

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

**A. 510(k) Number:**

k093107

**B. Purpose for Submission:**

Modification to device

**C. Measurand:**

Twelve Allergen Specific IgE (Brewer's Yeast, Cantaloupe, Cinnamon, Flounder, Green Bean, Green Pepper, Halibut, Mushroom, Pinto Bean, Red Kidney Bean, Sugar Cane, Yogurt)

**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) immunological test system
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. The test results are to be used in conjunction with clinical findings and other laboratory tests.
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:

<b>Similarities</b>		
Item	New Device	Predicate Device
Intended use	For <i>in vitro</i> 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	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

<b>Differences</b>		
Item	New Device	Predicate Device
Total number of Allergens	Twelve	One hundred and ten
Types of Specific Allergens	12 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):**

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

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

**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 (Brewer's Yeast, Cantaloupe, Cinnamon, Flounder, Green Bean, Green Pepper, Halibut, Mushroom, Pinto Bean, Red Kidney Bean, Sugar Cane, Yogurt) in duplicate twice a day for 20 different days (n = 80).

The sponsor's criterion for the negative sample was the average dose level must be <0.10 kU/L; all negative sample mean 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 2.21% to 5.93 % and 3.24% to 10.32%, respectively (see tables below).

## Allergen: Brewer's Yeast

Sample	Mean (kU/L)	Intra-assay		Inter-assay	
		SD (kU/L)	%CV	SD (kU/L)	%CV
Positive #1	0.78	0.028	3.59	0.031	3.97
Positive #2	3.67	0.125	3.41	0.164	4.47
Positive #3	13.57	0.451	3.32	0.547	4.03

## Allergen: Cantaloupe

Sample	Mean (kU/L)	Intra-assay		Inter-assay	
		SD (kU/L)	%CV	SD (kU/L)	%CV
Positive #1	1.27	0.048	3.78	0.051	4.02

Positive #2	1.17	0.035	2.99	0.041	3.50
Positive #3	0.50	0.014	2.80	0.027	5.40
Positive #4	0.36	0.014	3.72	0.019	5.16
Positive #5	8.14	0.350	4.30	0.397	4.87

## Allergen: Cinnamon

Sample	Mean (kU/L)	Intra-assay		Inter-assay	
		SD (kU/L)	%CV	SD (kU/L)	%CV
Positive #1	2.86	0.121	4.23	0.143	5.00
Positive #2	2.97	0.134	4.51	0.163	5.49
Positive #3	2.87	0.154	5.37	0.165	5.75
Positive #4	0.38	0.013	3.34	0.017	4.49
Positive #5	6.89	0.254	3.68	0.281	4.08

## Allergen: Flounder

Sample	Mean (kU/L)	Intra-assay		Inter-assay	
		SD (kU/L)	%CV	SD (kU/L)	%CV
Positive #1	7.40	0.294	3.97	0.309	4.18
Positive #2	11.13	0.384	3.45	0.420	3.77
Positive #3	21.89	0.985	4.50	1.157	5.29

## Allergen: Green Bean

Sample	Mean (kU/L)	Intra-assay		Inter-assay	
		SD (kU/L)	%CV	SD (kU/L)	%CV
Positive #1	1.06	0.043	4.06	0.048	4.53
Positive #2	2.08	0.076	3.65	0.105	5.05
Positive #3	9.05	0.360	3.98	0.414	4.57

## Allergen: Green Pepper

Sample	Mean (kU/L)	Intra-assay		Inter-assay	
		SD (kU/L)	%CV	SD (kU/L)	%CV
Positive #1	0.85	0.024	2.82	0.033	3.88
Positive #2	3.95	0.140	3.54	0.172	4.35
Positive #3	1.28	0.044	3.44	0.049	3.83

## Allergen: Halibut

Sample	Mean (kU/L)	Intra-assay		Inter-assay	
		SD (kU/L)	%CV	SD (kU/L)	%CV
Positive #1	5.34	0.200	3.75	0.221	4.14
Positive #2	7.68	0.288	3.75	0.306	3.98

