

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

A. 510(k) Number:

k101251

B. Purpose for Submission:

Addition of 13 new allergens to a cleared device

C. Measurand:

Thirteen new allergen-specific IgE: nDer p 1, rDer p 2, rDer 10, rFel d 1, nFel d 2, rAra h 1, rAra h 2, rAra h 3, rAra h 8, rAra h 9, nCyn d 1, rAlt a 1, and nAmb a 1

D. Type of Test:

Fluoroenzymeimmunoassay, Quantitative and Semi-quantitative

E. Applicant:

Phadia AB

F. Proprietary and Established Names:

ImmunoCAP Allergen d202, Allergen component nDer p 1, House dust mite
ImmunoCAP Allergen d203, Allergen component rDer p 2, House dust mite
ImmunoCAP Allergen d205, Allergen component rDer p 10, Tropomyosin, House dust mite

ImmunoCAP Allergen e94, Allergen component rFel d 1, Cat

ImmunoCAP Allergen e220, Allergen component nFel d 2, Cat serum albumin

ImmunoCAP Allergen f422, Allergen component rAra h 1, Peanut

ImmunoCAP Allergen f423, Allergen component rAra h 2, Peanut

ImmunoCAP Allergen f424, Allergen component rAra h 3, Peanut

ImmunoCAP Allergen f352, Allergen component rAra h 8, PR-10, Peanut

ImmunoCAP Allergen f427, Allergen component rAra h 9, LTP, Peanut

ImmunoCAP Allergen g216, Allergen component nCyn d 1, Bermuda grass

ImmunoCAP Allergen m229, Allergen component rAlt a 1, Alternaria alternata

ImmunoCAP Allergen w230, Allergen component nAmb a 1, Ragweed

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(s):

ImmunoCAP Specific IgE is an *in vitro* quantitative assay for the measurement of allergen specific IgE in human serum or plasma. ImmunoCAP Specific IgE is to be used with instruments Phadia 100, Phadia 250, and Phadia 1000. It is intended for *in vitro* diagnostic use as an aid in the clinical diagnosis of IgE mediated

allergic disorders in conjunction with other clinical findings, and is to be used in clinical laboratories.

2. Indication(s) for use:
Same as intended use.
3. Special conditions for use statement(s):
For prescription use only
4. Special instrument requirements:
ImmunoCAP Specific IgE is to be used with the instrument Phadia 100 Phadia 250 and Phadia 1000

I. Device Description:

The ImmunoCAP system is a fully integrated and automated system for the determination of specific IgE in human blood serum or plasma. It is comprised of instrument Phadia 100, Phadia 250 and Phadia 1000 test system modules (comprising general, test and method specific reagents), as well as instrument and data management software. The ImmunoCAP reagents include ImmunoCAP specific IgE Conjugate, ImmunoCAP Specific IgE Curve Control, ImmunoCAP Specific IgE Calibrators, Specific IgE anti-IgE ImmunoCAP, Allergen ImmunoCAP carriers, ImmunoCAP development solution and stop solution.

Individual allergen tests (the method specific reagents) are individual proteins covalently coupled to a support in a plastic housing. Individual allergens are purified native proteins or recombinantly produced and purified proteins.

J. Substantial Equivalence Information:

1. Predicate device name(s):
ImmunoCAP Specific IgE
2. Predicate K number(s):
k051218
3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Indications for Use	ImmunoCAP Specific IgE is an <i>in vitro</i> quantitative assay for the measurement of allergen specific IgE in human serum or plasma. It is intended for <i>in vitro</i> diagnostic use as an aid in the clinical diagnosis of IgE mediated allergic disorders in conjunction with other clinical findings, and is to be used in clinical laboratories, as well as physician office laboratories.	Same
Number of calibrators	Six	Same
Sample matrix	Serum and Plasma	Same
Antibody	β -Galactosidase-anti-IgE (mouse monoclonal antibody) for all ImmunoCAP	Same
Basic principle	Fluoroenzymeimmunoassay	Same

Similarities		
Item	Device	Predicate
Sample volume	40 µl	Same
Process time	2 hours 30 minutes for Phadia 100. 1 hour 45 minutes for Phadia 250 and 1000.	Same
Incubation temperature	37°C	Same

