

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

A. 510(k) Number:

k051677

B. Purpose for Submission:

This submission is for modification of the device. The product modifications consisted of: design changes that did not affect the indications for use or technology, several labeling changes added for clarifying the labeling, product name changed from CLA Allergen-Specific IgE Assay System to the OPTIGEN Allergen-Specific IgE Assay System, new control sera added for verifying allergen performance and the expiration date extended to 24 months.

C. Measurand:

Allergen specific anti-IgE antibodies.

D. Type of Test:

Semi-quantitative, solid phase immunoassay

E. Applicant:

Hitachi Chemical Diagnostics, Inc.

F. Proprietary and Established Names:

OPTIGEN Allergen-Specific IgE Assay System

G. Regulatory Information:

1. Regulation section:

21 CFR 866.5750 – Radioallergosorbent (RAST) Immunological Test System

21 CFR 866.5510 – Immunoglobulins A, G, M, D, E Immunological Test System

2. Classification:

Class II

3. Product code:

DHB- System, Test, Radioallergosorbent (RAST) Immunological

DGC- IgE, Antigen, Antiserum, Control

4. Panel:

Immunology 82

H. Intended Use:

1. Intended use(s):

The OPTIGEN Assay is an in vitro test for use in the semiquantitative determination of circulating allergen specific-IgE concentrations in human serum.

2. Indication(s) for use:

The OPTIGEN Assay is an in vitro test, which provides a semi quantitative measurement of circulating allergen-specific IgE antibodies in human serum. The OPTIGEN is intended to assist in the clinical diagnosis of IgE-mediated allergic disorders. The device is designed for use in clinical laboratories.

3. Special conditions for use statement(s):

The device is for prescription use only.

4. Special instrument requirements:

CLA-1 Luminometer System

I. Device Description:

The device is a solid phase in vitro test used for the semi quantitative measurement of circulating allergen-specific IgE antibodies to 20 allergens simultaneously in human serum. The 20 allergens are: Alternaria, Aspergillus, Birch- White, Cat, Cladosporium, Cockroach, Codfish, Dog, Egg White, Latex, Milk, Mite-Farinae, Mite- Pteronyssinus, Mugwort, Peanut, Ragweed Mix I, Rice, Soybean, Timothy and Wheat. The device consists of an OPTIGEN kit containing pette (test chambers), reagents (wash buffer, goat anti-human IgE and photoreagents), plugs; Positive Allergy Control Reagent and Negative Allergy Control Reagent and package insert.

J. Substantial Equivalence Information:

1. Predicate device name(s):
 - a. Hitachi Chemical Diagnostics, CLA Allergen- Specific IgE Assay- Latex Allergen K82
 - b. Pharmacia, Inc., UniCAP Specific IgE Assay
2. Predicate 510(k) number(s):
 - a. k030590
 - b. k962274
3. Comparison with predicate:

Item	New Device	Predicate	
	OPTIGEN Allergen-Specific IgE Assay System	CLA Allergen Specific IgE System	Pharmacia-UniCAP Specific IgE
Indication for Use	Assist in the clinical diagnosis of IgE-mediated allergic disorders	Same	Same
Results	Semi- quantitative interpretation	Same	Same
Sample type	Human Serum	Same	Same
Antisera specificity	No detectable cross reactivity w/ human IgG, IgM, IgD and IgA	Same	Same
Shelf life stability	Store @ 2-8°C until expiration date	Same	Same

Item	New Device	Predicate	
	OPTIGEN Allergen-Specific IgE Assay System	CLA Allergen Specific IgE System	Pharmacia-UniCAP Specific IgE
Assay Type	Chemiluminescence	Same	Fluoroenzyme immunoassay
Serum Volume	12.5 µL	37.5 µL	40 µL
Class Values	0, 1, 2, 3, 4	0, 1/0, 1, 2, 3, 4	0-6
Serum Incubation	~2 hrs	16-24 hrs	2.5 hrs
Analytical Range	0-300 LU	0-300 LU	0-100 Ku/L
Lowest detectable	26 LUs	10 LUs	0.35 Ku/L

Item	New Device	Predicate	
	OPTIGEN Allergen-Specific IgE Assay System	CLA Allergen Specific IgE System	Pharmacia-UniCAP Specific IgE
limit			
Chamber Components	Three Molded Parts: a Pette Body, a Coverslip and a Partition	Two components: a Molded Pette Body and a Extruded Polystyrene Coverslip	
Solid Phase	Polystyrene	Cotton Thread	
Allergen Attachment to Solid Phase	Non- Covalent	Covalent	
Total Serum Requirement per Device	0.5 ml	1.5 ml	
Reagent Volume	0.5 ml	1.5 ml	
Photoreagent Components	2 Photoreagents AB and CD	4 Photoreagents: A,B, C and D	
Photoreagent Composition	Enhancer	No Enhancer	
Wash Repetitions	1 time each wash	3 times each wash	
Wash Volume	10 ml	30 mL	
Re-Hydration Step	Yes, 10 ml	No	
Pette Storage	Dry	Moist	
Class 0	0-26 LU	0-11 LU	
Class 1/0	No Class Equivocal	12-26 LU	
Positive Control Sera	Positive to Some Allergens in the Panel and Negative to Others	Positive to all Allergens in the Panel	
Negative Blanking Control Cut-Off	69 LUs	33 LUs	
Test Chamber Pette and Reagent Stability	24 Months	12 Months	
Luminometer Program Card	Revision 2.3	Revision 2.2	

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

None provided.