Positive #3	8.69	0.309	3.56	0.368	4.23
Positive #4	0.45	0.015	3.22	0.019	4.07
Positive #5	2.52	0.093	3.71	0.100	3.96

## Allergen: Mushroom

Sample	Mean (kU/L)	Intra-assay		Inter-assay	
		SD (kU/L)	%CV	SD (kU/L)	%CV
Positive #1	1.42	0.044	3.10	0.049	3.45
Positive #2	2.07	0.048	2.32	0.079	3.82
Positive #3	0.86	0.029	3.37	0.057	6.63

## Allergen: Pinto Bean

Sample	Mean (kU/L)	Intra-assay		Inter-assay	
		SD (kU/L)	%CV	SD (kU/L)	%CV
Positive #1	1.41	0.047	3.33	0.052	3.69
Positive #2	1.79	0.079	4.41	0.089	4.97
Positive #3	8.11	0.230	2.84	0.293	3.61
Positive #4	0.59	0.024	4.15	0.025	4.30
Positive #5	20.28	0.639	3.15	0.688	3.39

## Allergen: Red Kidney Bean

Sample	Mean (kU/L)	Intra-assay		Inter-assay	
		SD (kU/L)	%CV	SD (kU/L)	%CV
Positive #1	1.32	0.070	5.30	0.077	5.83
Positive #2	0.62	0.064	3.87	0.064	10.32
Positive #3	2.46	0.120	4.39	0.120	4.88

## Allergen: Sugar Cane

Sample	Mean (kU/L)	Intra-assay		Inter-assay	
		SD (kU/L)	%CV	SD (kU/L)	%CV
Positive #1	1.72	0.102	5.93	0.133	7.73
Positive #2	1.87	0.077	4.12	0.088	4.71
Positive #3	1.60	0.055	3.44	0.094	5.88
Positive #4	0.51	0.023	4.47	0.029	5.69
Positive #5	4.30	0.168	3.91	0.256	5.95

## Allergen: Yogurt

Sample	Mean (kU/L)	Intra-assay		Inter-assay	
		SD (kU/L)	%CV	SD (kU/L)	%CV
Positive #1	0.68	0.015	2.21	0.022	3.24
Positive #2	0.41	0.013	3.17	0.023	5.61

Positive #3	6.94	0.251	3.62	0.315	4.54
Positive #4	1.07	0.028	2.58	0.060	5.58
Positive #5	8.31	0.268	3.22	0.419	5.03

Additional precision studies were performed on six allergens for the following concentration levels (see table below):

Class	Specific Allergen	Mean (kU/L)	Within-run		Total	
			SD	%CV	SD	%CV
Class I 0.35-0.69 kU/L	F102 Cantaloupe	0.36	0.014	3.72	0.019	5.16
Class III 3.50-17.49 kU/L	F102 Cantaloupe	8.14	0.350	4.30	0.397	4.87
Class I 0.35-0.69 kU/L	F21 Sugar Cane	0.51	0.023	4.47	0.029	5.69
Class III 3.50-17.49 kU/L	F21 Sugar Cane	4.30	0.168	3.91	0.256	5.95
Class I 0.35-0.69 kU/L	F220 Cinnamon	0.38	0.013	3.34	0.017	4.49
Class III 3.50-17.49 kU/L	F220 Cinnamon	6.89	0.254	3.68	0.281	4.08
Class I 0.35-0.69 kU/L	F300 Pinto Bean	0.59	0.024	4.15	0.025	4.30
Class IV 17.5-52.49 kU/L	F300 Pinto Bean	20.28	0.639	3.15	0.688	3.39
Class I 0.35-0.69 kU/L	F303 Halibut	0.45	0.015	3.22	0.019	4.07
Class II 0.70 – 3.49 kU/L	F303 Halibut	2.52	0.093	3.71	0.100	3.96
Class II 0.70 – 3.49 kU/L	F360 Yogurt	1.07	0.028	2.58	0.060	5.58
Class III 3.50-17.49 kU/L	F360 Yogurt	8.31	0.268	3.22	0.419	5.03

**Lot to lot imprecision:**

The three tested lots were analyzed for lot-to-lot precision using three positive and one negative samples. Within run imprecision between lots ranged from 2.46% to 18.98\*% and total imprecision from 3.77% to 19.51\*%. All three lots were within the sponsor's claimed acceptable criterion of  $\leq 20\%$  variability.

