September 11, 2020

Immucor GTI Diagnostics, Inc.
Allison Stray
Sr. Director QA/RA
20925 Crossroads Circle
Waukesha, Wisconsin 53186

Re: K201570
Trade/Device Name: PF4 Enhanced assay
Regulation Number: 21 CFR 864.7695
Regulation Name: Platelet Factor 4 Radioimmunoassay
Regulatory Class: Class II
Product Code: LCO
Dated: June 11, 2020
Received: June 11, 2020

Dear Allison Stray:

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)*
K201570

Device Name
PF4 Enhanced assay

Indications for Use *(Describe)*
PF4 Enhanced assay is designed as a solid phase enzyme linked immunosorbent assay (ELISA). The product is intended to be used as an in vitro diagnostic kit by hematology, coagulation, or other pathology laboratories to assist in screening patient samples, 3.2% sodium citrate (plasma) or without anticoagulant (serum), for the presence of heparin associated commonly found in patients with heparin induced thrombocytopenia (HIT) or thrombosis.

IVD

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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Section 5.0 Special 510(k) Summary

1. **Submission Type** Special 510(k)

2. **Submitter**

Owner's Name:	Immucor GTI Diagnostics, Inc.
Address:	20925 Crossroads Circle, Waukesha, WI 53186
Phone:	(262) 754-1000
Fax:	(262) 754-9831
Establishment Registration Number:	2183608
Name of Contact Person:	Allison Stray (astray@immucor.com)
Date Summary Prepared:	September 4, 2020

3. **Name of Device**

Device Name:	PF4/PVS Anti-IgG/A/M Antibody Detection Assay
Proprietary Name:	PF4 Enhanced Assay
Common Name:	Platelet Factor 4 Assay
Regulation Number:	21CFR 864.7695
Classification:	Class II
Product Code:	LCO
Establishment Registration Number:	2183608

4. **Name of Predicate Device for Claiming Equivalence**
PF4 Enhanced Assay (K053559)

5. **Description of Device**
PF4 Enhanced Assay is an Enzyme Linked Immunosorbent Assay (ELISA). The PF4 Enhanced ELISA is intended to detect antibodies in human serum or plasma that react with Platelet Factor 4 (PF4) when it is complexed to heparin or other polyanionic compounds. The PF4 Enhanced kit contains all of the reagents necessary to perform the assay.

Patients receiving heparin treatment for at least a week often develop thrombocytopenia. In some cases the platelet levels are reduced only slightly and return to normal even when heparin treatment is continued. This type of thrombocytopenia is termed "Type I" heparin-induced Thrombocytopenia (HIT) and is not antibody-mediated.

In other patients thrombocytopenia is usually more severe and is antibody-mediated. This condition is designated "Type II" HIT. Type I HIT is generally considered to be a benign condition, whereas patients with Type II HIT are at risk to develop more severe thrombocytopenia as well as arterial or venous thrombosis if heparin therapy is continued. Antibodies associated with Type II HIT can be detected in several ways. The most commonly used techniques are the platelet aggregation test, the serotonin release test and the platelet factor 4 ELISA.

It is now known that antibodies associated with Type II HIT recognize sites on a platelet protein designated "platelet factor 4" (PF4) that are created when PF4 is complexed with heparin or another linear polyanionic compound such as polyvinyl sulfonate (PVS).

PF4 Enhanced Solid Phase ELISA microwells provide immobilized PF4: PVS complexes as a target for the detection of antibodies associated with Type II HIT.

Test Procedure

Patient sample is added to microwells coated with platelet factor 4 (PF4) complexed to polyvinyl sulfonate (PVS). If an antibody recognizing a site on PF4:PVS is present, binding will occur. Unbound antibodies are then washed away. An alkaline phosphatase labeled anti-human globulin reagent (Anti-IgG/A/M) is added to the wells and incubated. The unbound Anti-IgG/A/M is washed away and the substrate PNPP (p-nitrophenyl phosphate) is added. After a 30-minute incubation period, the reaction is stopped with Stopping Solution. The optical density of the color that develops is measured in a spectrophotometer.

Engineering drawings or schematics are not applicable to the PF4 Enhanced Assay. The device consists of reagents and drawings are not pertinent to describe the device.

6. Intended Use

PF4 Enhanced Assay is a qualitative solid phase enzyme linked immunosorbent assay (ELISA) designed to detect antibodies in human serum or Sodium Citrate plasma reactive with platelet factor 4 (PF4) when it is complexed to polyanionic compounds such as Polyvinyl Sulfonate (PVS). These antibodies are found in some patients undergoing heparin therapy.

7. Substantial Equivalence

This Special 510(k) is for a Positive Serum Control raw material change and other changes the prior company did not file. The Positive Serum Control raw material modification in this submission is from human serum containing Bovine Albumin and 0.1% NaN_3 to human serum containing Bovine Albumin and 0.1% NaN_3 plus a chimeric (mouse Fab/Human Fc) monoclonal antibody in the PF4 Enhanced Assay positive control reagent.

