

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY**

A. 510(k) Number:

K071781

B. Purpose for Submission:

Clearance of a new device

C. Measurand:

PF4 IgG

D. Type of Test:

ELISA

E. Applicant:

Genetic Testing Institute

F. Proprietary and Established Names:

PF4 IgG™

G. Regulatory Information:

1. Regulation section:

21 CFR 864.7695

2. Classification:

Class II

3. Product code:

LCO

4. Panel:

81 Hematology

H. Intended Use:

1. Intended use(s):

The Genetic Testing Institute's (GTI) PF4 IgG™ is a qualitative solid phase enzyme linked immunosorbent assay (ELISA) designed to detect IgG 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.

2. Indication(s) for use:

3. Special conditions for use statement(s):

4. Special instrument requirements:

I. Device Description:

The Genetic Testing Institute's (GTI) PF4 IgG™ is available in 13 and 45 Test kits, and consists of microwell strips coated with immobilized PF4/PVS Complexes, Positive and Negative Controls, PNPP Substrate, Goat anti-human IgG conjugated to alkaline phosphatase enzyme, Wash Solution, Diluent, Buffer, and Stop solution.

J. Substantial Equivalence Information:

1. Predicate device name(s):

GTI PF4 Enhanced

2. Predicate K number(s):

K053559

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Methodology	ELISA	Same
Intended Use	Qualitative Assay for the detection of heparin associated antibodies	Same
Reagents	Microwell strips	Same

Similarities		
Item	Device	Predicate
	immobilized with PF4/PVS, PNPP substrate, Controls, Wash Solutions, Diluent, Buffer	

Differences		
Item	Device	Predicate
Conjugate	Goat anti-human IgG, IgA, IgM conjugated to alkaline phosphatase enzyme	Goat anti-human IgG conjugated to alkaline phosphatase enzyme

K. Standard/Guidance Document Referenced (if applicable):

CLSI - EP7, Interference testing in Clinical Chemistry; Approved Guideline

CLSI EP-5A2, Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline.

CLSI – EP12-A Vol.22, No 14, User Protocol for Evaluation of Qualitative Test Performance; Approved Guideline

CLSI EP9-A2; Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline

BS EN 13612:2002; Performance Evaluation of in vitro Diagnostic Medical Devices

BS EN 13640:2002; Stability Testing of in vitro Diagnostic Reagents

L. Test Principle:

Heparin induced antibodies are immunoglobulins which are present in the patient's serum suspected to have a Type II heparin induced thrombocytopenia (HIT). Type II HIT is an adverse drug reaction caused by platelet-activating antibodies that are produced as a result of heparin therapy.

Antibodies which bind to PF4/Heparin complexes also bind to PF4 when it is complexed with other polyanionic compounds such as polyvinyl sulfonate (PVS).

In the PF4 IgG™ assay, test serum is diluted 1:50 and is then added to microwells to which platelet Factor 4 (PF4) complexed to polyvinyl sulfonate (PVS) which has been immobilized. The sample is incubated for 30 mins during which any antibodies present in the test serum that recognizes a site on the PF4/PV complex will bind. Following incubation, a wash step removes any unbound antibodies. A goat anti-human IgG alkaline phosphatase conjugate is then added to the wells. Following incubation, another wash step is performed to remove any unbound conjugate. An alkaline phosphate substrate is added to the microwells, and following incubation, the reaction is stopped and the optical density of the color that develops is measured in a spectrophotometer at 405 or 410 nm using a reference wave length of 490 nm.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

Three samples were prepared by diluting a sample containing a high anti-PF4/heparin antibody. The sample was diluted to obtain 3 separate samples that had a low, medium, and high positive reactivity. These samples along with the positive and negative control provided in the kit, were tested in duplicate in the PF4 IgG™ assay in 10 separate assays.

The data were analyzed by ANOVA according to CLSI Document EP-5A2, Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline. The reportable result (positive or negative) was also analyzed for agreement within and between runs according to CLSI Document EP-12A Vol 22, No 14, User Protocol for Evaluation of Qualitative Test Performance; Approved Guideline. There was 100% agreement between the reportable results within run and between run for each sample tested.

Sample	Within Run % CV	Between Run % CV	Total % CV
Negative	5.6	8.9	10.0
Low Positive	4.1	10.0	10.3
Medium Positive	2.2	4.7	4.9
High Positive	2.6	3.4	3.8

b. Linearity/assay reportable range:

n/a

c. Traceability, Stability, Expected values (controls, calibrators, or methods):

The Positive Control is prepared from the serum of individual(s) known to contain an anti-PF4/heparin antibody based on a positive result in the Serotonin Release Assay. Assay OD values should be ≤ 0.300 .

The Negative Control is prepared from pools of normal human serum. Assay values should be ≥ 1.800 .

d. Detection limit:

n/a

e. Analytical specificity:

Interferants was spiked into a negative sample that contained no PF4/heparin antibodies, and 3 positive samples that contained varying reactivity (low, medium, and high) of PF4/heparin antibodies. The following concentrations were evaluated: hemoglobin – 500 mg/dL, triglycerides – 500 mg/dL, and bilirubin- 20 mg/dL. An equivalent aliquot of the compound used to prepare the interferant was also spiked in to a separate sample and used as the control. Samples containing the interfering substance and the control sample were tested in replicates of 5 in the PF4 IgGTM assay. Results demonstrated no significant difference in the mean value obtained for each of the test spiked samples when compared to the control.

f. Assay cut-off:

Assay cut-off was determined from the normal range study to be ≥ 0.400

2. Comparison studies:

a. Method comparison with predicate device:

A two site clinical study was conducted in which the PF4 IgGTM assay was compared to the predicate (PF4 Enhanced®), and the Serotonin Release Assay (SRA). At site 1, (n=229), and tested at GTI. At site 2 (n=171). All samples were collected from patients receiving heparin treatment, and frozen until testing. The SRA assay was conducted at the external sites.

	PF4 IgG™ versus PF4 Enhanced®	PF4 Enhanced® versus SRA	PF4 IgG™ versus SRA
Sensitivity (co-positivity)	60%	100%	91%
95% Confidence Interval	51.1 – 67.8%	88.4 - 99.6%	79.3 – 96.5%
Specificity (Co-negativity)	100%	76%	90%
95% Confidence Interval	98.6 – 100.0%	71.4 – 80.2%	86.3 – 92.6%
% Agreement	87%	79%	90%

b. Matrix comparison:

n/a

3. Clinical studies:

a. Clinical Sensitivity:

n/a

b. Clinical specificity:

n/a

c. Other clinical supportive data (when a. and b. are not applicable):

n/a

4. Clinical cut-off:

n/a

5. Expected values/Reference range:

120 serum samples from healthy individuals were tested in duplicate on the PF4 IgG™ assay. A non-parametric analysis determined the upper end of the normal range to be 0.352 O.D. units (95% reference interval, 90% confidence).

N. Proposed Labeling:

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

O. Conclusion:

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