510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

A. 510(k) Number:
k091984

B. Purpose for Submission:
Modification to device

C. Measurand:
Allergen Specific IgE (Black pepper, Broccoli, Cabbage, Cheese-Mold Type, Cherry, Chestnut, Chocolate, Coffee, Cucumber, Grape, Grapefruit, Haddock, Lamb, Lemon, Lima Bean, Peach, Pear, Pineapple, Plum, Pumpkin, Red Snapper, Sole, Spinach, Sweet Potato, Trout, Turkey meat, Watermelon)

D. Type of Test:
Quantitative, chemiluminiscent immunoassay

E. Applicant:
Siemens Healthcare Diagnostics, Inc.

F. Proprietary and Established Names:
IMMULITE® 2000 3gAllergy™ Specific IgE Assay kit

G. Regulatory Information:

1. Regulation section:
   21 CFR § 866.5750, Radioallergosorbent (RAST) test systems
2. Classification:
   Class II
3. Product code:
   DHB System, Test, Radioallergosorbent (RAST), Immunological
4. Panel:
   Immunology (82)

H. Intended Use:

1. Intended use:
   For *in vitro* diagnostic use with the IMMULITE 2000 Analyzer – for the quantitative measurement of allergen-specific IgE in human serum, as an aid in the clinical diagnosis of IgE-mediated allergic disorders.
2. Indication(s) for use:
   Same as Intended use.
3. Special conditions for use statement(s):
   For prescription only.
4. Special instrument requirements:
   IMMULITE 2000 Analyzer (k970227)

I. Device Description:
Each device contains the following: 3gAllergy™ specific IgE bead pack (3 packs of 200 beads coated with anti-ligand); specific IgE reagent wedge: 30 mL alkaline phosphatase (bovine calf intestine) conjugated to monoclonal murine anti-human IgE antibody in a human/nonhuman serum buffer matrix (equally dispensed in 1 wedge with B & C chambers); specific IgE adjustors: low and high (2 vials, 2 mL each) of human IgE in a nonhuman serum matrix with preservative; specific IgE adjustor

antibody: 2 tubes, 2.75 mL each) ready to use ligand-labeled polyclonal goat anti-human IgE antibody with preservative; specific IgE universal kit controls: (2 vials, 2 mL each) human IgE in a nonhuman sample matrix with preservative; specific IgE control antibody: (2 tubes, 2.75 mL each) ready to use ligand-labeled polyclonal goat anti-human IgE antibody with preservative. Kit components supplied separately: 3gAllergy™ specific IgE sample diluent (concentrated ready to use 1 vial, 25 mL); chemiluminiscent substrate; probe wash; probe cleaning kit; disposable reaction tubes; bar coded allergen holder wedges serially coded 1-33; 34 -66; 67-99; allergen tube caps and tube septa.

J. Substantial Equivalence Information:

1. Predicate device name(s):
   IMMULITE® 2000 3gAllergy™ Specific IgE
2. Predicate K number(s):
   k013134
3. Comparison with predicates:

Similarities		
Item	New Device	Predicate Device
Intended use	For *in vitro* diagnostic use with the IMMULITE 2000 Analyzer – for the quantitative measurement of allergen-specific IgE in human serum, as an aid in the clinical diagnosis of IgE-mediated allergic disorders.	Same
Technology	Chemiluminescence	Same
Assay performance	Assay to be specific to allergen-specific IgE	Same
Calibrators	Low and high	Same
Controls	Specific IgE and Antibody and Specific IgE Universal Controls	Same
Sample type	Serum	Same
Result Interpretation	Quantitative values in kU/L; Interpretation of class results for two scoring systems: Standard and Extended standard	Same

Differences		
Item	New Device	Predicate Device
Total number of Allergens	Twenty seven	One hundred and ten
Types of Specific Allergens	27 Specific Food Allergens	110 Specific Allergens: 8 Animal epithelia, 2 House dusts, 39 Food, 13 Grasses, 5 Insects, 5 Mites, 10 Molds, 1 Latex, 14 Trees, 13 Weeds

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

Standard documents:

CLSI I/LA 20-A: Evaluation Methods and Analytical Performance Characteristics of Immunological Assays for Human Immunoglobulin E (IgE)

CLSI EP5-A2: Evaluation of Precision Performance of Quantitative Methods; Approved Guideline – Second Edition

Guidance document:

FDA Guidance – Radioallergosorbent Test (RAST) Methods for Allergen-Specific Immunoglobulin E (IgE) 510(k); Final Guidance

L. Test Principle:

The assay is a solid-phase, two-step, chemiluminiscent immunoassay that exploits liquid phase kinetics in a bead format. The allergens are covalently bound to a soluble polymer/co-polymer matrix, which is labeled with a ligand. The assay specific antibody is labeled with alkaline phosphatase. The use of an amino acid co-polymer amplifies the amount of allergen that the matrix can support. The chemiluminiscent detection system is a phosphatase ester of stabilized dioxatane. Cleavage of the phosphate ester by alkaline phosphatase results in the decomposition of dioxatane and the emission of photons, which are quantified by a luminometer.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

   a. *Precision/Reproducibility:*

   Reproducibility of the assay was assessed by testing three positive samples and one negative control sample of each allergen (Black pepper, Broccoli, Cabbage, Cheese-Mold Type, Cherry, Chestnut, Chocolate, Coffee, Cucumber, Grape, Grapefruit, Haddock, Lamb, Lemon, Lima Bean, Peach, Pear, Pineapple, Plum, Pumpkin, Red Snapper, Sole, Spinach, Sweet Potato, Trout, Turkey meat, Watermelon) in duplicate twice a day for 20 different days (n = 80).