\* The two outlier 18.98% and 19.51% imprecision readings were due to sample #2 for Brewer's Yeast allergen on lot #117; which on repeat gave readings of 3.76% and 4.50% respectively. If the two outliers were excluded from calculations, within run imprecision between lots range would be 2.46% to 5.29% and total imprecision from 3.77% to 12.34%.

**b. Linearity/assay reportable range:**

Linearity studies: For each allergen, two clinical 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. Results from both clinical samples were combined (so  $n = 12$ ) and analyzed for linearity. Regression statistics for each allergen comparing the observed results to expected results are presented below:

Allergen	Regression Equation	Slope 95% CI	Intercept 95% CI
Brewer's Yeast	$y = 0.99x + 0.032$	0.991 – 1.000	0.018 - 0.046
Cantaloupe	$y = 0.98x + 0.109$	0.951 – 1.027	0.038 - 0.182
Cinnamon	$y = 0.98x + 0.019$	0.964 – 1.011	0.002 - 0.036
Flounder	$y = 0.99x + 0.015$	0.983 - 1.005	-0.002 - 0.032
Green Bean	$y = 0.99x + 0.273$	0.960– 1.020	0.111 - 0.435
Green Pepper	$y = 0.99x + 0.214$	0.957 – 1.034	0.041 - 0.387
Halibut	$y = 0.98x - 0.008$	0.961 - 1.015	0.025 - 0.045
Mushroom	$y = 0.97x + 0.080$	0.859–1.084	-0.0002 - 0.160
Pinto Bean	$y = 0.99x + 0.145$	0.957–1.023	0.036 - 0.256
Red Kidney Bean	$y = 0.99x + 0.142$	0.977–1.015	-0.032 - 0.251
Sugar Cane	$y = 0.98x + 0.077$	0.914–1.041	0.0045- 0.151
Yogurt	$y = 1.009x + 0.098$	0.967–1.050	-0.019- 0.215

IMMULITE 2000 3gAllergy Universal Kit Total IgE 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 2<sup>nd</sup> IRP 75/502 reference standard for human IgE.

Stability:

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

*On-board/ open stability:* Testing was performed for 21 days. On-going data collection is for >90 days. Current study supports the 21 day stability claim.

*Adjustment interval (calibration curve) stability:* Testing was performed at days 1 and 14 to validate the 2-week adjustment interval. The calibration curve stability study supports the 2 weeks stability claim.

*Sample stability:* Stress conditions representing the storage claims were set up at 3 and 7 days at 2-8°C and 6 months at -20 °C. No significant variation to the reference samples that were run at day 0 was observed. The sample stability study supports the 7 days at 2-8°C and 6 months at -20 °C stability claims.

- d. *Detection limit:*

Limit of Blank (LoB): Three runs assaying the blank sample (zero calibrator) were performed to estimate the 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 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 tested 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  $\mu$ L of undiluted and 4 levels of 5-fold serially diluted inhibitor extract (at 5, 1, 0.2, 0.04, and 0.008 mg/mL) were mixed with 250  $\mu$ L of sample or pool. In some instances, additional levels of inhibitor extract (at 0.0016, 0.00032, and 0.000064 mg/mL) were also used. 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:

$$\frac{(\text{Response of pos. control}_{(\text{pos. sample} - \text{neg. sample})} - \text{sample response with inhibitor extract})}{(\text{Response of pos. control}_{(\text{pos. sample} - \text{neg. sample})})} \times 100$$

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:

Brewer's Yeast		Cinnamon		Flounder	
Inhibitor Concentration (mg/mL)	% Inhibition	Inhibitor Concentration (mg/mL)	% Inhibition	Inhibitor Concentration (mg/mL)	% Inhibition
5	100.00	5	89.66	5	100.00
1	100.00	1	91.38	1	97.90
0.2	100.00	0.2	79.31	0.2	94.84
0.04	92.23	0.04	63.79	0.04	88.15
0.008	82.43	0.008	56.03	0.008	79.54
0.0016	73.31	0.0016	53.45	0.0016	69.22
0.00032	32.43	0.00032	45.69	0.00032	59.66
0.000064	8.78	0.000064	24.57	0.000064	25.81

