510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY TEMPLATE

A. 510(k) Number:

K071255

B. Purpose for Submission:

clearance of a new device

C. Measurand:

IgG, IgA, and IgM heparin-dependent antibodies

D. Type of Test:

Enzyme linked immunosorbent assay

E. Applicant:

Hyphen BioMed

F. Proprietary and Established Names:

ZYMUTEST HIA IgG

ZYMUTEST HIA IgGAM

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 ZYMUTEST HIA IgGAM ELISA is a qualitative screening assay intended for the global detection of heparin-dependent antibodies, whether the isotype is: IgG IgM, and IgA, in human plasma, by clinical laboratories. It is intended for *in vitro* diagnostic use.

The ZYMUTEST HIA IgG ELISA is a qualitative assay intended for the detection of heparin-dependent antibodies of the IgG isotope, in human plasma, by clinical laboratories. It is intended for *in vitro* diagnostic use.

2. Indication(s) for use:

   ZYMYUTEST HIA IgG AND IgGAM KITS are designed as a solid phase enzyme-linked immunosorbent assay (ELISA). These products are intended to be used as an *in vitro* diagnostics kit by Hematology, coagulation or other pathology laboratories to assist in screening patient samples for the presence of heparin-associated antibodies commonly found in patients with heparin induced thrombocytopenia or thrombosis (HIT).

3. Special conditions for use statement(s):

4. Special instrument requirements:

I. Device Description:

The assay kit consists of a 96 welled micro ELISA plate coated with unfractionated heparin, 3 vials each of lyophilized Positive and Negative controls, 3 vials lyophilized Platelet lysate, 3 vials of Immunoconjugate, 25 mL of TMB substrate, 1 vial of sulfuric Acid Stop solution, buffer, diluents, and wash solution.

J. Substantial Equivalence Information:

1. Predicate device name(s):

1. DIAGNOSTICA STAGO ASSERCHROM® HPIA TEST KIT

2. GTI PF4 ENHANCED SOLID PHASE ELISA

2. Predicate 510(k) number(s):

1. K003767

2. K053559

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Intended Use	A qualitative *in vitro diagnostic* screening assay intended for the global detection of IgG, IgM, and IgA heparin-dependent antibodies in human plasma, by clinical laboratories.	same
test principle	ELISA	same
sample requirements	citrated plasma	same

Differences		
Item	Device	Predicate
materials	Microtiter plate coated with unfractionated heparin	microtiter plate coated with purified PF4 complexed to polyvinly sulfonate

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

L. Test Principle:

When a diluted plasma sample and platelet lysate is added to one of the microwells of the coated plate, if present, heparin-dependent antibodies present in the sample will form complexes with unfractionated heparin immobilized on the plate. Following a washing step, bound antibodies are mixed with the immunoconjuuagate, which will bind to IgG, IgM, and IgA isotypes. Following another washing step, the TMB peroxidase substrate is added, and a blue color develops which turns yellow upon the addition of the stop

solution. The color that develops is directly proportional to the amount of heparin-dependent antibodies present in the tested sample.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Intra-assay- ZYMUTEST HIA IgG and ZYMUTEST HIA IgGAM were tested in duplicate using positive control material.

Positive control	N	Mean A450	CV%
Anti PF4-IgG Lot 061027D	6	1.31	3.07
Anti PF4-IgG Lot 061214A	9	1.10	4.46
Anti PF4-IgGAM Lot 061214D	9	1.74	4.75

Inter-assay-

Positive control	N	Mean A450	CV%
Anti PF4-IgG Lot 061027D	7	1.34	7.11
Anti PF4-IgGAM Lot 061027G	7	1.84	7.50

b. Linearity/assay reportable range:

n/a

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

Negative controls are derived from normal human plasma with an A450 of mean ± 2 SD.

The positive control is derived from chimeras made by coupling anti-PF4 polyclonal antibodies with human Igs (IgG, IgA or IGM, or the mixture of the three), with an A450 of mean ± 5 SD.

d. Detection limit:

n/a

e. Analytical specificity: The effect of varying concentrations of heparin in the assay was tested on 3 pathological plasmas with and without heparin addition,

ranging from 0 to 5 IU/ml. After heparin addition, plasma was diluted 1:100 and tested. Results demonstrated no heparin interference up to 1 IU/ml.

f. Assay cut-off:

The assay was evaluated in hospital patients with no HIT, ACC patients with circulating anticoagulant antibodies with no HIT, and normal healthy donors with no autoimmunity background. Cut-off was established as mean + 3SD for the normal hospital patients and ACC patients, which corresponded to + 5 SD for normal healthy donors.

2. Comparison studies:

a. Method comparison with predicate device:

ZYMUTEST IgGAM compared with Asserachrom. N= 44.

In-house Study		Asserachrom	
		Positive	Negative
Zymutest IgGAM	Positive	28	2
	Negative	0	14
Agreement		100%	88%

2 site clinical study ZYMUTEST IgGAM compared with Asserachrom

Combined		Asserachrom	
Site 1 & 2		Positive	Negative
Zymutest IgGAM	Positive	48	32
	Negative	27	136
Agreement		76%	
Co-positivity		64%	
Co-negativity		81%	
Sample Size		243	

3 site clinical study ZYMUTEST IgGAM compared with GTI PF4 Enhanced

Combined		GTI PF4-Enhanced	
Site 1, 2, &3		Positive	Negative
Zymutest IgGAM	Positive	101	17
	Negative	74	153
Agreement		74%	
Co-positivity		58%	
Co-negativity		90%	
Sample Size		345	

2 site clinical study- ZYMUTEST IgG compared with Asserachrom

Combined		Asserachrom	
Site 1 & 2		Positive	Negative
Zymutest IgG	Positive	33	17
	Negative	42	151
Agreement		76%	
Co-positivity		44%	
Co-negativity		90%	
Sample Size		243	

ZYMUTEST IgG compared with Serotonin Release Assay (SRA) n=174

# Matches	131
% Matching	75.3%

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:

n/a

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.