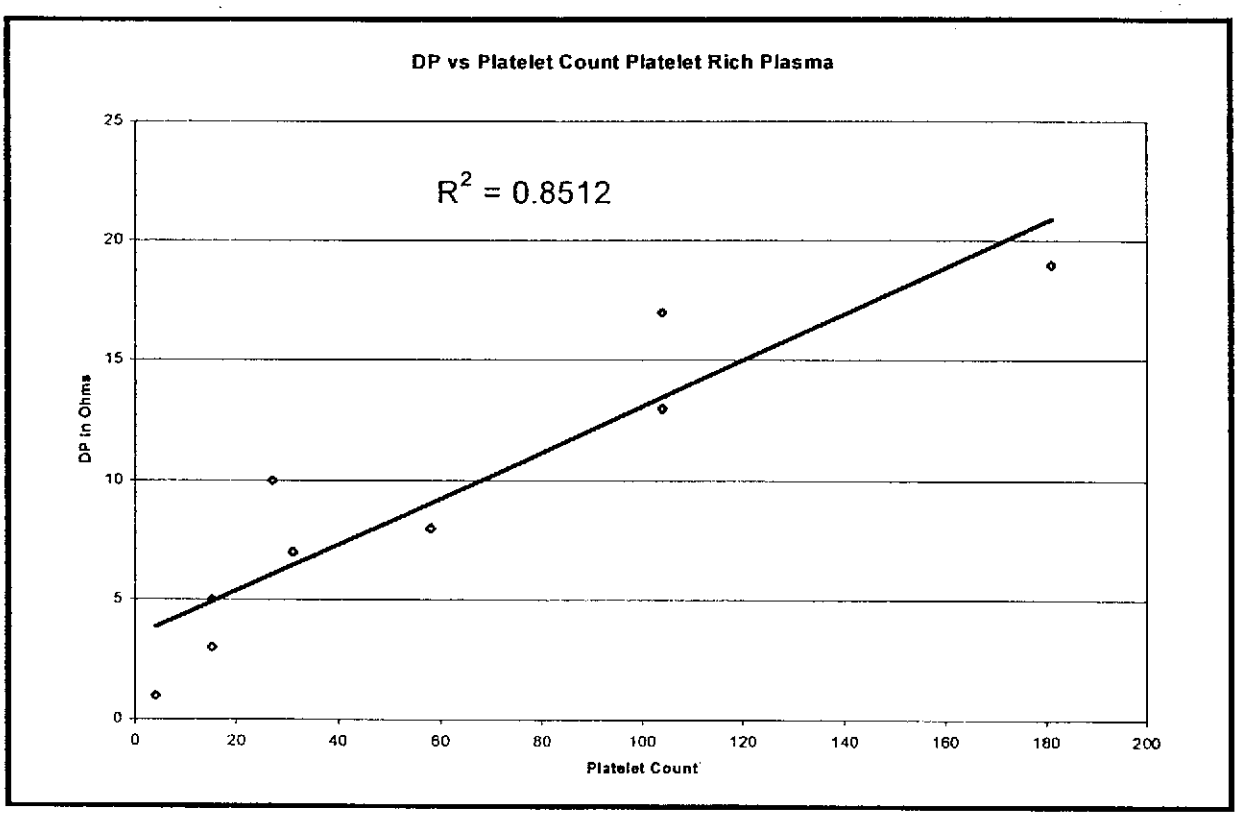


FIGURE 11.4

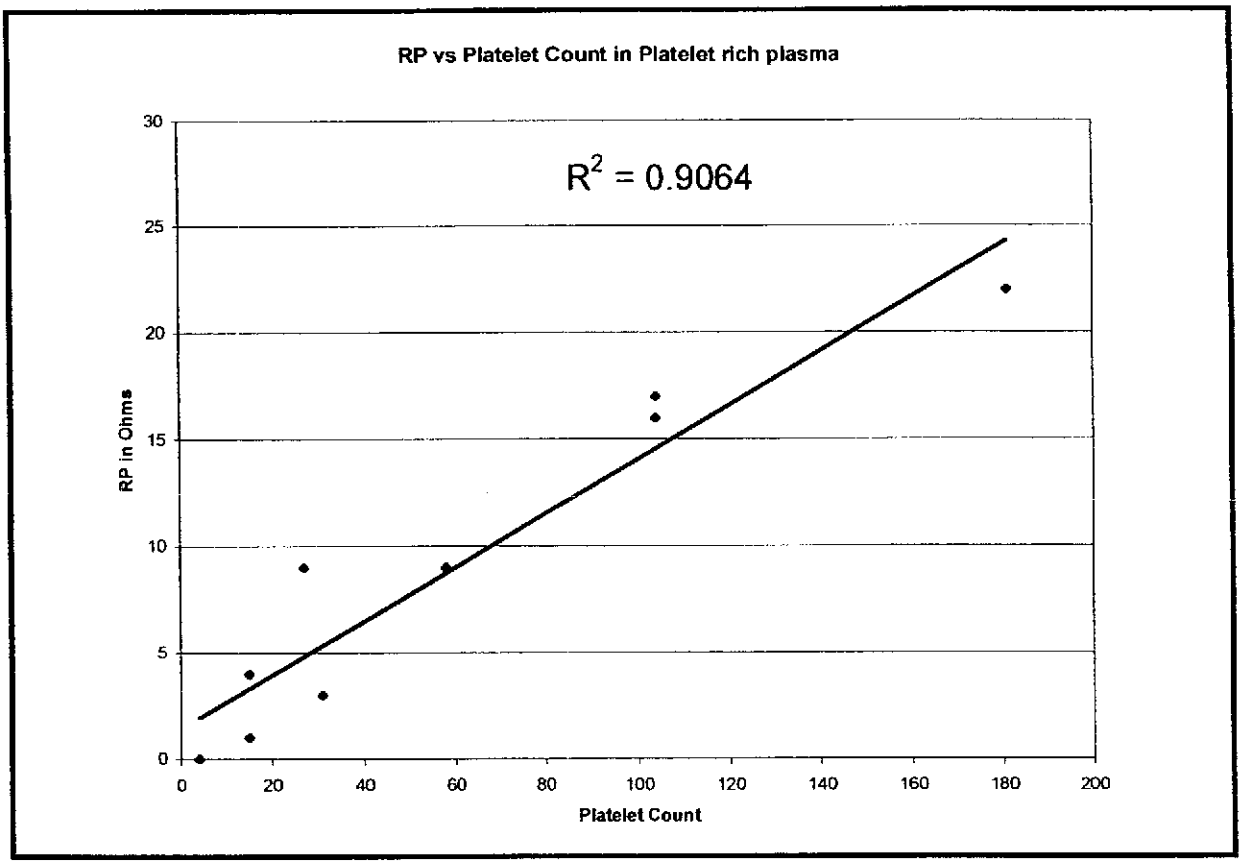


FIGURE 11.5

These graphs show a strong relationship between platelet count and each instrument in both Whole Blood and PRP as marked, demonstrating that the Model 591A/592A can detect lesser and greater amounts of platelet aggregation with similar results as are seen in the Model 591/592.

The physical differences between the reusable and disposable electrodes caused a slight shift in the normal range. We establish a new normal range to reflect this shift. The normal ranges established in this study for the Model 591A/592A are as follows:

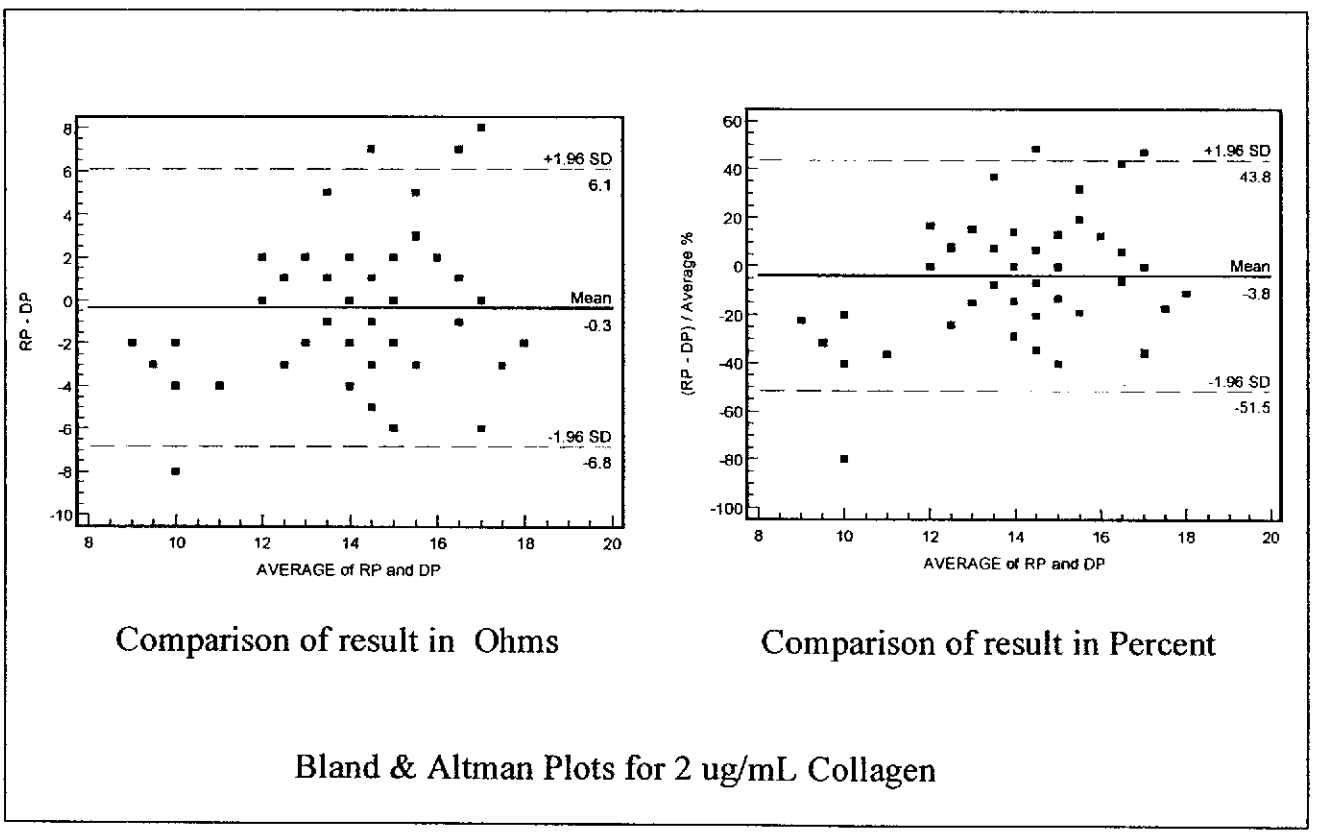
Collagen	5µg/mL	12-23
Collagen	2µg/mL	10-21
ADP	20µM	9-18
Ristocetin	0.4mg/mL	>5Ω

The previously established normal ranges for the Model 591/592 are as follows:

Collagen	5 µg/mL	16-29
ADP	10µM	9-14
Ristocetin	1mg/mL	17-38

Although the two sets of normal ranges are not exact, the normals are close to the previously established normal range in both value and range.

We analyzed the results of the two methods using the Bland-Altman comparison plot using reagent concentrations of 2 μg/mL Collagen, 5 μg/mL Collagen and 20μM ADP. Figures 11.6, 11.7 and 11.8 are the plot difference in ohms and the plot difference in percent for the three reagent concentrations.