   The sponsor's criterion for the negative sample was the average dose must be <0.10 kU/L; all negative sample results were within the acceptance criterion. The sponsor's acceptance criterion for the positive samples was ≤15% CV for both within-run and total precision. Three allergen lots were tested for each allergen; representative data from one lot is shown below for the positive samples. The intra-assay and inter-assay %CV ranges were from 2.68% to 11.08% and 3.94% to 12.30%, respectively (see tables below).

Allergen: Black Pepper

Sample	Mean (kU/L)	Intra-assay		Inter-assay	
		SD (kU/L)	%CV	SD (kU/L)	%CV
Positive #1	1.41	0.59	4.18	0.073	5.18
Positive #2	3.43	0.380	11.08	0.422	12.30
Positive #3	6.81	0.250	3.67	0.571	8.38

Allergen: Broccoli

Sample	Mean (kU/L)	Intra-assay		Inter-assay	
		SD (kU/L)	%CV	SD (kU/L)	%CV
Positive #1	12.02	0.546	4.54	0.759	6.31
Positive #2	5.68	0.251	4.42	0.338	5.95
Positive #3	2.37	0.091	3.84	0.127	5.36

Allergen: Cabbage

Sample	Mean (kU/L)	Intra-assay		Inter-assay	
		SD (kU/L)	%CV	SD (kU/L)	%CV
Positive #1	0.78	0.023	2.95	0.053	6.79
Positive #2	14.40	0.591	4.10	0.971	6.74
Positive #3	22.92	0.801	3.49	1.422	6.20

Allergen: Cheese-Mold Type

Sample	Mean (kU/L)	Intra-assay		Inter-assay	
		SD (kU/L)	%CV	SD (kU/L)	%CV
Positive #1	1.20	0.037	3.08	0.059	4.92
Positive #2	1.66	0.052	3.13	0.067	4.04
Positive #3	6.04	0.241	3.99	0.287	4.75

Allergen: Cherry

Sample	Mean (kU/L)	Intra-assay		Inter-assay	
		SD (kU/L)	%CV	SD (kU/L)	%CV
Positive #1	3.31	0.130	3.93	0.221	6.68
Positive #2	1.10	0.036	3.27	0.70	6.36
Positive #3	11.19	0.390	3.49	0.981	8.77

Allergen: Chestnut

Sample	Mean (kU/L)	Intra-assay		Inter-assay	
		SD (kU/L)	%CV	SD (kU/L)	%CV
Positive #1	7.93	0.238	3.00	0.396	4.99
Positive #2	2.86	0.108	3.78	0.135	4.72
Positive #3	5.81	0.181	3.12	0.261	4.49

Allergen: Chocolate

Sample	Mean (kU/L)	Intra-assay		Inter-assay	
		SD (kU/L)	%CV	SD (kU/L)	%CV
Positive #1	0.43	0.931	7.21	0.038	8.84
Positive #2	1.13	0.085	7.52	0.095	8.41
Positive #3	0.41	0.029	7.07	0.038	9.27

Allergen: Coffee

Sample	Mean (kU/L)	Intra-assay		Inter-assay	
		SD (kU/L)	%CV	SD (kU/L)	%CV
Positive #1	0.58	0.020	3.45	0.041	7.07
Positive #2	1.84	0.075	4.08	0.128	6.96
Positive #3	0.61	0.024	3.93	0.048	7.87

Allergen: Cucumber

Sample	Mean (kU/L)	Intra-assay		Inter-assay	
		SD (kU/L)	%CV	SD (kU/L)	%CV
Positive #1	2.85	0.097	3.40	0.167	5.86
Positive #2	2.10	0,082	3.90	0.168	8.00
Positive #3	8.38	0.256	3.05	0.621	7.41

Allergen: Grape

Sample	Mean (kU/L)	Intra-assay		Inter-assay	
		SD (kU/L)	%CV	SD (kU/L)	%CV
Positive #1	5.21	0.189	3.63	0.292	5.60
Positive #2	1.29	0.047	3.64	0.064	4.96
Positive #3	14.20	0.464	3.27	0.707	4.98

Allergen: Grapefruit

Sample	Mean (kU/L)	Intra-assay		Inter-assay	
		SD (kU/L)	%CV	SD (kU/L)	%CV
Positive #1	2.68	0.092	3.43	0.160	5.97
Positive #2	1.07	0.031	2.90	0.088	8.22
Positive #3	13.79	0.524	3.80	0.988	7.16

Allergen: Haddock

Sample	Mean (kU/L)	Intra-assay		Inter-assay	
		SD (kU/L)	%CV	SD (kU/L)	%CV
Positive #1	0.084	0.031	3.69	0.038	4.52
Positive #2	5.21	0.176	3.38	0.268	5.14
Positive #3	8.66	0,387	4.47	0.413	4.77