Halibut		Red Kidney Bean		Green Bean	
Inhibitor Concentration (mg/mL)	% Inhibition	Inhibitor Concentration (mg/mL)	% Inhibition	Inhibitor Concentration (mg/mL)	% Inhibition
5	100.00	5	93.03	5	96.52
1	100.00	1	93.80	1	94.56

Halibut		Red Kidney Bean		Green Bean	
Inhibitor Concentration (mg/mL)	% Inhibition	Inhibitor Concentration (mg/mL)	% Inhibition	Inhibitor Concentration (mg/mL)	% Inhibition
0.2	94.40	0.2	94.39	0.2	92.60
0.04	87.47	0.04	92.16	0.04	86.79
0.008	77.33	0.008	88.96	0.008	48.48
0.0016	65.60	0.0016	74.15	0.0016	15.97
0.00032	33.33	0.00032	29.43	0.00032	0.00
0.000064	3.73	0.000064	10.94		

Cantaloupe		Green Pepper		Mushroom	
Inhibitor Concentration (mg/mL)	% Inhibition	Inhibitor Concentration (mg/mL)	% Inhibition	Inhibitor Concentration (mg/mL)	% Inhibition
5	97.54	5	96.19	5	60.00
1	97.39	1	92.23	1	58.67
0.2	93.70	0.2	91.04	0.2	37.33
0.04	76.65	0.04	82.90	0.04	0.00
0.008	39.02	0.008	36.59	0.008	0.00
0.000064	3.73	0.000064	10.94		

Pinto Bean		Sugar Cane		Yogurt	
Inhibitor Concentration (mg/mL)	% Inhibition	Inhibitor Concentration (mg/mL)	% Inhibition	Inhibitor Concentration (mg/mL)	% Inhibition
5	96.23	5	72.30	5	87.50
1	93.05	1	58.45	1	92.21
0.2	85.43	0.2	28.53	0.2	70.08
0.04	64.77	0.04	11.36	0.04	0.00
0.008	34.83	0.008	8.59	0.008	0.00

Additional inhibition studies were conducted to show that the specific allergens are not cross-reacting to the unrelated allergens. Testing was performed using one positive sample with three unrelated allergen extracts at 1 mg/ml. A negative sample was used to measure the background response. Results on the positive sample are listed in Table below for the following specific allergen: Brewer's Yeast, Cantaloupe, Cinnamon, Flounder, Green Bean, Green Pepper, Halibut, Mushroom, Pinto Bean, Red Kidney Bean, Sugar Cane, Yogurt:

Brewer's Yeast (Positive Control = 3.76 KU/L)

Unrelated Inhibitor Extract USED	Inhibitor (mg/mL)	Observed Dose (KU/L)	Net Dose Reduction (KU/L)	% Inhibition

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W43 (Common Sagebrush)	1	3.32	0.44	11.70
T23 (Italian Cypress)	1	3.49	0.27	7.18
F182 (Lima Bean)	1	4.05	-0.29	0.00

Cantaloupe (Positive Control = 5.26 KU/L)

Unrelated Inhibitor Extract USED	Inhibitor (mg/ml)	Observed Dose (KU/L)	Net Dose Reduction (KU/L)	% Inhibition
C1 (Penicilloyl G)	1	5.00	0.26	4.94
M6 (Alternaria tenuis)	1	4.65	0.61	11.60
F42 (Haddock)	1	4.90	0.36	6.84

Cinnamon (Positive Control = 1.62 KU/L)

Unrelated Inhibitor Extract USED	Inhibitor (mg/ml)	Observed Dose (KU/L)	Net Dose Reduction (KU/L)	% Inhibition
C203 (Ampicillin)	1	2.19	-0.57	0.00
I206 (American Cockroach)	1	1.64	-0.02	0.00
M88 (Stemphylium solani)	1	1.73	-0.11	0.00