L. Test Principle:

The OPTIGEN assay employs a small plastic device known as a pette or test chamber to expose patient serum simultaneously to a number of allergens or allergen mixes.

The pette contains polystyrene solid phase and integrated lenslets, as well as one Negative Blanking Control and one Positive Procedural Control.

The OPTIGEN assay is run by filling a pette with patient serum after a pre-wash step. As the serum incubates, IgE in the patient serum binds to the allergen coated wells.

After an incubation period, the pette is washed with buffer solution to remove unbound serum. Next, an enzyme labeled anti-IgE antibody is added to the pette and the antibody couples with the serum IgE bound to the wells. After a second wash, the pette is filled with a photo-reagent mixture which reacts with the enzyme labeled

antibody to produce chemiluminescence. The amount of light emitted is proportional to the amount of allergen-specific IgE in the patient serum. The light emitted is read in the CLA-1 Luminometer and reported as Light Units (LU).

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

Within Assay: Ten serum replicates were run in one batch. The average mean coefficient of variation of the responses was calculated per class.

Class	% CV
1	31
2	16
3	16
4	5

Between Assays: Ten replicates of a serum were run on five different days. The mean coefficient of variation of the responses of all allergens tested was calculated per class.

Class	% CV
1	25
2	15
3	9
4	1

b. *Linearity/assay reportable range:*

Assay reportable range is 0-300 LU

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

No claim was made for traceability to a reference standard.

d. *Detection limit:*

The detection limit was calculated by running negative patient sera in the OPTIGEN assay with different lots of devices. The detection limit was calculated from the average signal obtained with all the sera in all the allergens wells plus 3 times the Standard Deviation (Std) as shown below:

$N = 273$

Average = 2.4 LU

Std = 7.95 LU

Average +3(Std) = 26.25 LU

The detection limit of the assay is 26 LUs.

e. *Analytical specificity:*

Cross-reactivity: The manufacturer states there is no detectable cross-reactivity with human serum immunoglobulins IgG, IgM, IgA or IgD at normal physiological levels.

f. *Assay cut-off:*

To calculate patient's IgE response, the Luminometer automatically subtracts the emission level of the Negative Control from the emission level of each

allergen. CLA Class Values are assigned based on the amount of light emitted by the individual allergens in the pette. The concentrations of IgE associated with CLA class values and instrument readings are listed in the table below.

Class cut-offs for the OPTIGEN Assay are the following:

Class	LU
0	0-26
1	27-65
2	66-142
3	143-242
4	243-300

CLA Class 0 represents absence of non-detectable levels of allergen-specific antibodies.

2. Comparison studies:

a. *Method comparison with predicate device:*

Comparison studies were performed in 3 sites (France, Germany, and USA) with the OPTIGEN Universal Panel 20 Allergen Specific IgE Assay and the predicate device Pharmacia CAP System Specific IgE Assay. A total of 1753 determinations were made and results are summarized in the comparison table below.

		Pharmacia CAP		Total
		(+)	(-)	
Hitachi OPTIGEN	(+)	678	77	755
	(-)	81	917	998
Total		759	994	1753

Positive percent agreement: 89.3% (678/759)
 Negative percent agreement: 92.9% (917/994)
 Overall agreement: 91.0% (1595/1753)

The comparison data below shows the Class determination of specific IgE to 20 allergens with the OPTIGEN Allergen-Specific IgE Assay and the Pharmacia CAP Specific IgE Assay.

Hitachi Class	PHARMACIA CAP CLASS				
	0	1	2	3	4,5 & 6
4	0	3	86	133	98
3	7	3	61	33	12
2	20	19	83	37	9
1	50	20	56	21	4
0	917	45	30	6	0
TOTAL DATA POINTS: 1753					

- b. Matrix comparison:*
Both assays use human serum.
- 3. Clinical studies:
 - a. Clinical Sensitivity:*
Not provided.
 - b. Clinical Specificity:*
Not provided.
 - c. Other clinical supportive data (when a and b are not applicable):*
Not applicable.
- 4. Clinical cut-off:
See Assay Cut-off.
- 5. Expected values/Reference range:
Expected value in the normal, non-allergic population is negative (<26 LU-Class 0). The manufacturer recommends that each laboratory establish its own expected range of values for the population of interest. The cut-off threshold between positive and negative results was established as three standard deviations above the mean value of the normal population.

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 substantial equivalence decision.