Allergen: Lamb

Sample	Mean (kU/L)	Intra-assay		Inter-assay	
		SD (kU/L)	%CV	SD (kU/L)	%CV
Positive #1	2.96	0.105	3.55	0.180	6.08
Positive #2	9.50	0.359	3.78	0.591	6.22
Positive #3	7.87	0.319	4.05	0.509	6.47

Allergen: Lemon

Sample	Mean (kU/L)	Intra-assay		Inter-assay	
		SD (kU/L)	%CV	SD (kU/L)	%CV
Positive #1	12.13	0.407	3.36	0.621	5.12
Positive #2	1.16	0.048	4.14	0.065	5.60
Positive #3	3.88	0.147	3.79	0.266	6.86

Allergen: Lima Bean

Sample	Mean (kU/L)	Intra-assay		Inter-assay	
		SD (kU/L)	%CV	SD (kU/L)	%CV
Positive #1	3.89	0.176	4.52	0.257	6.61
Positive #2	5.85	0.229	3.91	0.320	5.47
Positive #3	14.77	0.539	3.65	0.668	4.52

Allergen: Peach

Sample	Mean (kU/L)	Intra-assay		Inter-assay	
		SD (kU/L)	%CV	SD (kU/L)	%CV
Positive #1	3.80	0.159	4.18	0.197	5.18
Positive #2	3.87	0.176	4.55	0.212	5.48
Positive #3	11.15	0.442	3.96	0.666	5.97

Allergen: Pear

Sample	Mean (kU/L)	Intra-assay		Inter-assay	
		SD (kU/L)	%CV	SD (kU/L)	%CV
Positive #1	1.63	0.058	3.56	0.105	6.44
Positive #2	4.36	0,117	2.68	0.268	6.15
Positive #3	6.61	0.212	3.21	0.428	6.48

Allergen: Pineapple

Sample	Mean (kU/L)	Intra-assay		Inter-assay	
		SD (kU/L)	%CV	SD (kU/L)	%CV
Positive #1	2.21	0.098	4.43	0.168	7.60
Positive #2	1.50	0.049	3.27	0.107	7.13
Positive #3	0.83	0.024	2.89	0.081	9.76

Allergen: Plum

Sample	Mean (kU/L)	Intra-assay		Inter-assay	
		SD (kU/L)	%CV	SD (kU/L)	%CV
Positive #1	1.38	0.117	8.48	0.136	9.86
Positive #2	3.93	0.127	3.23	0.211	5.37
Positive #3	2.81	0.087	3.10	0.147	5.23

Allergen: Pumpkin

Sample	Mean (kU/L)	Intra-assay		Inter-assay	
		SD (kU/L)	%CV	SD (kU/L)	%CV
Positive #1	0.98	0.063	6.43	0.076	7.76
Positive #2	3.33	0.136	4.08	0.187	5.62
Positive #3	8.92	0.306	3.43	0.413	4.63

Allergen: Red Snapper

Sample	Mean (kU/L)	Intra-assay		Inter-assay	
		SD (kU/L)	%CV	SD (kU/L)	%CV
Positive #1	15.92	0.612	3.84	0.723	4.54
Positive #2	3.74	0.129	3.45	0.182	4.87
Positive #3	15.14	0.427	2.82	0.700	4.62

Allergen: Sole

Sample	Mean (kU/L)	Intra-assay		Inter-assay	
		SD (kU/L)	%CV	SD (kU/L)	%CV
Positive #1	1.50	0.51	3.40	0.077	5.13
Positive #2	4.75	0.219	4.61	0.276	5.81
Positive #3	18.62	0.577	3.10	0.734	3.94

Allergen: Spinach

Sample	Mean (kU/L)	Intra-assay		Inter-assay	
		SD (kU/L)	%CV	SD (kU/L)	%CV
Positive #1	0.91	0.027	2.97	0.039	4.29
Positive #2	1.73	0.054	3.12	0.085	4.91
Positive #3	14.80	0.405	2.74	0.685	4.63

Allergen: Sweet Potato

Sample	Mean (kU/L)	Intra-assay		Inter-assay	
		SD (kU/L)	%CV	SD (kU/L)	%CV
Positive #1	6.71	0.238	4.22	0.352	5.25
Positive #2	4.09	0.178	4.35	0.273	6.67
Positive #3	1.97	0.081	4.11	0.102	5.18

Allergen: Trout

Sample	Mean (kU/L)	Intra-assay		Inter-assay	
		SD (kU/L)	%CV	SD (kU/L)	%CV
Positive #1	30.71	0.945	3.08	1.825	5.94
Positive #2	1.72	0.058	3.37	0.097	5.64
Positive #3	17.28	0.646	3.74	0.926	5.36

Allergen: Turkey Meat

Sample	Mean (kU/L)	Intra-assay		Inter-assay	
		SD (kU/L)	%CV	SD (kU/L)	%CV
Positive #1	1.36	0.045	3.31	0.117	8.60
Positive #2	4.80	0.150	3.25	0.211	4.40
Positive #3	6.99	0.233	3.33	0.642	9.18

Allergen: Watermelon

Sample	Mean (kU/L)	Intra-assay		Inter-assay	
		SD (kU/L)	%CV	SD (kU/L)	%CV
Positive #1	1.62	0.064	3.95	0.122	7.53
Positive #2	5.03	0.172	3.42	0.345	6.86
Positive #3	19.25	0.561	2.91	1.250	6.49

Lot to lot reproducibility:
The above results were reanalyzed for lot-to-lot reproducibility. Within run imprecision between lots ranged from 3.04% to 12.02% and total imprecision from 3.95% to 16.55%. All three lots were within the acceptable criterion of ≤ 20% variability.

b. *Linearity/assay reportable range:*
Linearity studies: For each allergen, two samples were diluted in 2-fold serial dilutions to 5 levels. The undiluted (neat) and diluted samples were tested with the specific allergen to demonstrate linearity at concentrations within the assay limits. Regression statistics for each allergen comparing the observed results to expected results are presented below.