Differences		
Item	Device	Predicate
Modification	Existing allergen tests consist of multiple proteins from the allergen source. The new devices are individual proteins from this mix. Some are purified native proteins and some are recombinantly produced and purified. Recombinant proteins are: rDer p 2, rDer 10, rFel d 1, rAra h 1, rAra h 2, rAra h 3, rAra h 8, rAra h 9, rAlt a 1	Existing allergen tests are to whole allergens comprising multiple proteins from the allergen source

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

CLSI I/LA20-A: Evaluation Methods and Analytical Performance Characteristics of Immunological Assays for Human Immunoglobulin E (IgE) Antibodies of Defined Allergen Specificities; Approved Guideline (1997) I/LA20-A.

CEN 13640: Stability Testing of *in vitro* Diagnostic Reagents.

CLSI EP17-A: Protocols for Determination of Limits of Detection and Limits of Quantitation.

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

L. Test Principle:

The allergen of interest covalently coupled to the ImmunoCAP solid phase, reacts with the specific IgE in the patients plasma/serum sample. After washing away non specific IgE, enzyme labeled antibodies against IgE are added to form a complex. After incubation, unbound enzyme-anti-IgE is washed away and the bound complex is then incubated with the developing agent. After stopping the reaction, the fluorescence of the eluate is measured. The higher the response value, the more specific IgE present in the specimen. To evaluate the test results, the response for the patient samples are transformed to concentrations with the use of a calibration curve.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Within-Lot imprecision:

Imprecision of the individual allergen components were tested by using two

plasma samples ($0.35 \pm 25\%$ and ≥ 0.7 kU_A/l) tested four times per run, two runs per day, for ten days (a total of 80 replicates per allergen). The studies shown below were performed on a Phadia 250 instrument according to the ImmunoCAP Specific IgE, Directions for Use. In data not shown here, the applicant demonstrated similar assay precision on the Phadia 100 and Phadia 1000 instruments.

Allergen Group: **House Dust Mite** (*Dermatophagoides pteronyssinus*)

Allergen	Component Number	Mean (kU _A /l)	Between days CV%	Between runs within day CV%	Within run CV%	Total CV%
nDer p 1	d202	0.34	0.66	3.12	2.91	4.31
		1.82	2.93	2.59	2.93	4.89
rDer p 2	d203	0.33	2.02	2.46	2.35	3.96
		2.02	0.42	3.76	1.70	4.14
rDer 10	d205	0.36	1.99	3.24	2.90	4.78
		2.36	1.86	4.67	2.23	5.50

Allergen Group: **Cat** (*Felis catus*)

Allergen	Component Number	Mean (kU _A /l)	Between days CV%	Between runs within day CV%	Within run CV%	Total CV%
rFel d 1	e94	0.33	0.00	2.89	3.21	4.32
		2.58	0.00	6.53	1.98	6.82
nFel d 2	e220	0.36	0.85	2.77	2.22	3.66
		2.14	1.85	1.91	2.24	3.48

Allergen Group: **Peanut** (*Arachis hypogea*)

Allergen	Component Number	Mean (kU _A /l)	Between days CV%	Between runs within day CV%	Within run CV%	Total CV%
rAra h 1	f422	0.35	0.66	3.82	1.90	4.32
		1.96	5.43	3.82	1.65	6.84
rAra h 2	f423	0.31	3.83	4.03	10.05	11.49
		2.82	2.62	6.48	7.04	9.92
rAra h 3	f424	0.36	1.49	2.76	6.04	6.80

Allergen	Component Number	Mean (kU _A /l)	Between days CV%	Between runs within day CV%	Within run CV%	Total CV%
		3.47	1.49	3.10	3.17	4.68
rAra h 8	f352	0.37	0.67	1.65	2.11	2.76
		2.55	0.00	3.49	3.97	5.29
rAra h 9	f427	0.33	1.80	2.82	1.99	3.90
		2.35	6.03	5.02	2.38	8.20

Allergen Group: **Bermuda grass** (*Cynodon dactylon*)

Allergen	Component Number	Mean (kU _A /l)	Between days CV%	Between runs within day CV%	Within run CV%	Total CV%
rCyn d 1	g216	0.35	1.93	1.88	2.25	3.51
		2.07	0.00	3.02	2.23	3.75