The modification of the PF4 Enhanced Assay and need for this submission is due to supply of the predicate PF4 Enhanced Assay positive control material. The current supply of the PF4 Enhanced Assay positive control material is depleting and will not be available in the future.

Two (2) additional reportable changes, the prior company, did not file are being included. Those changes include: 1) Addition of plasma as a sample type, 2) Stopping Solution changed from 3M NaOH to a buffered EDTA solution. The prior company did document a 510(k) Letter to File for both the sample type change and Stopping Solution change. Their rationale for not filing with the Food and Drug Administration included the changes did not have any significant impact to the safety or effectiveness of the device.

There were no design or functionality changes. All elements of the Design History File (DHF) for the proposed device were used as possible and design outputs were created for the proposed device.

8. Special 510(k) Evaluation

The changes to Immucor GTI Diagnostics, Inc.'s device required performance data to evaluate the change. The three changes described above included defined methods to evaluate the change. In addition, the changes were reviewed and evaluated as part of the Immucor Risk Management Process.

The Similarities between the Predicate and Candidate Device:

- The technology (ELISA) and assay steps have not changed
- Reportable results have not changed
- The packaging configuration has not changed
- There are no design or functionality changes between the predicate and candidate device
- All reagents are identical with the exception of the Positive Serum Control and the Stopping Solution

The Differences between the Predicate and Candidate Device:

- The Intended Use has been revised to include plasma as a sample type
- The formulation of the Stopping Solution for PF4 Enhanced is different from the predicate device. The PF4 Enhanced Stopping Solution is a buffered EDTA solution which is ready for use, whereas the predicate device utilizes 3M NaOH.
- The candidate device contains Positive Serum Control as Human serum containing Bovine Albumin and 0.1% NaN_3. The predicate device contains Positive Serum Control as Human serum containing Bovine Albumin and 0.1% NaN_3 plus chimeric (mouse Fab/Human Fc) monoclonal antibody.
- The candidate device has changes to the IFU as a result of the specimen collection type change and Stopping Solution type change.
- The candidate device has non-reportable changes to the IFU as described in Sections 11.0, Executive Summary and 13.0, Proposed Labeling.

The table below provides the comparison between the current version of PF4 Enhanced and the proposed device.

#	Features / Characteristics	Predicate Device	Candidate Device	Comments
1	Intended Use	PF4 Enhanced assay is a qualitative solid phase enzyme linked immunosorbent assay (ELISA) designed to detect antibodies reactive with platelet factor 4 (PF4) when it is complexed to polyanionic compounds such as Polyvinyl Sulfonate (PVS). These antibodies are found in some patients undergoing heparin therapy.	PF4 Enhanced assay is a qualitative solid phase enzyme linked immunosorbent assay (ELISA) designed to detect antibodies in human serum or Sodium Citrate plasma reactive with platelet factor 4 (PF4) when it is complexed to polyanionic compounds such as Polyvinyl Sulfonate (PVS). These antibodies are found in some patients undergoing heparin therapy.	N/A

#	Features / Characteristics	Predicate Device	Candidate Device	Comments
2	Indications for Use	PF4 Enhanced is designed as a solid phase enzyme linked immunosorbent assay (ELISA). The product is intended to be used as an in vitro diagnostic kit by hematology, coagulation, or other pathology laboratories to assist in screening patients for the presence of heparin associated commonly found in patients with heparin induced thrombocytopenia (HIT) or thrombosis.	PF4 Enhanced is designed as a solid phase enzyme linked immunosorbent assay (ELISA). The product is intended to be used as an in vitro diagnostic kit by hematology, coagulation, or other pathology laboratories to assist in screening patients for the presence of heparin associated commonly found in patients with heparin induced thrombocytopenia (HIT) or thrombosis.	N/A
3	Technology	ELISA with a colorimetric measurement system	Same	N/A
4	Specimen Collection	Serum	Without anticoagulant (Serum) and 3.2% sodium citrate (Plasma)	Prior company made this change in 2010
5	Reportable Results	Qualitative assay; results are reported as positive or negative	Same	N/A
6	Packaging Configuration	13 and 45 Test kits	Same	N/A
7	Reagents			
	Microwell Strips	Immobilized PF4/PVS Complex	Same	N/A
	Concentrated Wash Solution	10X Tris Buffer, NaCl, Tween 20, 1% NaN_3	Same	N/A
	Specimen Diluent	Phosphate Buffered Saline, 0.05% NaN_3	Same	N/A
	Substrate Buffer	Diethanolamine and magnesium chloride, 0.02% NaN_3	Same	N/A

	Substrate	PNPP (crystalline powder)	Same	N/A
	Stopping Solution	3 M NaOH	Buffered EDTA Solution	Prior company made this change in 2010
	Positive Serum Control	Human serum containing Bovine Albumin and 0.1% NaN_3	Human serum containing Bovine Albumin and 0.1% NaN_3 plus Chimeric (mouse Fab/Human Fc) monoclonal antibody	N/A
	Negative Serum Control	Human serum containing 0.1% NaN_3	Same	N/A
	Conjugate	Goat anti-human IgG/A/M conjugated to alkaline phosphatase enzyme	Same	N/A
8	Instructions for Use (IFU)	PF4 Enhanced Direction Insert	Positive Serum Control raw material modification – no changes to the IFU	N/A
			Addition of plasma as a sample type – changes to IFU Sections: Intended Use, Specimen Collection and Storage, Limitations	
			Stopping Solution change – changes to IFU sections: Reagents and Precautions	
			Two (2) statements in the Interpretation of Results section moved to Limitations Section	