Allergen	Regression Equation	N	Slope	95% CI	Intercept	95% CI
Black pepper	Y= 0.9975X +0.0404	12	0.9975	0.9761–1.0188	-0.0404	–0.0165-0.0973
Broccoli	Y= 1.0035X + 0.2560	12	1.0035	0.9666–1.045	0.2560	–0.0089-0.5209
Cabbage	Y= 0.9976X + 0.0231	12	0.9976	0.9883–1.0068	0.0231	-0.0077-0.0540
Cheese-Mold Type	Y= 0.9929X + 0.0656	12	0.9929	0.9594–1.0264	0.0656	-0.0110-0.1202
Cherry	Y= 1.0165X + 0.2024	12	1.0165	0.9719–1.0612	0.2024	-0.1789-0.5838
Chestnut	Y= 1.0074X +0.2158	12	1.0074	0.9748–1.0399	0.2158	-0.0857-0.5173
Chocolate	Y= 1.0047X - 0.0163	9	1.0047	0.9833–1.0261	-0.0163	–0.0349-0.0022
Coffee	Y= 0.9876X + 0.0824	11	0.9876	0.9168–1.0584	0.0824	–0.0008-0.1655
Cucumber	Y= 1.0003X + 0.1336	12	1.0003	0.9736–1.0249	0.1336	-0.1292-0.3963
Grape	Y= 1.0117X + 0.1622	12	1.0117	0.9811–1.0423	0.1622	-0.1933-0.5177
Grapefruit	Y= 0.9967X + 0.0264	12	0.9967	0.9816–1.0119	0.0264	-0.0277-0.0804
Haddock	Y= 1.0010X + 0.0653	12	1.0010	0.9852–1.0169	0.0653	-0.1583-0.2888
Lamb	Y= 1.0233X - 0.2153	12	1.0233	0.9966–1.0499	-0.2153	–0.4527-0.0221
Lemon	Y= 0.9995X + 0.1424	12	0.9995	0.9836–1.0153	0.01424	0.0300-0.2549
Lima Bean	Y= 0.9973X + 0.0791	12	0.9973	0.9778–1.0167	0.0791	0.0067-0.1514
Peach	Y= 0.9916X + 0.1351	12	0.9916	0.9647–1.0185	0.1351	-0.2444-0.5145
Pear	Y= 1.0073X + 0.4035	12	1.0073	0.9667–1.0480	0.4035	-0.1411-0.9481
Pineapple	Y= 0.9871X + 0.0561	12	0.9871	0.9782–0.9960	0.0561	0.0373-0.0749
Plum	Y= 1.0175X + 0.0408	12	1.0175	0.9819–1.0531	0.0408	–0.2704-0.3521
Pumpkin	Y= 1.0033X + 0.0589	12	1.0033	0.9805–1.0262	0.0589	–0.0278-0.1455

Allergen	Regression Equation	N	Slope	95% CI	Intercept	95% CI
Red Snapper	Y= 0.9914X + 0.0753	12	0.9914	0.9822–1.0006	0.0753	0.0421-0.1085
Sole	Y= 0.9966X + 0.0610	12	0.9966	0.9825–1.0106	0.0610	-0.0042-0.1262
Spinach	Y= 1.0046X + 0.1871	12	1.0046	0.9568–1.0523	0.1871	-0.0821-0.4563
Sweet Potato	Y= 0.9999X +0.1379	11	0.9999	0.9529–1.0469	0.1379	0.0074-0.2683
Trout	Y= 1.0038X – 0.0478	12	1.0038	0.9896–1.0181	-0.0478	-0.2083-0.1127
Turkey meat	Y= 1.0129X + 0.1070	12	1.0129	0.9823–1.0436	0.1070	-0.0919-0.3058
Watermelon	Y= 1.0138X + 0.0405	12	1.0138	0.9856–1.0420	0.0405	-0.2677-0.3486

Assay working ranges: 0.1 – 100 kU/L.

c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*
Traceability: The calibrators and controls are traceable to the WHO 2nd IRP 75/502 reference standard for human IgE.

Stability: Accelerated allergen stability testing (15-25ºC for 57 days; assay kits stored at recommended temperature 2-8ºC). The accelerated study supports a two year shelf-life stability claim.

d. *Detection limit:*
Limit of Blank (LoB): Three runs assaying the blank sample (zero calibrator) were performed to estimate the Limit of Blank (LoB). A total of three instruments were used per run. The maximum dose of the LoB was selected as the most conservative LoB: $LoB_{MAX} = 0.026$. The claimed LoB is 0.1 kU/L.