Allergen Group: **Alternaria alternata**

Allergen	Component Number	Mean (kU _A /l)	Between days CV%	Between runs within day CV%	Within run CV%	Total CV%
rAlt a 1	w230	0.37	3.10	2.35	1.82	4.29
		2.32	2.16	2.60	2.27	4.07

Allergen Group: **Ragweed** (*Ambrosia artemisiifolia*)

Allergen	Component Number	Mean (kU _A /l)	Between days CV%	Between runs within day CV%	Within run CV%	Total CV%
nAmb a 1	m229	0.35	1.58	3.05	1.89	3.92
		2.36	2.22	2.75	1.88	4.00

Lot-to-lot imprecision:

Three lots of each individual allergen were tested using two positive samples ($0.35 \pm 25\%$ and ≥ 0.7 kU_A/L) and one negative sample (< 0.1 kU_A/L). For each lot the samples were tested in 12 replicates in one assay run. Each lot represented a different preparation of the allergen from routine production.

Allergen Group: **House Dust Mite** (*Dermatophagoides pteronyssinus*)

Allergen (Component number)	Lot	Sample				
		Positive 1		Positive 2		Negative
		Mean (kU _A /l)	CV (%)	Mean (kU _A /l)	CV (%)	Mean (kU _A /l)
nDer p 1 (d202)	1	2.49	4.1	0.39	3.4	0.00
	2	2.73	6.0	0.40	4.9	0.00
	3	2.35	8.8	0.37	3.4	0.00
rDer p 2 (d203)	1	2.10	2.6	0.35	2.5	0.00
	2	2.27	2.9	0.38	1.8	0.00
	3	2.11	1.5	0.35	2.6	0.00
rDer 10 (d205)	1	2.63	1.2	0.44	2.2	0.00
	2	2.47	2.2	0.42	2.6	0.00
	3	2.58	2.0	0.41	2.2	0.00

Allergen Group: **Cat** (*Felis catus*)

Allergen (Component number)	Lot	Sample				
		Positive 1		Positive 2		Negative
		Mean (kU _A /l)	CV (%)	Mean (kU _A /l)	CV (%)	Mean (kU _A /l)
rFel d 1 (e94)	1	3.10	1.7	0.40	3.3	0.00
	2	2.77	2.1	0.37	2.0	0.00
	3	3.07	2.7	0.40	1.8	0.00
nFel d 2 (e220)	1	2.16	1.9	0.33	2.0	0.00
	2	2.18	2.7	0.38	1.8	0.00
	3	2.15	1.5	0.37	2.8	0.00

Allergen Group: **Peanut** (*Arachis hypogea*)

Allergen (Component number)	Lot	Sample				
		Positive 1		Positive 2		Negative
		Mean (kU _A /l)	CV (%)	Mean (kU _A /l)	CV (%)	Mean (kU _A /l)
rAra h 1 (f422)	1	2.35	1.4	0.41	1.2	0.00
	2	2.29	2.2	0.39	1.7	0.00
	3	2.23	2.6	0.39	2.5	0.00
rAra h 2 (f423)	1	3.60	3.8	0.32	2.6	0.03
	2	3.27	4.5	0.29	3.5	0.03

Allergen (Component number)	Lot	Sample				
		Positive 1		Positive 2		Negative
		Mean (kU _A /l)	CV (%)	Mean (kU _A /l)	CV (%)	Mean (kU _A /l)
	3	2.99	6.6	0.26	2.9	0.02
rAra h 3 (f424)	1	3.77	3.1	0.32	1.9	0.00
	2	3.81	1.8	0.34	2.6	0.00
	3	4.06	2.8	0.34	3.7	0.00
rAra h 8 (f352)	1	2.57	4.1	0.33	1.9	0.00
	2	2.44	5.1	0.32	2.3	0.00
	3	2.70	3.6	0.33	1.9	0.00
rAra h 9 (f427)	1	2.85	3.5	0.38	2.1	0.00
	2	3.00	3.7	0.39	1.9	0.00
	3	2.53	1.9	0.34	1.2	0.00

Allergen Group: **Bermuda grass** (*Cynodon dactylon*)

