February 14, 2020

Fujimori Kogyo Co., Ltd.
Jeffrey Dahlen
Project Leader
11435 Merritage Court
San Diego, California 92131

Re: K191364
Trade/Device Name: T-TAS 01 System with PL Chip
Regulation Number: 21 CFR 864.5700
Regulation Name: Automated platelet aggregation system
Regulatory Class: Class II
Product Code: JOZ
Dated: May 20, 2019
Received: May 22, 2019

Dear Jeffrey Dahlen:

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. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. 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 Part 801 and Part 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Takeesha Taylor-Bell
Chief
Division of Immunology
and Hematology Devices
OHT7: Office of In Vitro Diagnostics
and Radiological Health
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2020
See PRA Statement below.

510(k) Number *(if known)*

Device Name
T-TAS 01 System with PL chip

Indications for Use *(Describe)*

The T-TAS 01 Instrument is intended for use with T-TAS reagent chips in the clinical laboratory.

The T-TAS 01 PL chip is intended for use in the clinical laboratory for the analysis of the platelet thrombus formation process (primary hemostatic function) in patients age 21 and older with a history of conditions associated with impaired primary hemostatic function or use of antiplatelet therapy. The test uses BAPA-anticoagulated whole blood specimens to measure platelet adhesion to a thrombogenic collagen-coated surface and aggregation, which causes an increase in flow pressure inside the PL chip. The test measures primary hemostatic function as the area under the pressure-time curve (AUC), with AUC < 260 suggesting abnormal primary hemostatic function. Additional testing may be necessary to identify the cause(s) of abnormal primary hemostatic function. The test has been evaluated in patients taking antiplatelet therapy, in patients with von Willebrand disease, and in patients with Glanzmann's thrombasthenia. Other primary hemostasis disorders have not been evaluated.

The BAPA tube for T-TAS 01 is intended to be used for the collection, transport, and storage of blood specimens for use with the T-TAS 01 system.

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.

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510(k) Summary [as required by 21 CFR 807.92(c)]

Submitter information:

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Contact Name:	Jeffrey Dahlen, Ph.D.
Contact Email:	jeff-dahlen@zacros.co.jp

Date Summary was Prepared:	2020-02-14

Product information:

510(k) Number	K191364
Trade/Proprietary Name(s):	Total Thrombus-formation Analysis (T-TAS) 01 System, which consists of: • T-TAS 01 Instrument (Catalog #18001) • PL chip for T-TAS 01 (Catalog #18002) • PL chip Reservoir Set for T-TAS 01 (Catalog #18003) • BAPA tube for T-TAS 01 (Catalog #18004)
Common/Usual Name(s):	Automated Platelet Aggregation System
Product Code:	JOZ
Regulation:	21 CFR 864.5700
Regulatory Classification:	Class II
Panel:	Hematology

Predicate Method:

Product Name:	Dade Behring (now Siemens) PFA-100
510(k) Document Number:	K060489

Device Description:

The T-TAS 01 system is an in vitro diagnostic device that is comprised of tabletop instrument controlled by a dedicated PC and a disposable, single-use flow chamber. The PL Chip for T-TAS 01 is designed to specifically measure platelet thrombus formation (PTF) under physiological conditions on a collagen-coated analytical path consisting of 26 microcapillary channels. Platelet thrombus formation is a direct indicator of the patient's primary hemostatic function. The assay is performed under arterial flow conditions using benzylsulfonyl-D-Arg-Pro-4-amidinobenzylamide (BAPA)-anticoagulated whole blood samples. BAPA is an anticoagulant that inhibits thrombin and factor Xa, blocking the coagulation cascade and allowing the PL assay to specifically measure only the platelet thrombus formation process (primary hemostasis). During the assay, the blood sample is exposed to arterial shear stresses at 1,500 s^{-1} in the presence of a collagen-coated surface, which causes platelet attachment to collagen mediated by von Willebrand factor (vWF), and platelet activation. Platelet activation causes the release of endogenous factors contained within the platelets that recruit and activate other platelets and cause aggregation, and platelet thrombus formation. The growing platelet thrombus causes occlusion of the microcapillary channels, which increases the flow pressure within the assay chip. The process of platelet thrombus formation in the flow chamber is continuously monitored by a pressure sensor that tracks pressure changes in the flow path. Results are

calculated automatically within 10 minutes or when the pressure a reading reaches 60 kPa above the baseline pressure, whichever occurs first. Results are displayed as AUC, which is the area under the flow pressure curve over 10 minutes.