Flounder (Positive Control = 4.08 KU/L)

Unrelated Inhibitor Extract USED	Inhibitor (mg/ml)	Observed Dose (KU/L)	Net Dose Reduction (KU/L)	% Inhibition
C1 (Penicilloyl G)	1	4.18	-0.10	0.00
M6 (Alternaria tenuis)	1	4.52	-0.44	0.00
O201 (Tobacco)	1	3.84	0.24	5.88

Green Bean (Positive Control = 14.91 KU/L)

Unrelated Inhibitor Extract USED	Inhibitor (mg/ml)	Observed Dose (KU/L)	Net Dose Reduction (KU/L)	% Inhibition
C1 (Penicilloyl G)	1	15.20	-0.29	0.00
F2 (Milk)	1	15.24	-0.33	0.00
M6 (Alternaria tenuis)	1	15.28	0.37	5.88

Green Pepper (Positive Control = 13.42 KU/L)

Unrelated Inhibitor Extract USED	Inhibitor (mg/ml)	Observed Dose (KU/L)	Net Dose Reduction (KU/L)	% Inhibition
C1 (Penicilloyl G)	1	14.19	-0.77	0.00
F2 (Milk)	1	11.36	2.06	15.35

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M6 ( <i>Alternaria tenuis</i> )	1	14.04	-0.62	0.00
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Halibut (Positive Control = 2.81 KU/L)

Unrelated Inhibitor Extract USED	Inhibitor (mg/ml)	Observed Dose (KU/L)	Net Dose Reduction (KU/L)	% Inhibition
C1 (Penicilloyl G)	1	3.12	-0.31	0.00
M6 ( <i>Alternaria tenuis</i> )	1	2.80	0.01	0.36
O201 (Tobacco)	1	2.65	0.16	5.69

Mushroom (Positive Control = 1.94 KU/L)

Unrelated Inhibitor Extract USED	Inhibitor (mg/ml)	Observed Dose (KU/L)	Net Dose Reduction (KU/L)	% Inhibition
M88 ( <i>Stemphylium solani</i> )	1	1.63	0.31	15.98
C203 (Ampicillin)	1	2.07	-0.13	0.00
T83 (Mango Tree)	1	1.77	0.17	8.76

Pinto Bean (Positive Control = 11.31 KU/L)

Unrelated Inhibitor Extract USED	Inhibitor (mg/ml)	Observed Dose (KU/L)	Net Dose Reduction (KU/L)	% Inhibition
C1 (Penicilloyl G)	1	13.29	-1.98	0.00
F2 (Milk)	1	11.20	0.11	0.97
M6 ( <i>Alternaria tenuis</i> )	1	12.06	-0.75	0.00

Red Kidney Bean (Positive Control = 11.04 KU/L)

Unrelated Inhibitor Extract USED	Inhibitor (mg/ml)	Observed Dose (KU/L)	Net Dose Reduction (KU/L)	% Inhibition
C1 (Penicilloyl G)	1	11.37	-0.33	0.00
F2 (Milk)	1	10.05	0.99	8.97
M6 ( <i>Alternaria tenuis</i> )	1	10.49	0.55	4.98

Sugar Cane (Positive Control = 2.69 KU/L)

Unrelated Inhibitor Extract USED	Inhibitor (mg/ml)	Observed Dose (KU/L)	Net Dose Reduction (KU/L)	% Inhibition
C1 (Penicilloyl G)	1	2.98	-0.29	0.00
F2 (Milk)	1	2.63	0.06	2.23
M6 ( <i>Alternaria tenuis</i> )	1	2.79	-0.10	0.00

Yogurt (Positive Control = 0.60 KU/L)

Unrelated Inhibitor Extract USED	Inhibitor (mg/ml)	Observed Dose (KU/L)	Net Dose Reduction (KU/L)	% Inhibition
F222 (Tea)	1	0.79	-0.19	0.00
I206 (American Cockroach)	1	0.66	-0.06	0.00
T83 (Mango Tree)	1	0.56	0.04	6.67