Allergen (Component number)	Lot	Sample				
		Positive 1		Positive 2		Negative
		Mean (kU _A /l)	CV (%)	Mean (kU _A /l)	CV (%)	Mean (kU _A /l)
nCyn d 1 (g216)	1	1.78	4.5	0.37	2.7	0.00
	2	2.19	2.1	0.39	3.4	0.00
	3	2.16	2.8	0.38	2.3	0.00

Allergen Group: **Alternaria alternata**

Allergen (Component number)	Lot	Sample				
		Positive 1		Positive 2		Negative
		Mean (kU _A /l)	CV (%)	Mean (kU _A /l)	CV (%)	Mean (kU _A /l)
rAlt a 1 (w230)	1	2.30	1.8	0.37	2.2	0.00
	2	2.28	2.2	0.37	2.1	0.00
	3	2.24	2.0	0.36	1.5	0.00

Allergen Group: **Ragweed** (*Ambrosia artemisiifolia*)

Allergen (Component number)	Lot	Sample				
		Positive 1		Positive 2		Negative
		Mean (kU _A /l)	CV (%)	Mean (kU _A /l)	CV (%)	Mean (kU _A /l)

nAmb a 1 (m229)	1	2.52	2.1	0.39	1.4	0.00
	2	2.33	1.6	0.37	2.2	0.00
	3	2.52	2.3	0.40	2.6	0.00

b. *Linearity/assay reportable range:*

The linearity of the 13 individual allergens was assessed by diluting three positive plasma samples per allergen in negative plasma to provide at least five 2-fold consecutive dilutions. Undiluted and diluted samples were tested in four replicates in one assay run. The assay was performed according to the ImmunoCAP Specific IgE, Directions for Use using instrument Phadia 250. For each product one lot of ImmunoCAP Allergen Component was used. The ImmunoCAP Specific Total IgE working range is LoD – 100 kUA/L.

For each allergen, the replicates from all three samples were pooled and analyzed for linearity. Regression statistics for each allergen comparing the observed results to expected results are presented below:

Allergen Group: **House Dust Mite** (*Dermatophagoides pteronyssinus*)

Allergen (Component Number)	Regression Equation	R2	95% CI Slope	95% CI Intercept
nDer p 1 (d202)	$y = 0.99x + 0.04$	0.99	0.97 – 1.00	0.04 – 0.02
rDer p 2 (d203)	$y = 1.00x$	1.00	0.99 – 1.01	-0.01 – 0.01
rDer 10 (d205)	$y = 1.00x + 0.03$	1.00	0.97 – 1.02	0.01 – 0.05

Allergen Group: **Cat** (*Felis catus*)

Allergen (Component Number)	Regression Equation	R2	95% CI Slope	95% CI Intercept
rFel d 1 (e94)	$y = 0.97x + 0.03$	0.99	0.95 – 0.98	0.02 – 0.04
nFel d 2 (e220)	$y = 0.94x + 0.08$	0.99	0.93 – 0.96	0.06 – 0.09

Allergen Group: **Peanut** (*Arachis hypogea*)

Allergen (Component Number)	Regression Equation	R2	95% CI Slope	95% CI Intercept
rAra h 1 (f422)	$y = 1.00x - 0.05$	1.00	1.00 – 1.01	-0.05 - -0.04
rAra h 2 (f423)	$y = 0.91x + 0.09$	0.99	0.90 – 0.93	0.08 – 0.11
rAra h 3 (f424)	$y = 0.99x + 0.02$	0.99	0.96 – 1.01	0 – 0.04
rAra h 8 (f352)	$y = 1.00x$	1.00	0.99 – 1.01	-0.01 – 0.01
rAra h 9 (f427)	$y = 1.01x - 0.03$	1.00	1.00 – 1.03	-0.04 - -0.02

Allergen Group: Bermuda grass, Alternaria alternata, and Ragweed

Allergen (Component Number)	Regression Equation	R2	95% CI Slope	95% CI Intercept
nCyn d (g216)	$y = 0.96$	1.00	0.95 – 0.97	0.04 – 0.05
rAlt a 1 (m229)	$y = 0.96x$	0.99	0.96 – 0.99	-0.01 – 0.01
nAmb a 1 (w230)	$y = 0.97x + 0.02$	1.00	0.96 – 0.98	0.02 – 0.03

- c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*
The IgE calibrators are traceable (via an unbroken chain of calibrations) to the 2nd International Reference Preparation (IRP) 75/502 of Human Serum Immunoglobulin E from World Health Organization (WHO).