AUC results less than 260 are associated with abnormal primary hemostatic function.

Intended Use/Indications for Use:

The T-TAS 01 Instrument is intended for use with T-TAS reagent chips in the clinical laboratory.

The T-TAS 01 PL chip is intended for use in the clinical laboratory for the analysis of the platelet thrombus formation process (primary hemostatic function) in patients age 21 and older with a history of conditions associated with impaired primary hemostatic function or use of antiplatelet therapy. The test uses BAPA-anticoagulated whole blood specimens to measure platelet adhesion to a thrombogenic collagen-coated surface and aggregation, which causes an increase in flow pressure inside the PL chip. The test measures primary hemostatic function as the area under the pressure-time curve (AUC), with AUC < 260 suggesting abnormal primary hemostatic function. Additional testing may be necessary to identify the cause(s) of abnormal primary hemostatic function. The test has been evaluated in patients taking antiplatelet therapy, in patients with von Willebrand disease, and in patients with Glanzmann's thrombasthenia. Other primary hemostasis disorders have not been evaluated.

The BAPA tube for T-TAS 01 is intended to be used for the collection, transport, and storage of blood specimens for use with the T-TAS 01 system

Comparison with Predicate:

Parameter	PFA-100 CEPI cartridge (Predicate Device)	T-TAS 01 System with PL-chip (Subject Device)
Intended Use	The Dade® PFA-100® Platelet Function Analyzer and Dade® PFA-100® Reagents are in vitro diagnostic devices intended to aid in the detection of platelet dysfunction in citrated human whole blood. (Note: the PFA-100 was originally marketed by Dade and is now marketed by Siemens Healthineers)	The T-TAS 01 Instrument is intended for use with T-TAS reagent chips in the clinical laboratory. The T-TAS 01 PL chip is intended for use in the clinical laboratory for the analysis of the platelet thrombus formation process (primary hemostatic function) in patients age 21 and older with a history of conditions associated with impaired primary hemostatic function or use of antiplatelet therapy. The test uses BAPA-anticoagulated whole blood specimens to measure platelet adhesion to a thrombogenic collagen-coated surface and aggregation, which causes an increase in flow pressure inside the PL chip. The test measures primary hemostatic function as the area under the pressure-time curve (AUC), with AUC < 260 suggesting abnormal primary hemostatic function. Additional testing may be necessary to identify the cause(s) of abnormal primary hemostatic function. The test has been evaluated in patients taking antiplatelet therapy, in patients with von Willebrand disease, and in patients with Glanzmann's thrombasthenia. Other primary hemostasis disorders have not been evaluated. The BAPA tube for T-TAS 01 is intended to be used for the collection, transport, and storage of blood specimens for use with the T-TAS 01 system
Location of Intended Use	Clinical laboratory	**Same**
Intended Use Population	• Normal population • Patients taking aspirin • Patients with vWD • Patients with Glanzmann's thrombasthenia • Adult & pediatric populations	• Patients taking antiplatelet therapy • Patients with vWD • Patients with Glanzmann's thrombasthenia • Adult population
Pre-analytic Considerations		
Specimen Type	Buffered sodium citrate-anticoagulated whole blood	BAPA-anticoagulated whole blood
Sample Preparation	None	**Same**
Reagent Preparation	None	**Same**

