DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
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Silver Spring, MD 20993-0002

December 2, 2016

Chrono-log Corporation
Nicholas J. Veriabo
Executive Director
2 West Park Road
Havertown, PA 19083-4691

Re: K161329
Trade/Device Name: Chrono-log Platelet Aggregometer, Model 490 4+4
Regulation Number: 21 CFR 864.5700
Regulation Name: Platelet aggregometer
Regulatory Class: Class II
Product Code: JOZ
Dated: November 2, 2016
Received: November 4, 2016

Dear Mr. Veriabo:

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. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. 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); medical device reporting (reporting of

medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely,

Leonthena R. Carrington -S

Leonthena R. Carrington, MS, MBA, MT(ASCP)
Director
Division of Immunology and Hematology Devices
Office of *In Vitro* Diagnostics and Radiological Health
Center for Devices and Radiological Health

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*
K161329

Device Name
Chrono-log Platelet Aggregometer, Model 490 4+4

Indications for Use *(Describe)*
The Chrono-log Model 490 4+4 Aggregometer is intended for use for in-vitro diagnostic use for measuring Platelet Aggregation in Platelet Rich Plasma.
This device is intended to be used in a clinical laboratory environment by laboratory technicians.
For use only with light transmission aggregometry assays cleared for use with the Chrono-log Platelet Aggregometry systems.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

11. 510(k) Summary

Device: Chrono-log™ Platelet Aggregometer, Model 490 4+4

Date: March 17, 2016

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™ Platelet Aggregometer Model 490 4+4

Common/Usual Name - Platelet Aggregometer

Classification Name – System, Automatic Platelet Aggregation 21CFR 864.5700

Regulatory Class – Class II

Product Code – JOZ

510(k) Review Panel - Hematology

Predicate Device:

Trade/Proprietary Name - Chrono-log™ Whole Blood Lumi-Aggregometer Model 700

Common/Usual Name - Platelet Aggregometer, Whole Blood Aggregometer, Lumi-Aggregometer

Classification Name – System, Automatic Platelet Aggregation 21CFR 864.5700

Regulatory Class – Class II

Product Code – JOZ

510(k) Review Panel - Hematology

11.1 Device Description:

The Chrono-log™ Model 490 4+4 Aggregometer measures platelet function on patient samples using LTA which measures a change in optical density of platelet rich plasma. The Model 490 4+4 is also used to run the Ristocetin Cofactor Assay to aid in diagnosis of patients with von Willebrand disease. The instrument comes with a starter kit of reagents and supplies. The output of the Model 490 4+4 can be connected to either a strip chart recorder or to a Computer. Software is provided with the computer interface option. The computer interface option is used to collect data only. The computer is not used for diagnosis or treatment and does not have any control over or input into the Model 490 4+4 Aggregometer.

LTA or Born method of platelet aggregation measures the change in optical density of a Platelet Rich Plasma (PRP) sample in comparison to optical density of a Platelet Poor Plasma (PPP) sample. The PRP sample, platelets in a suspension of plasma, is isolated from an anticoagulated blood sample by a relatively low centrifugal force centrifugation. The PPP sample is prepared by centrifuging the blood sample at a relatively high force. The Chrono-log sample chambers are designed so that a beam of infra red light shines through two cuvettes, one containing PRP (the sample) and one containing PPP (the reference). Silicon photodiodes detect the light able to pass through the samples: PRP is arbitrarily considered to be 0% light transmission or 0% aggregation; PPP is considered to be 100% light transmission or 100% aggregation. When a stimulus is added to the cuvette containing PRP and the platelets respond forming aggregates, more light is allowed to pass through the PRP sample. The change in light transmission, recorded over time, shows a trend towards the platelet poor plasma, or 100% light transmission. A graphical tracing of the change in optical density during the course of platelet aggregation is produced either on a strip chart recorder or on a computer using Chrono-log provided software. This device is designed to be used in the clinical laboratory as an in vitro diagnostic tool. The 490 4+4 varies from the predicate devices only in the number of channels.

11.2 Intended Use:

The Chrono-log Model 490 4+4 Aggregometer is intended for use for in-vitro diagnostic use for measuring platelet aggregation in platelet rich plasma. This device is intended to be used in a clinical laboratory environment by laboratory technicians. For use only with light transmission aggregometry assays cleared for use with the Chrono-log™ Platelet Aggregometry systems.

11.3 Technical Description:

The Chrono-log™ Model 490 4+4 Aggregometer is an instrument used in the Laboratory for the determination of Platelet Aggregation in samples of PRP. The 490 4+4 is a modified Model 700. Substantial equivalency between the Model 490 4+4 and the Model 700 (K050265) currently in commercial distribution by Chrono-log Corp is claimed.