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 Brewer's Yeast, Cantaloupe, Cinnamon, Flounder, Green Bean, Green Pepper, Halibut, Mushroom, Pinto Bean, Red Kidney Bean, Sugar Cane, Yogurt 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 specific allergen or allergen group of interest and/or a positive skin prick test. 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 144 samples for Brewer's Yeast, 173 samples for Cantaloupe, , 131 samples for Cinnamon, , 168 samples for Flounder, 184 samples for Green Bean, 137 samples for Green Pepper , 205 samples for Halibut, 137 samples for Mushroom, 181 samples for Pinto Bean, 212 samples for Red Kidney Bean, 232 samples for Sugar Cane, 166 samples for Yogurt.

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

<u>Allergen:</u> Brewer's Yeast		Clinical Diagnosis		
		Atopic	Non-atopic	Total
IMMULITE 2000	positive	17	0	17
	negative	27	100	127
	Total	44	100	144

*Sensitivity:* 39% (17/44) (95% CI: 24-53%)

*Specificity:* 100% (100/100)

<u>Allergen: Cantaloupe</u>		Clinical Diagnosis		
		Atopic	Non-atopic	Total
IMMULITE 2000	positive	17	1	18
	negative	27	128	155
	Total	44	129	173

*Sensitivity: 39% (17/44) (95% CI: 24-53 %)*

*Specificity: 99 % (128/129) (95% CI: 98-100 %)*

<u>Allergen: Cinnamon</u>		Clinical Diagnosis		
		Atopic	Non-atopic	Total
IMMULITE 2000	positive	14	1	15
	negative	17	99	116
	Total	31	100	131

*Sensitivity: 45% (14/31) (95% CI: 28-63%)*

*Specificity: 99% (99/100) (95% CI: 97-101%)*

<u>Allergen: Flounder</u>		Clinical Diagnosis		
		Atopic	Non-atopic	Total
IMMULITE 2000	positive	15	7	22
	negative	23	123	146
	Total	38	130	168

*Sensitivity: 39% (15/38) (95% CI: 24-55%)*

*Specificity: 95% (123/130) (95% CI: 91-98%)*

<u>Allergen: Green Bean</u>		Clinical Diagnosis		
		Atopic	Non-atopic	Total
IMMULITE 2000	positive	32	10	42
	negative	23	119	142
	Total	55	129	184

*Sensitivity: 58% (32/55) (95% CI: 45-71%)*

*Specificity: 92% (119/129) (95% CI: 88-97%)*

<u>Allergen: Green Pepper</u>		Clinical Diagnosis		
		Atopic	Non-atopic	Total
IMMULITE 2000	positive	32	3	35
	negative	5	97	102
	Total	37	100	137

*Sensitivity: 86% (32/37) (95% CI: 75-98%)*

*Specificity: 97% (97/100) (95% CI: 94/100%)*

<u>Allergen: Halibut</u>		Clinical Diagnosis		
		Atopic	Non-atopic	Total
IMMULITE 2000	positive	15	14	29
	negative	15	161	176

	Total	30	175	205
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*Sensitivity: 50% (15/30) (95% CI: 32-68%)*

*Specificity: 92% (161/175) (95% CI: 88-96%)*

<u>Allergen: Mushroom</u>		Clinical Diagnosis		
		Atopic	Non-atopic	Total
IMMULITE 2000	positive	17	8	25
	negative	20	92	112
	Total	37	100	137

*Sensitivity: 46% (17/37) (95% CI: 30-62%)*

*Specificity: 92% (92/100) (95% CI: 87-97%)*

<u>Allergen: Pinto Bean</u>		Clinical Diagnosis		
		Atopic	Non-atopic	Total
IMMULITE 2000	positive	33	12	45
	negative	29	107	136
	Total	62	119	181

*Sensitivity: 53% (33/62) (95% CI: 41-66%)*

*Specificity: 90% (107/119) (95% CI: 85--95%)*

<u>Allergen: Red Kidney Bean</u>		Clinical Diagnosis		
		Atopic	Non-atopic	Total
IMMULITE 2000	positive	26	11	37
	negative	36	139	175
	Total	62	150	212