Limit of Detection (LoD): Five samples were used to estimate the Limit of Detection (LoD). Sixty replicates of each sample were assayed per run. A total of 2 runs were completed with testing performed on 2 different instruments. The LoD was calculated for each sample using the formula: $LoD = LoB_{MAX} + (1.65 * SD_{LOD})$. The claimed LoD is 0.1 kU/L

e. *Analytical specificity:*
Inhibition studies: Specificity of each allergen was verified through competitive inhibition testing using a single serum sample or a serum pool. A negative sample was used to measure the background response.
To initiate the inhibition experiment, 70 µL of undiluted and 4 levels of 5-fold serially diluted inhibitor extract were mixed with 250 µL of sample or pool. This mixture was incubated at room temperature (15-28°C) for 1 hour allowing the immunological reaction to occur. Each sample mixture containing the inhibitor extract and the appropriate controls was assayed with one lot of each allergen. The percent (%) inhibition was calculated according to the following formula:

$$\left(\frac{\text{(Response of pos. control}_{\text{(pos. sample – neg. sample)}} \text{ – sample response with inhibitor extract)}}{\text{(Response of pos. control}_{\text{(pos. sample – neg. sample)}}\text{)}} \right) \text{ X } 100$$

The inhibition study demonstrated that the allergens tested are inhibited by the

relevant inhibitor extract in a concentration dependent fashion. Summary inhibition table is presented below.

Black pepper			Broccoli			Cabbage	
Inhibitor Concentration (mg/mL)	% Inhibition		Inhibitor Concentration (mg/mL)	% Inhibition		Inhibitor Concentration (mg/mL)	% Inhibition
5	93.01		5	95.21		5	96.75
1	77.62		1	91.51		1	95.56
0.2	56.99		0.2	85.56		0.2	91.34
0.04	22.38		0.04	74.17		0.04	70.45
0.008	1.40		0.008	24.75		0.008	16.30

Cheese-Mold Type			Cherry			Chestnut	
Inhibitor Concentration (mg/mL)	% Inhibition		Inhibitor Concentration (mg/mL)	% Inhibition		Inhibitor Concentration (mg/mL)	% Inhibition
5	89.34		5	98.94		5	95.98
1	88.83		1	92.40		1	90.12
0.2	80.71		0.2	76.56		0.2	49.64
0.04	74.11		0.04	57.76		0.04	0.00
0.008	16.75		0.008	46.57		0.008	2.70

Chocolate			Coffee			Cucumber	
Inhibitor Concentration (mg/mL)	% Inhibition		Inhibitor Concentration (mg/mL)	% Inhibition		Inhibitor Concentration (mg/mL)	% Inhibition
5	79.53		5	74.53		5	97.89
1	82.46		1	66.98		1	96.22
0.2	50.29		0.2	39.62		0.2	91.22
0.04	27.49		0.04	13.21		0.04	84.76
0.008	5.26		0.008	10.85		0.008	35.31
						0.0016	9.35

Grape,			Grapefruit			Haddock	
Inhibitor Concentration (mg/mL)	% Inhibition		Inhibitor Concentration (mg/mL)	% Inhibition		Inhibitor Concentration (mg/mL)	% Inhibition
5	85.56		5	97.78		0.2	97.33
1	52.22		1	93.13		0.04	90.80
0.2	23.33		0.2	82.32		0.008	83.47
0.04	26.67		0.04	15.76		0.0016	80.20
0.008	14.44		0.008	0.81		0.0032	70.73
						0.000064	18.47

Lamb			Lemon			Lima Bean	
Inhibitor Concentration (mg/mL)	% Inhibition		Inhibitor Concentration (mg/mL)	% Inhibition		Inhibitor Concentration (mg/mL)	% Inhibition
5	95.86		5	91.50		5	96.94
1	92.88		1	86.82		1	91.68
0.2	84.86		0.2	83.36		0.2	82.49
0.04	62.10		0.04	59.91		0.04	54.49
0.008	34.02		0.008	7.57		0.008	21.66

Peach			Pear			Pineapple	
Inhibitor Concentration (mg/mL)	% Inhibition		Inhibitor Concentration (mg/mL)	% Inhibition		Inhibitor Concentration (mg/mL)	% Inhibition
5	97.28		5	85.31		5	88.36
1	92.41		1	71.19		1	83.60
0.2	83.46		0.2	57.06		0.2	72.49
0.04	74.25		0.04	49.72		0.04	42.86
0.008	45.01		0.008	27.68		0.008	20.11

Plum			Pumpkin			Red Snapper	
Inhibitor Concentration (mg/mL)	% Inhibition		Inhibitor Concentration (mg/mL)	% Inhibition		Inhibitor Concentration (mg/mL)	% Inhibition
5	97.86		5	93.18		0.2	83.58
1	82.91		1	83.36		0.04	74.68
0.2	67.67		0.2	57.98		0.008	76.29
0.04	46.50		0.04	33.97		0.0016	76.50
0.008	16.70		0.008	14.19		0.0032	46.46
						0.000064	5.79

Sole			Spinach			Sweet Potato	
Inhibitor Concentration (mg/mL)	% Inhibition		Inhibitor Concentration (mg/mL)	% Inhibition		Inhibitor Concentration (mg/mL)	% Inhibition
1	97.04		5	80.10		5	60.57
0.2	90.31		1	81.20		1	42.86
0.04	77.55		0.2	62.02		0.2	0.00
0.008	63.52		0.04	36.58		0.04	0.00
0.0016	47.50		0.008	15.75		0.008	3.43
0.0032	39.34						