Parameter	PFA-100 CEPI cartridge (Predicate Device)	T-TAS 01 System with PL-chip (Subject Device)
Other Reagents Necessary for Assay	Trigger solution	Mineral oil (for instrument micropump)
Assay Calibration	None required by user; all calibration performed at factory.	**Same**
Introduction of Blood Sample	Manual transfer of sample from blood collection tube to assay cartridge by pipette.	**Same**
Blood Sample Volume Required	800 µL	300-330 µL (320 µL recommended)
Sample Incubation Time Prior to Assay	15 minutes at room temperature	30 minutes
Chip/Cartridge Warm-up Time in Instrument Prior to Assay	< 2.5 minutes	**Same**
Maximum Allowable Sample Stability Time Prior to Assay (ambient temperature)	4 hours	6 hours
Assay Temperature	37.9 ± 1 °C	36 °C
Recommended Operating Temperature	64 °F to 90 °F (18 °C to 29 °C)	68 °F to 86 °F (20 °C to 30 °C)
Recommended Operating Relative Humidity	20-90%	20-80%
Altitude (maximum)	2,000 m (6,500 ft)	**Same**
Assay Cartridge Storage Conditions	2-25 °C, allow cold cartridge to warm to room temperature for 15 minutes prior to testing.	2-8 °C, allow cold cartridge to warm to room temperature for 15 minutes prior to testing.
Open Pouch Stability	4 hours at ambient temperature	8 hours at ambient temperature
Quality Control Considerations		
Internal Quality Control	Yes, self-test performed at least once per shift at the start of each shift.	**Same**
External Quality Control	Yes, external quality control using known control donor blood samples.	**Same**

Parameter	PFA-100 CEPI cartridge (Predicate Device)	T-TAS 01 System with PL-chip (Subject Device)
Analytic Considerations		
Detection Principle	Measures time required for platelets to adhere and aggregate, resulting in occlusion of an aperture under high shear flow conditions.	Measures integrated area under the curve of pressure over time as platelets adhere to a thrombogenic surface under high shear flow conditions.
Principal Assay Components Involved in Generating Result	Platelets, collagen, exogenous epinephrine, endogenous plasma and platelet components, aperture.	Platelets, collagen, endogenous plasma and platelet components, capillary channels.
Mechanism of Platelet Activation	Soluble exogenous agonist + vWF-mediated binding to collagen at high shear rate	vWF-mediated binding to collagen at high shear rate
Solution-phase Exogenous Platelet Agonist	Epinephrine	None
Platelet Adhesion Matrix	Collagen	**Same**
Shear Rate During Assay	5,000 s^{-1}	1,500 s^{-1}
Post-analytic Considerations		
Time to Result	4-8 minutes	≤ 10 minutes
Units	Closure time (seconds)	AUC
Reference Range	94-193 seconds	AUC 270.0-447.7
Recommended Cutoff	> 170 seconds	AUC < 260
Interpretation of Result	Prolonged closure times (above the cutoff) are considered abnormal, and indicative of platelet dysfunction.	AUC ≥ 260 indicates that that primary hemostatic defects are not identified. AUC < 260 is considered abnormal and indicates impaired primary hemostatic function (reduced platelet thrombus formation).
Instrument Technical Considerations		
Supports Use of Operator IDs	No	**Same**
Supports Use of Patient IDs	Yes	**Same**
Method for Controlling Instrument	LCD screen and keypad	External computer with touchscreen
Number of Results Stored in Memory	20 Patient Results 50 Control Results	Thousands (limited by PC memory)
Instrument Dimensions (LxWxH)	15.1” x 9” x 14.2” (38 x 23 x 36 cm)	14.2” x 12.6” x 9.7” (36 x 32 x 24.7 cm)
Instrument Weight	24 lbs (10.9 kg)	13.2 lbs (6.0 kg)

Summary of Non-clinical Data:

Precision:
Assay precision was evaluated using three operators, three T-TAS 01 instruments, and three PL chip lots. BAPA-anticoagulated whole blood specimens collected from one control donor and two donors taking aspirin were tested. The blood specimens had AUC results representing specimens with normal primary hemostatic ability (High), abnormal primary hemostatic ability (Low), and hemostatic ability near the assay cutoff (Middle). The results were within the specification of CV ≤ 15% or SD ≤ 39 and are summarized below.

Sample	N	Mean	Repeatability Within-Run (SD, %CV)	Between-Operator (SD, %CV)	Between-Lot (SD, %CV)	Between-Instrument (SD, %CV)	Total (SD, %CV)
High	36	428.1	10.7, 2.5	2.0, 0.5	4.7, 1.1	1.6, 0.4	11.9, 2.8
Middle	36	237.3	31.7, 13.4	6.4, 2.7	10.5, 4.4	0.0, 0.0	34.0, 14.3
Low	36	130.7	18.4, 14.1	11.8, 9.0	13.5, 10.3	0.0, 0.0	25.7, 19.6

Between-site reproducibility was also studied by performing 5 replicate PL assay measurements per day over 5 days at each of three different locations using BAPA-anticoagulated whole blood samples from four donors. The donors included a healthy control donor and three donors taking aspirin therapy that had high, middle, and low AUC results similar to the precision study. All results within each day of tested were within the specification of CV ≤ 15% or SD ≤ 39.