*Sensitivity: 42% (26/62) (95% CI: 30-54 %)*

*Specificity: 93% (139/150) (95% CI: 88-97 %)*

<u>Allergen: Sugar Cane</u>		Clinical Diagnosis		
		Atopic	Non-atopic	Total
IMMULITE 2000	positive	25	15	40
	negative	32	160	192
	Total	57	175	232

*Sensitivity: 44% (25/57) (95% CI: 31-57%)*

*Specificity: 91% (160/175) (95% CI: 87-96%)*

<u>Allergen: Yogurt</u>		Clinical Diagnosis		
		Atopic	Non-atopic	Total
IMMULITE 2000	positive	23	12	35
	negative	13	118	131
	Total	36	130	166

*Sensitivity: 64% (23/36) (95% CI: 48-80%)*

*Specificity: 91% (118/130) (95% CI: 86-96%)*

Literature support was provided on allergens with low prevalence and %

sensitivity as shown below:

Specific Allergen Clinical Sen (%)	Allergen Name	Literature Cited:	Prevalence Found	Clinical Sensitivity
F403 (39%)	Brewer's Yeast	1.Mari A, Schneider P, Wally V, Breitenbach M, Simon-Nobbe B. Sensitization to fungi: epidemiology, comparative skin tests, and IgE reactivity of fungal extracts. Clin Exp Allergy. 2003; 33(10):1429-38. 2.Cholez C, Contet-Audonneau N, Schmutz JL, Virion JM, Barbaud A. Role of Malassezia species in head and neck dermatitis. Rev Fr Allergol Immunol Clin 2004; 44(4):372-378.	Yeast - 1.4% (46 out of 3248) population with suspected allergies <sup>1</sup>	3-30% (S. Cerevisiae) <sup>2</sup>
F102 (39%)	Cantaloupe	1.Osterballe M, Hansen TK, Mortz CG, Høst A, Bindslev-Jensen C. The prevalence of food hypersensitivity in an unselected population of children and adults. Pediatr Allergy Immunol. 2005; 16(7):567-73. 2.García Ortiz JC, Cosmes Martín P, Lopez-Asunolo A. Melon sensitivity shares allergens with Plantago and grass pollens. Allergy. 1995; 50(3):269-73. 3.Calkhoven PG, Aalbers M, Koshte VL, Pos O, Oei HD, Aalberse RC. Cross-reactivity among birch pollen, vegetables and fruits as detected by IgE antibodies is due to at least three distinct cross-reactive structures. Allergy. 1987;42(5):382-90	17-32% food hypersensitivity (in populations of pollen sensitized adults) <sup>1,2</sup>	Melon - 9-39.5% (24 out 262 patients with pollinosis) <sup>2</sup> and (17 out of 43 birch/food sensitized patients) <sup>3</sup>
F220 (45%)	Cinnamon	1.Osterballe M, Hansen TK, Mortz CG, Høst A, Bindslev-Jensen C. The prevalence of food hypersensitivity in an unselected population of children and adults. Pediatr Allergy Immunol. 2005;16(7):567-73. 2.García Ortiz JC, Cosmes Martín P, Lopez-Asunolo A. Melon sensitivity shares allergens with Plantago and grass pollens. Allergy. 1995;50(3):269-73. 3.Döner F, Yarıktas M, Demirci M. The role of allergy in recurrent otitis media with effusion. J Investig Allergol Clin Immunol. 2004;14(2):154-8.	17-32% food hypersensitivity (in populations of pollen sensitized adults) <sup>1,2</sup>	4.5-10% (1 out of 22 patients with food allergy) <sup>3</sup> and (9 out of 88 with allergen group that included cinnamon) <sup>1</sup>
F147 (39%)	Flounder	1. O'Neil C, Helbling AA, Lehrer SB. Allergic reactions to fish. Clin Rev Allergy. 1993; 11(2):183-200. 2. Pereira B, Venter C, Grundy J, Clayton CB, Arshad SH, Dean T. Prevalence of sensitization to food allergens, reported adverse reaction to foods, food avoidance, and food hypersensitivity among teenagers. J	6.9-10.3% fish (in children) <sup>1</sup> 8-15% fish (young adults) <sup>2</sup>	33% (in a fish sensitive population) <sup>1</sup>