Trout			Turkey meat			Watermelon	
Inhibitor Concentration (mg/mL)	% Inhibition		Inhibitor Concentration (mg/mL)	% Inhibition		Inhibitor Concentration (mg/mL)	% Inhibition
5	99.03		5	96.52		5	100.00
1	97.71		1	93.99		1	93.53
0.2	96.10		0.2	90.51		0.2	87.30
0.04	91.36		0.04	68.20		0.04	83.37
0.008	83.99		0.008	20.09		0.008	62.59
0.0016	78.25						12.70
0.0032	60.21						5.08
0.000064	12.99						

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

f. Assay cut-off:
Not applicable

2. Comparison studies:
   a. Method comparison with predicate device:
   Refer to Clinical studies
   b. Matrix comparison:
   Not applicable. Serum is the only matrix.
3. Clinical studies:
   a. Clinical Sensitivity and specificity
   Clinical performance of the IMMULITE® 2000 3gAllergy Specific IgE assay for Black pepper, Broccoli, Cabbage, Cheese-Mold Type, Cherry, Chestnut, Chocolate, Coffee, Cucumber, Grape, Grapefruit, Haddock, Lamb, Lemon, Lima Bean, Peach, Pear, Pineapple, Plum, Pumpkin, Red Snapper, Sole, Spinach, Sweet Potato, Trout, Turkey meat, Watermelon allergens was demonstrated by testing samples from non-atopic and atopic individuals. Atopic patients were selected from patients who had documented history of allergies to mold and/or pollen and/or skin prick tested. Information on the skin test allergen extracts (crude or purified) was not documented. Non-atopic patients were clinically known non-allergenic or total IgE <130 ng/mL or 54 IU/mL (2.4 ng = 1 IU). Testing was performed on 156 samples for Black pepper, 156 samples for Broccoli, 155 samples for Cabbage, 158 samples for Cheese-Mold Type, 155 samples for Cherry, 153 samples for Chestnut, 190 samples for Chocolate, 130 samples for Coffee, 156 samples for Cucumber, 161 samples for Grape, 151 samples for Grapefruit, 139 samples for Haddock, 154 samples for Lamb, 161 samples for Lemon, 158 samples for Lima Bean, 156 samples for Peach, 152 samples for Pear, 152 samples for Pineapple, 152 samples for Plum, 151 samples for Pumpkin, 131 samples for Red Snapper, 136 samples for Sole, 149 samples for Spinach, 157 samples for Sweet Potato, 158 samples for Trout, 145 samples for Turkey meat, 156 samples for Watermelon .

Literature support was provided on allergens with low prevalence and % sensitivity as shown below:

Specific Allergen/ % Clinical Sen.	Literature(s)	Prevalence	Literature(s)	%Clinical Sensitivity Ranges
F82: Cheese-Mold Type / 45%	Pereira B, Venter C, Grundy J, Clayton CB, Arshad SH, Dean T. J Allergy Clin Immunol. 2005 Oct;116(4):884-92	24-28% milk and dairy (young adults)	1. Eriksson NE. Allergy. 1978 Aug;33(4):189-96. 2. Pereira B, Venter C, Grundy J, Clayton CB, Arshad SH, Dean T. J Allergy Clin Immunol. 2005 Oct;116(4):884-92	3% 8%
F105: Chocolate / 46%	1. Osterballe M, Hansen TK, Mortz CG, Høst A, Bindslev-Jensen C. Pediatr Allergy Immunol. 2005 Nov;16(7):567-73. 2. Pereira B, Venter C, Grundy J, Clayton CB, Arshad SH, Dean T. J Allergy Clin Immunol. 2005 Oct;116(4):884-92	7-12% 23%	Eriksson NE. Allergy. 1978 Aug;33(4):189-96.	2.3%
F42: Haddock / 32%	1. O'Neil C, Helbling AA, Lehrer SB. Clin Rev Allergy. 1993 Summer;11(2):183-200. 2. Pereira B, Venter C, Grundy J, Clayton CB, Arshad SH, Dean T. J Allergy Clin Immunol. 2005 Oct;116(4):884-92	6.9-10.3% fish (in children)[1] 8-15% fish (young adults)[2]	O'Neil C, Helbling AA, Lehrer SB. Clin Rev Allergy. 1993 Summer;11(2):183-200.	5-49%
F337: Sole / 37%	1. O'Neil C, Helbling AA, Lehrer SB. Clin Rev Allergy. 1993 Summer;11(2):183-200. 2. Pereira B, Venter C, Grundy J, Clayton CB, Arshad SH, Dean T. J Allergy Clin Immunol. 2005 Oct;116(4):884-92	6.9-10.3% fish (in children)[1] 8-15% fish (young adults)[2]	O'Neil C, Helbling AA, Lehrer SB. Clin Rev Allergy. 1993 Summer;11(2):183-200.	3-44%
F284: Turkey Meat / 48%	Zacharisen MC. WMJ. 2006 Jul;105(5):50-2.	17% (chicken meat)	Zacharisen MC. WMJ. 2006 Jul;105(5):50-2.	40% (chicken/ turkey meat)