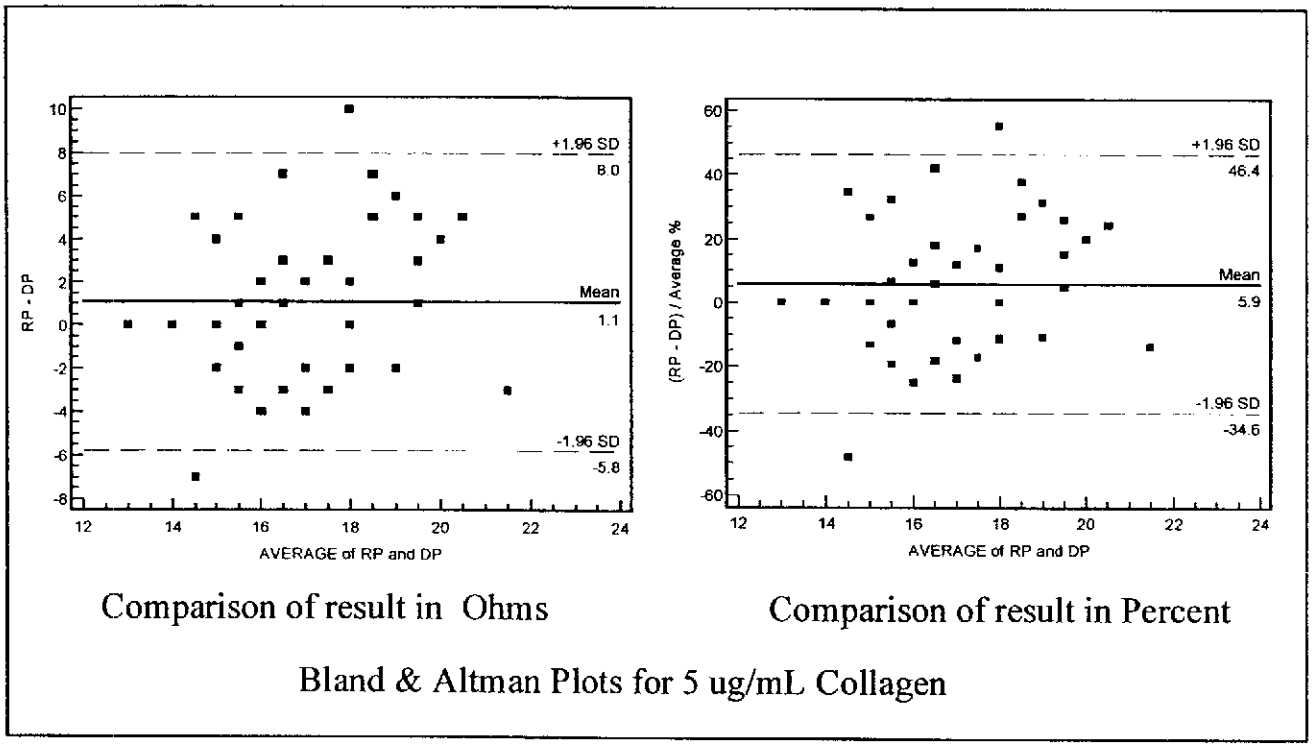


Comparison of result in Ohms

Comparison of result in Percent

Bland & Altman Plots for 2 ug/mL Collagen

FIGURE 11.6

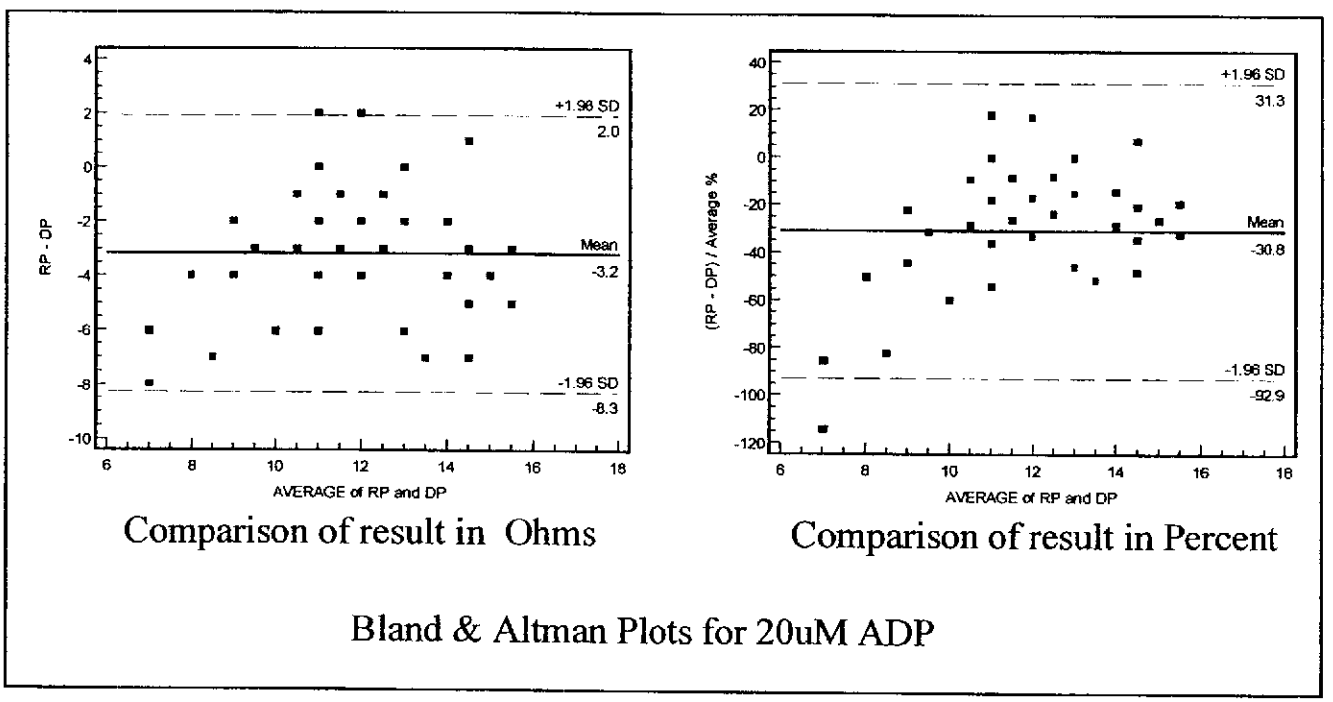


Comparison of result in Ohms

Comparison of result in Percent

Bland & Altman Plots for 5 ug/mL Collagen

FIGURE 11.7



Comparison of result in Ohms

Comparison of result in Percent

Bland & Altman Plots for 20uM ADP

FIGURE 11.8

Examining the graphs, we see that there is a wide range for the 2SD cut-off; however, this is not beyond what is historically seen with platelet aggregation in whole blood on normal subjects. Since these donors are all normal subjects, we are able to establish a normal range from the data. As stated previously in this report, the normal range is close in value and range to the normal range established for the Model 591/592.

The results of these tests indicate that the two models of Whole Blood Aggregometer give comparable results and raise no new issues of safety or effectiveness.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

APR - 2 2004

Mr. Nicholas J. Verabo
Executive Director
Chrono-Log Corp.
2 West Park Rd.
Havertown, PA 19083

Re: k032951
Trade/Device Name: Chrono-Log Whole Blood Aggregometer (WBA)
Model 591A/592A
Regulation Number: 21 CFR 864.5700
Regulation Name: Automated platelet aggregation system
Regulatory Class: Class II
Product Code: JOZ
Dated: February 10, 2004
Received: February 11, 2004

Dear Mr. Verabo

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820).

If you desire specific information about the application of labeling requirements to your device, or questions on the promotion and advertising of your device, please contact the Office of In Vitro Diagnostic Device Evaluation and Safety at (301) 594-3084. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its Internet address http://www.fda.gov/cdrh/dsma/dsmamain.html.

Sincerely yours,

Joseph L. Hackett

Joseph L. Hackett, Ph.D.
Acting Director
Division of Immunology and Hematology Devices
Office of In Vitro Diagnostic Device Evaluation and Safety
Center for Devices and Radiological Health

Enclosure

6. INDICATIONS FOR USE

Device Name: Chrono-log Whole Blood Aggregometer (WBA)
Model 591A/592A

Indications for Use: For Platelet Function testing of Whole Blood specimens using Impedance Aggregometry.

For Prescription Use ✓

Division Sign-Off

Office of In Vitro Diagnostic Device Evaluation and Safety

510(k) K032951