9. Company Name Change

Genetic Testing Institute Inc. was purchased by Gen-Probe Inc. in December 2010 and the company name was changed to Gen-Probe GTI Diagnostics, Inc. Immucor purchased Gen-Probe GTI Diagnostics Inc. in March 2013. The company name was subsequently changed to Immucor GTI Diagnostics, Inc.

10. Non-Clinical Studies Supporting Safety and Effectiveness of the Candidate Device

The details of each of the following studies are covered in Sections 14.0 (Sterilization and Shelf Life) and 18.0 (Performance Testing Bench). Only a brief summary of these studies is provided in this section.

The manufacturing facility is in conformance with the design control procedure requirements as specified in 21 CFR 820.30 and the records are available for review.

10.1 Modification, Positive Serum Control Raw Material Change

Process Validation

Three validation batches of PF4 Positive Serum Control were manufactured for this process validation.

The three validation batches were tested per the PF4 Enhanced Instructions For Use (IFU-303288.IFUEN, Rev. E) and all acceptance criteria were met.

Based upon the data generated, the PF4 Positive Serum Control manufacturing process consistently delivers product meeting established acceptance criteria and is acceptable for use in the production of the PF4 Enhanced Assay.

Precision Study

Testing was performed by 3 operators and five assays were conducted by each operator.

Testing was completed using a single lot of the PF4 Enhanced kit. Each of the three validation lots of the Positive Serum Control were tested concurrently on each of the 5 assays (days).

The acceptance criteria for 30 vials tested, as stated in the protocol, indicated that for each vial tested, the average OD value must be greater than or equal to 1.800 OD and the OD values of the duplicate test wells must be less than or equal to 20% of the mean of the two values.

10.2 Modification, Addition of Plasma as a Sample Type

Comparison of Serum and Plasma Sample Types

The objective of the Comparison of Serum and Plasma Sample Types was to demonstrate that using serum or plasma in the PF4 Enhanced Assay obtain equivalent results meeting established acceptance criteria.

Florida Hospital conducted a study using 174 paired (serum vs plasma) fresh serum and plasma samples. Genetic Testing Institute used the transcribed raw data to perform the analysis according to the PF4 Enhanced Instructions For Use.

94.8% Agreement (164/173) was observed between the qualitative results obtained with serum and plasma. For 8 of the 9 samples that were discrepant, the OD values were near the 0.400 cutoff. Upon investigation of the ninth discrepant sample, additional testing for the plasma and serum sample both matched that of the fresh plasma sample. Therefore, it was likely the fresh serum result was incorrect. With removal of the incorrect sample, the agreement was 95.4% (164/172).

Percent agreement between results using serum or plasma was acceptable and comparison of OD values showed positive agreement with a slope greater than 0.9 (up to 4.0 OD). Therefore, both sample types are acceptable for use in the PF4 Enhanced Assay.

10.3 Modification, Stopping Solution Change

Lot to Lot Comparison
A lot to lot comparison study was performed to demonstrate the new Stopping Solution (ESS) performs equivalent to the predicate Stopping Solution (3 M NaOH) meeting established acceptance criteria.

Three lots of ESS (referred to as the test solution) were manufactured according to SOP-292 and tested per QAP-017A. The predicate Stopping Solution, 3 M NaOH, was used as a reference in the study.

All acceptance criteria were met demonstrating the new Stopping Solution (ESS) is acceptable to use in the PF4 Enhanced Assay.

Process Validation
Three lots of the new Stopping Solution (ESS) were manufactured according to SOP-292 and tested with the PF4 Enhanced Assay according to the IFU.

Well-to-well variation and expected qualitative results were evaluated to determine if the new Stopping Solution (ESS) was equivalent to the predicate 3 M NaOH Stopping Solution. The predicate Stopping Solution, 3 M NaOH, was used as the reference in the study.

For Well-to-well variation, all wells met acceptance criteria. For qualitative results, the finished product QC panel was tested with all four lots of Stopping Solution. All 21 positive samples and 24 negative samples met their expected qualitative result on all three lots of the new Stopping Solution and the one lot of 3M NaOH Stopping Solution. All assays met the QC requirements in the IFU.

The data demonstrate the new Stopping Solution (ESS) can be used in the PF4 Enhanced Assay.

10.4 Shelf Life

The PF4 Enhanced Assay has a shelf life of 24 months. See Section 14.0, Sterilization and Shelf Life for stability studies performed to support this premarket submission. All acceptance criteria were met.

Conclusion
Based on the non-clinical performance and stability studies, the data demonstrate the modifications to the PF4 Enhanced device does not present new issues of safety and effectiveness.