Sensitivity and specificity of the new device, based on diagnosis of atopic status, are shown in the tables below:

Allergen: Black pepper		Clinical Diagnosis		
		Atopic	Non-atopic	Total
IMMULITE 2000	positive	27	0	27
	negative	24	105	129
	Total	51	105	156

Sensitivity: 53% (27/51) (95% CI: 39-67%)
Specificity: 100 % (105/105)

Allergen: Broccoli		Clinical Diagnosis		
		Atopic	Non-atopic	Total
IMMULITE 2000	positive	35	1	36
	negative	16	104	120
	Total	51	105	156

Sensitivity: 69% (35/51) (95% CI: 56-81 %)
Specificity: 99 % (104/105) (95% CI: 97-101 %)

Allergen: Cabbage		Clinical Diagnosis		
		Atopic	Non-atopic	Total
IMMULITE 2000	positive	35	1	36
	negative	15	104	119
	Total	50	105	155

Sensitivity: 70% (35/50) (95% CI: 57-83%)
Specificity: 99% (104/105) (95% CI: 97-101%)

Allergen: Cheese-Mold Type		Clinical Diagnosis		
		Atopic	Non-atopic	Total
IMMULITE 2000	positive	24	0	24
	negative	29	105	134
	Total	53	105	158

Sensitivity: 45% (24/53) (95% CI: 32-59%)
Specificity: 100% (105/105)

Allergen: Cherry		Clinical Diagnosis		
		Atopic	Non-atopic	Total
IMMULITE 2000	positive	36	1	37
	negative	14	104	118
	Total	50	105	155

Sensitivity: 72% (36/50) (95% CI: 60-84%)
Specificity: 99% (104/105) (95% CI: 97-101%)

Allergen: Chestnut		Clinical Diagnosis		
		Atopic	Non-atopic	Total
IMMULITE 2000	positive	47	1	48
	negative	1	104	105
	Total	48	105	153

Sensitivity: 98% (47/48) (95% CI: 94-102%)
Specificity: 99% (104/105) (95% CI: 97-101%)

Allergen: Chocolate		Clinical Diagnosis		
		Atopic	Non-atopic	Total
IMMULITE 2000	positive	17	0	17
	negative	20	153	173
	Total	37	153	190

Sensitivity: 46% (17/37) (95% CI: 30-62%)
Specificity: 100% (153/153)

Allergen: Coffee,		Clinical Diagnosis		
		Atopic	Non-atopic	Total
IMMULITE 2000	positive	19	6	25
	negative	9	96	105
	Total	28	102	130

Sensitivity: 68% (19/28) (95% CI: 51-85%)
Specificity: 94% (96/102) (95% CI: 90-99%)

Allergen: Cucumber		Clinical Diagnosis		
		Atopic	Non-atopic	Total
IMMULITE 2000	positive	35	1	36
	negative	16	104	120
	Total	51	105	156

Sensitivity: 69% (35/51) (95% CI: 56-81%)
Specificity: 99% (104/105) (95% CI: 97-101%)

Allergen: Grape		Clinical Diagnosis		
		Atopic	Non-atopic	Total
IMMULITE 2000	positive	42	1	43
	negative	14	104	118
	Total	56	105	161

Sensitivity: 75% (42/56) (95% CI: 64-86 %)
Specificity: 99% (104/105) (95% CI: 97-101 %)

Allergen: Grapefruit		Clinical Diagnosis		
		Atopic	Non-atopic	Total
IMMULITE 2000	positive	33	2	35
	negative	13	103	116
	Total	46	105	151

Sensitivity: 72% (33/46) (95% CI: 59-85%)
Specificity: 98% (103/105) (95% CI: 95-101%)

Allergen: Haddock		Clinical Diagnosis		
		Atopic	Non-atopic	Total
IMMULITE 2000	positive	12	1	13
	negative	25	101	126
	Total	37	102	139

Sensitivity: 32% (12/37) (95% CI: 17-48%)
Specificity: 99% (101/102) (95% CI: 97-101%)

Allergen: Lamb		Clinical Diagnosis		
		Atopic	Non-atopic	Total
IMMULITE 2000	positive	33	0	33
	negative	16	105	121
	Total	49	105	154

Sensitivity: 67% (33/49) (95% CI: 54-80%)
Specificity: 100% (105/105)

Allergen: Lemon		Clinical Diagnosis		
		Atopic	Non-atopic	Total
IMMULITE 2000	positive	39	1	40
	negative	17	104	121
	Total	56	105	161

Sensitivity: 70% (39/56) (95% CI: 58-82%)
Specificity: 99% (104/105) (95% CI: 97-101%)

Allergen: Lima Bean		Clinical Diagnosis		
		Atopic	Non-atopic	Total
IMMULITE 2000	positive	24	9	33
	negative	18	107	128
	Total	42	116	158

Sensitivity: 55% (24/42) (95% CI: 40-69%)
Specificity: 92% (107/116) (95% CI: 87-97%)

Allergen: Peach		Clinical Diagnosis		
		Atopic	Non-atopic	Total
IMMULITE 2000	positive	42	2	44
	negative	9	103	112
	Total	51	105	156