The fundamental scientific technology of the modified device was unchanged. The energy type is the same. Environmental specifications are the same. Performance specifications are the same as the optical method of the predicate device. The ergonomics of the user interface is the same and the firmware is the same.

The critical components of the Model 490 4+4 are exactly the same as the predicate device. The circuits that drive these components are the same as the circuits used in the Model 700. Due to various parts in the predicate device becoming obsolete, some circuit parts were upgraded in the Model 490 4+4. The chart on the following page gives a detailed description of the component differences between the Model 490 4+4 and the Model 700.

The chassis has also been redesigned to accommodate four channels. The front panel for both use a Liquid Crystal Display (LCD) for displaying Temperature and Stirring Speed. Both instruments have front panel controls which are tactile membrane switches.

The output of the Model 490 4+4 can be connected to either a strip chart recorder or to a Computer. Chrono-log provides software for the computer interface option as an accessory. The computer interface option is used to collect data and is not used for diagnosis or treatment and does not have any control over or input into the Model 490 4+4 Aggregometer.

490 4+4 Component change					
Component	**Functionality**	**Description of change**	**Material Change**	**Impact of change**	**Mitigation**
Heater Block	Holds sample Heats sample	Heater Block was made smaller. Remove holes for luminescence measurements	None	Minimal - LED and photodiodes are closer to sample	Verification testing was performed by measuring optical density samples and recording voltage readings. All samples measured to specifications.
Photodiode Amplifier	Measures the amount of light shining through the samples	Resistors R1, R2, R3 & R4 were changed from 20MΩ to 10MΩ to reduce the gain on the amplifier. A lower gain was needed because the heater blocks are closer.	None	No known impact. The output voltage is the same for various optical density	Verification testing was performed by measuring optical density samples and recording voltage readings. All samples measured to specifications.
Heater Control Board	Heats the heater blocks and has the Door switch for Luminescence	The following parts are removed: U5, C8, C11, D1, D2, D3, D4, D5, D6, D7. These components are used for luminescence in the Model 700. In the Model 490 4+4 there isn't a luminescence	None	Luminescence feature removed. Cannot measure ATP release, which is within the design specifications.	Verification not needed for the removal of the Luminescence feature.

		feature. These components are removed to reduced costs.			
Analog Control Board	Processes the output from the detection devices.	The following parts were removed U10, U11, C10, C11, R17, R18, R19, R20, R21, R26, P1 & P2. These components are for the luminescence and the selection between optical and Impedance methods in the Model 700. In the Model 490 4+4, the luminescence and impedance features are not used, so these components were removed to reduce costs.	None	Luminescence and Impedance features removed. Cannot measure ATP release or Impedance aggregation, which is within the design specifications.	Verification not needed for the removal of the Luminescence and Impedance features.
Switch Circuit on Heater Block Board	Turns power on to PMT when heater block door is closed, shuts off power when door is opened. The PMT is used for luminescence measurement of ATP release.	The following parts are removed U1, C1, C2, R2, R4, R5, R6, RL1, Con 2, Con 3, and Con 4,. All components above are for the door switch circuit used for luminescence in the Model 700. In the Model 490 4+4 there isn't a luminescence feature, so this circuit is not needed. These components are removed to reduce cost.	None	Luminescence feature removed. Cannot measure ATP release, which is within the design specifications.	Verification not needed for the removal of the Luminescence feature.
Heater block circuit	Heats the heater blocks to the temperature set on the front panel.	R2 was removed and R1 resistance was increased. The circuits for heating the block are the same except the Model 700 uses two resistors to heat the block where as the Model 490 4+4 needs only 1 resistor to heat the smaller block. This is why R2 was removed. The value of R1 was increased because less current is needed to heat smaller block size in the Model 490 4+4.	None	Minimal - The heater block temperature is maintained at the temperature set on the front panel, usually 37^{o}C.	Verification testing was performed by measuring the temperature of the blocks for every possible setting. All temperature settings tested to specifications.

Four Motor Driver Board	Drives the stirring motors. Controls the stirring motors speed. Monitors the motor speed.	The combination of U2, R1, R2, R3, R4, C8 and C9 on Drawing 6811 replaces components U2, T1, T2, T3, T4, D1, D2, D3, D4, D5, C1, C2, C3, C4, C5, C6, C7, R1, R2, R3, R4, R5, R6, R7, R8, R9, R10, R11, R12, R13, R14 and R15 on Drawing 6597 and also replaces U3, Q 1, R1, R2, R3, C10 and C11 on Drawing 6718.The rest of the circuit is the same.	None	Minimal- Stirrer driver operates as a Phase-locked circuit keeping the stirrer speed locked to the reference frequency provided by a Microcontroller. Both circuits (original and revised) accomplish this and are functionally equal.	Verification testing was performed by measuring the frequency of the signals and revolution rate of the motors. Fault conditions were induced to test the error checking feature. All conditions tested to specifications.