Specific Allergen Clinical Sen (%)	Allergen Name	Literature Cited:	Prevalence Found	Clinical Sensitivity
		Allergy Clin Immunol. 2005 116(4):884-92		
F303 (50%)	Halibut	1. O'Neil C, Helbling AA, Lehrer SB. Allergic reactions to fish. Clin Rev Allergy. 1993; 11(2):183-200. 2. Pereira B, Venter C, Grundy J, Clayton CB, Arshad SH, Dean T. Prevalence of sensitization to food allergens, reported adverse reaction to foods, food avoidance, and food hypersensitivity among teenagers. J Allergy Clin Immunol. 2005;116(4):884-92	6.9-10.3% fish (in children) <sup>1</sup> 8-15% fish (young adults) <sup>2</sup>	10-33% (in a fish sensitive population) <sup>1</sup>
F212 (46%)	Mushroom	1. Mari A, Schneider P, Wally V, Breitenbach M, Simon-Nobbe B. Sensitization to fungi: epidemiology, comparative skin tests, and IgE reactivity of fungal extracts. Clin Exp Allergy. 2003; 33(10):1429-38. 2. Dauby PA, Whisman BA, Hagan L. Cross-reactivity between raw mushroom and molds in a patient with oral allergy syndrome. Ann Allergy Asthma Immunol. 2002 Sep;89(3):319-21. 3. Herrera-Mozo I, Ferrer B, Luís Rodriguez-Sanchez J, Juarez C. Description of a novel panallergen of cross-reactivity between moulds and foods. Immunol Invest. 2006; 35(2):181-97.	Fungi - 19.1% (621 out of 3248) population with suspected allergies <sup>1</sup> Mushroom - 1% (in oral food allergy syndrome population) <sup>2</sup>	25-73.3% (3/12 patients with general inhalant allergies and 22/30 patients with mold allergies) <sup>3</sup>
F287 (42%)	Red Kidney Bean	1. Zuidmeer L, Goldhahn K, Rona R, Gislason D, Madsen C, Summers C, et al. The prevalence of plant food allergies: A systematic review. Journal of Allergy and Clinical Immunology, 2008; 121(5):1210-1218. 2. Geraldés L, Carrapatoso I, Santos A, Rodrigues F, Todo-Bom A, Faria E, Chieira C. Sensitization patterns in legume hypersensitivity. A study from the central region of Portugal. Rev Port Imunoalergologia 2009; 17(1):37-55.	0.1 - 1.4% (vegetable allergy) <sup>1</sup> 14.3% (13 out of 91 allergy clinic patients in a region of high legume consumption) <sup>2</sup>	38-92% (in a population with symptoms upon ingestion of 1 or more legumes) <sup>2</sup>

Specific Allergen Clinical Sen (%)	Allergen Name	Literature Cited:	Prevalence Found	Clinical Sensitivity
F21 (44%)	Sugar Cane	<p>1.Osterballe M, Hansen TK, Mortz CG, Høst A, Bindslev-Jensen C. The prevalence of food hypersensitivity in an unselected population of children and adults. <i>Pediatr Allergy Immunol.</i> 2005; 16(7):567-73.</p> <p>2.García Ortiz JC, Cosmes Martín P, Lopez-Asunolo A. Melon sensitivity shares allergens with Plantago and grass pollens. <i>Allergy.</i> 1995; 50(3):269-73.</p> <p>3.Chakraborty P, Gupta-Bhattacharya S, Chowdhury I, Majumdar MR, Chanda S. Differences in concentrations of allergenic pollens and spore at different heights on an agricultural farm in West Bengal, India. <i>Ann Agric Environ Med.</i> 2001;8(2):123-30</p>	17-32% food hypersensitivity (in populations of pollen sensitized adults) <sup>1,2</sup>	21-50% (in a study population with frequent exposure) <sup>3</sup>

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 <sup>†</sup>
	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.

<sup>†</sup> 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 <sup>†</sup>
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	

<sup>†</sup> 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.