Sensitivity: 82% (42/51) (95% CI: 72-93%)
Specificity: 98% (103/105) (95% CI: 95-101%)

Allergen: Pear		Clinical Diagnosis		
		Atopic	Non-atopic	Total
IMMULITE 2000	positive	41	0	41
	negative	6	105	111
	Total	47	105	152

Sensitivity: 87% (41/47) (95% CI: 78-97%)
Specificity: 100% (105/105)

Allergen: Pineapple		Clinical Diagnosis		
		Atopic	Non-atopic	Total
IMMULITE 2000	positive	30	0	30
	negative	17	105	122
	Total	47	105	152

Sensitivity: 64% (30/47) (95% CI: 50-78%)
Specificity: 100% (105/105)

Allergen: Plum		Clinical Diagnosis		
		Atopic	Non-atopic	Total
IMMULITE 2000	positive	31	1	32
	negative	16	104	120
	Total	47	105	152

Sensitivity: 66% (31/47) (95% CI: 52-80 %)
Specificity: 99% (104/105) (95% CI: 97-101%)

Allergen: Pumpkin		Clinical Diagnosis		
		Atopic	Non-atopic	Total
IMMULITE 2000	positive	34	1	35
	negative	12	104	116
	Total	46	105	151

Sensitivity: 74% (34/46) (95% CI: 61-87%)
Specificity: 99% (104/105) (95% CI: 97-101%)

Allergen: Red Snapper		Clinical Diagnosis		
		Atopic	Non-atopic	Total
IMMULITE 2000	positive	15	1	16
	negative	15	100	115
	Total	30	101	131

Sensitivity: 50% (15/30) (95% CI: 32-68%)
Specificity: 99% (100/101) (95% CI: 97-101%)

Allergen: Sole		Clinical Diagnosis		
		Atopic	Non-atopic	Total
IMMULITE 2000	positive	13	1	14
	negative	22	100	122
	Total	35	101	136

Sensitivity: 37% (13/35) (95% CI: 21-53%)
Specificity: 99% (100/101) (95% CI: 97-100%)

Allergen: Spinach		Clinical Diagnosis		
		Atopic	Non-atopic	Total
IMMULITE 2000	positive	35	1	36
	negative	9	104	113
	Total	44	105	149

Sensitivity: 80% (35/44) (95% CI: 68-91%)
Specificity: 99% (104/105) (95% CI: 97-101%)

Allergen: Sweet Potato		Clinical Diagnosis		
		Atopic	Non-atopic	Total
IMMULITE 2000	positive	44	1	45
	negative	8	104	112
	Total	52	105	157

Sensitivity: 85% (44/52) (95% CI: 75-94%)
Specificity: 99% (104/105) (95% CI: 97-101%)

Allergen: Trout		Clinical Diagnosis		
		Atopic	Non-atopic	Total
IMMULITE 2000	positive	31	0	31
	negative	22	105	127
	Total	53	105	158

Sensitivity: 58% (31/53) (95% CI: 45-72%)
Specificity: 100% (105/105)

Allergen: Turkey Meat		Clinical Diagnosis		
		Atopic	Non-atopic	Total
IMMULITE 2000	positive	19	0	19
	negative	21	105	126
	Total	40	105	145

Sensitivity: 48% (19/40) (95% CI: 32-63%)
Specificity: 100% (105/105)

Allergen: Watermelon		Clinical Diagnosis		
		Atopic	Non-atopic	Total
IMMULITE 2000	positive	30	6	36
	negative	16	104	120
	Total	46	110	156

Sensitivity: 65% (30/46) (95% CI: 51-79%)
Specificity: 95% (104/110) (95% CI: 90-99%)

b. Other clinical supportive data (when a. is not applicable):
Not applicable.

4. Clinical cut-off**:**
Not applicable.
5. Expected values/Reference range:

Not detected.
Refer to the Hoffman's 'Standard' and 'Extended Standard' classification system utilizing Class 0 to Class IV cut-offs (see Tables I and II below).

Table I: The Standard classification system utilizes the following class cutoffs:

Class	kU/L	Reactivity for Individual/Component Allergen(s)
0*	< 0.10	Absent or ND†
	0.10 – 0.34	Very Low
I	0.35 – 0.69	Low
II	0.70 – 3.49	Moderate
III	3.50 – 17.49	High
IV	17.5 – 52.49	Very High
V	52.5 – 99.99	
VI	≥ 100	

* Class 0 in the standard system signifies: not detectable by second-generation assays.
† ND: not detectable by IMMULITE 2000 3gAllergy.

Table II: The Extended standard classification system utilizes the following class cutoffs.

Class	kU/L	Reactivity for Individual/Component Allergen(s)
0	< 0.10	Absent or ND†
0/1	0.10 – 0.24	Very Low
I	0.25 – 0.39	Low
II	0.40 – 1.29	Moderate
III	1.30 – 3.89	High
IV	3.90–14.99	Very High
V	15.00– 24.99	
VI	≥ 25	

† ND: not detectable by IMMULITE 2000 3gAllergy

The choice of classification systems can be made by the user within the IMMULITE 2000 operational software.
Reference: Hoffman, DR. Comparison of methods of performing the Radioallergosorbent test: Phadebas, Fadal-Nalebuff and Hoffman protocols. Ann Allergy. 1980 Dec; 45(6)

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.