11.4 Performance:

Design control activities conforming to 21.CFR 820.30 were implemented in the device modification process. As demonstrated by risk analysis and by verification and validation activities, no questions of safety and effectiveness were raised. Verification and validation activities were performed and the results show conformance with predetermined acceptance criteria. These nonclinical tests suggest that the modified device is substantially equivalent to the predicate device.

A Comparison study was run to compare the performance of the Model 490 4+4 to the Model 700. Platelet Rich Plasma samples from four normal, healthy, drug free subjects and a subject taking aspirin, a known inhibitor of platelet aggregation by acetylation of the platelet cyclooxygenase pathway. These samples were tested with both instruments.

To demonstrate abnormal results with ADP and Collagen, samples were treated with ticagrelor and GPIIb/IIIa antagonist (Hart Biologicals, Hartlepool, UK), as per manufacturer's instructions. The ticagrelor blocks the $P2Y_{12}$ ADP-receptor, which reduces the aggregation with ADP. GPIIb/IIIa antagonist blocks the GPIIb/IIIa receptor which reduces aggregation by collagen.

To demonstrate abnormal Ristocetin results, samples were run using deficient vw plasma and lyophilized platelets.

The samples were tested using CHRONO-PAR™ Arachidonic Acid, Epinephrine, Collagen, ADP and Ristocetin. The following concentrations of reagents were run; Arachidonic Acid 0.5 mM, Epinephrine 5µM, Collagen 1µg/mL, Collagen 5µg/mL, ADP 5µM, ADP 10µM, Ristocetin 0.25mg/mL and Ristocetin 1.25 mg/mL. Tests were run using Platelet Rich Plasma samples of both 500µL and 250µL volume.

In total, there were 114 comparison tests using optical aggregation. To demonstrate sample size equivalence, a small subset of tests was used to compare the results for 500µL and 250µL volume samples from a normal donor and a donor taking aspirin. These two sample volumes were run because these are the two recommended sample

sizes in the instructions. For both donors, one test with each reagent for both sample sizes was run using the recommended concentrations in the IFU.

The Tables below show the correlation between the Model 490 4+4 and the Model 700.

ALL SAMPLES

No. of Samples	Coefficient of Variation
114	0.9771

NORMAL SAMPLES IN 500 µL

No. of Samples	Coefficient of Variation
8	0.9648

ASPIRIN SAMPLES IN 500 µL

No. of Samples	Coefficient of Variation
8	0.9943

NORMAL SAMPLES IN 250 µL

No. of Samples	Coefficient of Variation
8	0.9758

ASPIRIN SAMPLES IN 250 µL

No. of Samples	Coefficient of Variation
8	0.9871

When comparing the results of the 490 4+4 to the predicate device with each individual reagent, there is a strong correlation with each reagent.

Reagent	Coefficient of Variation
Arachidonic Acid	0.9945
Epinephrine	0.9509
Collagen	0.9786
ADP	0.9421
Ristocetin	0.9863

11.5 Conclusion:

The results of the study show strong correlation between the Model 490 4+4 and the predicate device. The R^2 Value of all samples run is 0.9771. There is also a strong correlation when comparing each reagent. In a subset of samples, values for the two recommended sample sizes were compared and strong correlation was found with the normal donors and donors on aspirin. Normal donors gave an R^2 result of 0.9648 for the 500 µL samples and 0.9758 for the 250 µL samples. Aspirin donors gave an R^2 result of 0.9943 for the 500 µL samples and 0.9871 for the 250 µL samples.

An agreement analysis using a Bland Altman Plot showed good agreement between the 490 4+4 and the predicate device. There is a small bias of -4.56 which is not clinically significant for this assay. The Bland Altman Plot shows agreement and the 2SD cut-off is not beyond what is historically seen with platelet aggregation.[1,2]

Since the assay is the same for the 490 4+4 and the predicate device, the aim is to show equivalence results for the two devices. The enclosed data supports the claim of substantial equivalence.

1. Riess et al: Clinical Evaluation of Platelet Aggregation in Whole Human Blood American Journal of Clinical Pathology (1986) 85 (1): 50-56

2. Alshameeri et al (1995): Comparisons of Platelet Aggregation in Platelet Rich Plasma and Whole Blood. Disorders of Thrombosis & Hemostasis, Abstract.