Assay Interference:
The following substances were tested for their ability to interfere with the PL assay AUC result and did not significantly affect the AUC results when present at the plasma concentrations indicated.

Compound	Concentration	Compound	Concentration
Acetaminophen	7.8 mg/dL	Heparin	525 U/mL
Bilirubin	40 mg/dL	L-Thyroxine	0.0858 mg/dL
Caffeine	21.6 mg/dL	Metformin	2.4 mg/dL
Captopril	0.528 mg/dL	Omeprazole	1.68 mg/dL
Catechin	5 mg/dL	Pravastatin	0.414 mg/dL
Cilostazol	1.25 mg/dL	Propranolol	0.202 mg/dL
Dabigatran	0.047 mg/dL	Rivaroxaban	0.044 mg/dL
Dextran 40	2400 mg/dL	Streptokinase	50,000 U/dL
Diltiazem	0.18 mg/dL	Theophylline	6 mg/dL
Dipyridamole	0.25 mg/dL	Tirofiban	N/A
Fish Oil	25.6 mg/dL	Triglycerides	750 mg/dL
Ibuprofen	0.438 mg/dL	Warfarin	7.5 mg/dL

Cilostazol, dipyridamole, ibuprofen, and tirofiban are all known to reduce platelet activity, and cause a dose-dependent reduction in AUC result. The maximum tirofiban concentration without interference was not determined.
Hemodilution up to 20% and under-filling of the BAPA collection tube up to 50% did not significantly affect PL assay AUC results.

Stability Studies:
Stability of the T-TAS 01 PL assay chip and stability of BAPA-anticoagulated blood samples were evaluated using fresh blood samples collected from healthy control donors and donors taking aspirin. PL assay chip stability was evaluated using an isochronous design. Stability of the BAPA tube was determined by measuring the fill volume over time according to CLSI standard GP39-A6.

Closed pouch PL chip stability: 12 months from the date of manufacture @ 2-8 °C
Open pouch PL chip stability: 8 hours @ ambient temperature (20-25 °C)
BAPA tube stability: 10 months from the date of manufacture @ ambient temperature (15-30 °C)
BAPA-anticoagulated blood sample stability: 6 hours @ ambient temperature (20-25 °C)

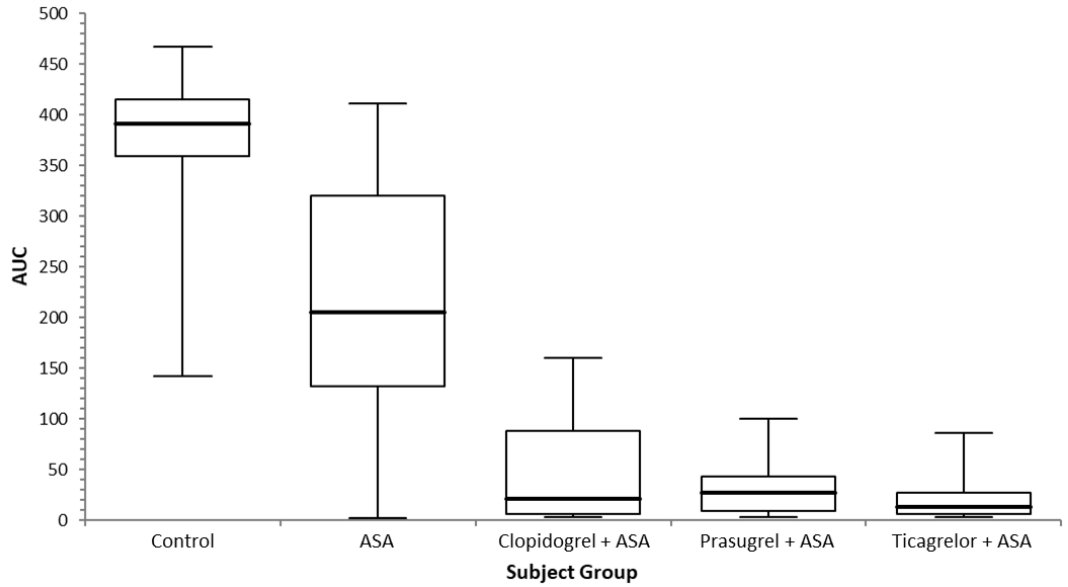
Summary of Clinical Data:

Reference Interval:
The AUC reference interval for the T-TAS 01 PL assay is 270.0 – 447.7.
The reference interval was determined from the 5th to 95th percentile (central 90%) of AUC results obtained from PL assay measurements at three clinical sites using a population of 142 individuals (96 females, 46 males, age 38.0 ± 11.3 years) without a history of inherited or acquired platelet dysfunction, and without laboratory evidence of von Willebrand disease. PL assay AUC results were not influenced by age, gender, ethnicity, or race.

Clinical Performance:
Sensitivity and negative agreement of the PL assay for detecting conditions associated with associated with abnormal primary hemostatic function were calculated from data obtained from a total of 274 subjects enrolled at a total of 6 investigational sites. Negative agreement was calculated using PL assay results from healthy donors confirmed to have normal primary hemostatic function because they did not have laboratory evidence or prior diagnosis of disorders affecting primary hemostatic function, nor were they taking medications that affect primary hemostatic function. Sensitivity was calculated using PL assay results from the following patient groups with conditions associated with impaired primary hemostatic function: subjects taking antiplatelet therapy (81 mg aspirin monotherapy and dual antiplatelet therapy), subjects diagnosed with von Willebrand disease, and subjects diagnosed with Glanzmann's thrombasthenia. Within the vWD patient group, 12 patients had vWD type 1, 10 patients had vWD type 2, and 3 patients had vWD type 3.
A summary of T-TAS 01 PL assay AUC results for the various subject groups is provided below.

Group	N	Mean	SD	Median	Range
Healthy Donors	142	381.5	55.5	390.9	142.5 – 467.7
Aspirin Monotherapy	57	218.4	114.4	205.7	2.7 – 410.9
Clopidogrel + ASA	18	46.2	47.3	21.7	3.6 – 159.8
Prasugrel + ASA	15	31.1	26.7	27.1	3.6 – 100.2
Ticagrelor + ASA	14	23.1	25.1	13.6	3.2 – 86.6
von Willebrand Disease	25	149.3	152.7	64.1	7.2 – 422.3
Glanzmann's Thrombasthenia	3	7.1	10.7	1.6	0.3 – 19.5

The distribution of AUC results from healthy controls and subjects taking antiplatelet therapy is shown below.



A summary of negative agreement and sensitivity of the AUC < 260 cutoff for aspirin monotherapy (ASA), dual antiplatelet therapy (DAPT, separated by DAPT type), von Willebrand disease (vWD), and Glanzmann's thrombasthenia (GT) is provided in the table below.

Parameter	N	Value	95% CI
Negative Agreement	142	95.8%	91.1-98.0%
Sensitivity (ASA)	57	68.4%	55.5-79.0%
Sensitivity (clopidogrel + ASA DAPT)	18	100.0%	81.5-100.0%
Sensitivity (prasugrel + ASA DAPT)	15	100.0%	78.2-100.0%
Sensitivity (ticagrelor + ASA DAPT)	14	100.0%	76.8-100.0%
Sensitivity (vWD)	25	72.0%	50.6-87.9%
Sensitivity (GT)	3	100.0%	43.9-100.0%

Von Willebrand disease severity can be highly variable, particularly in Type 1 vWD, and patients with mild vWD may not present with clinically significant bleeding. Within the vWD patient group, abnormal PFA-100 Col/EPI and Col/ADP demonstrated sensitivity that was similar to the PL assay (80%, [95% CI 61-90%]) and there was excellent overall agreement between the PL assay and PFA-100 assay (overall 88% [69-97%], percent positive agreement 72% [51-88%], percent negative agreement 100% [40-100%]). All 7 of the vWD patients with AUC results above 260 had either normal PFA-100 results or vWF antigen, vWF activity, and FVIII:C results that were all higher than levels considered to be strongly associated with vWD (30%).

Conclusions:

The data and information provided in this submission demonstrate that the T-TAS 01 System with PL chip is at least as safe and as effective as the legally marketed predicate device, therefore supporting a substantial equivalence determination.