Real-time stability study results were available for rFel d 1, nFel d 2, rAlt a 1, rAra h 1, rAra h 2, rAra h 3 and rAra h 8 PR-10 and support an unopened shelf-life of 24 months from the date of manufacture when stored at 2-8°C. For the real-time study, more than one lot of each component allergen was stored at 2-8°C. At different times a positive and a negative plasma sample were tested in three replicates in one assay; the results were compared to the results of the same samples tested at time = 0.

Accelerated stability studies performed on allergen components nDer p 1, rDer p 2, rDer 10, nAmb a 1, nCyn d 1, and rAra h 9 LTP support an

unopened shelf-life of 24 months from the date of manufacture when stored at 2-8°C. For the accelerated study, three lots of component allergens were stored at 30°C for eight weeks. The same lot stored at 2-8°C was used as reference. At four weeks and at eight weeks two positive and one negative control samples (stored human plasma) were tested in duplicate in each storage condition/lot combination. The results support the manufacture's claim of 24 months. Real-time stability studies are underway for these components and currently support a claim of 13 months.

The stability of the calibration curve, real time, and on-board stability of ImmunoCAP Specific IgE calibrator are detailed in k100999.

d. *Detection limit:*

The Limit of Blank (LoB) and the Limit of Detection (LoD) were determined for each allergen component on the Phadia 250 in alignment with CLSI EP17-A. The LoB was based on single determinations of 100 negative samples (blank samples); the LoB was estimated as the 95% percentile of the distribution. LoD was calculated according to the equation: $LoD = LoB + c_{\beta} \times SD$ where SD, the standard deviation, was based on 20 determinations of 3 low positive samples, in total 60 determinations. In data not shown here, the applicant demonstrated that the Phadia 100 and the Phadia 1000 instruments had similar LoBs and LoDs for a subset of the allergens below.

Allergen Group	Allergen component	LoB	LoD
House Dust Mite	d202	0.025	0.036
	d203	0.000	0.010
	d205	0.000	0.009
Cat	e94	0.010	0.024
	e220	0.002	0.020
Peanut	f422	0.004	0.010
	f423	0.008	0.066
	f424	0.006	0.029
	f352	0.008	0.020
	f427	0.007	0.019
Bermuda Grass	g216	0.016	0.030
Alternaria alternata	w230	0.007	0.018

Allergen Group	Allergen component	LoB	LoD
Ragweed	m229	0.007	0.014

e. Analytical specificity:

Specificity of each allergen was verified through competitive inhibition studies planned in accordance with CLSI I/LA20-A. Inhibition studies should show an overall dose dependent decrease of free specific IgE antibodies available to bind to the ImmunoCAP Allergen. This dose dependent decrease indicates the presence of antibodies that recognize the allergen; no, or little, decrease in response indicates that there are no antibodies specific to the allergen. The specific inhibition demonstrates the presence of immunologically relevant and reactive allergen bound to the solid phase.

To establish the minimum theoretical response level for the sample (100% inhibition, “100%”), equal volumes of negative sample and buffer were premixed and tested with the assay. This should mimic the state where all IgE antibodies are bound by the added soluble inhibitor (allergen) so that no specific IgE antibodies are available to bind to the solid phase.

The maximum response level for the sample (0% inhibition, “0%”), is established by pre-mixing equal volumes of positive sample and buffer and testing with the assay.

Overall dose dependent inhibition of specific allergens was demonstrated by premixing 100 µl of positive sample with varying dilutions of allergen solution (inhibitor). As a control, three unrelated antigens were also tested at one concentration each in separate experiments.

The mixtures were incubated in a sample tube at room temperature for 1 hour before being analyzed with the ImmunoCAP Allergen Component according to the manufacturer’s instructions. The testing was performed in duplicates in one assay run. Mean values were calculated.

The results of the studies (not shown) demonstrate that the allergens tested are inhibited by the relevant inhibitor extract in a concentration dependent fashion; all allergens were able to be inhibited by more than 50%. Most allergens could be inhibited more than 90% by the highest concentration of inhibitor (i.e. the least dilute dilution).

Additional inhibition studies were conducted to show that the specific allergens are not cross-reacting to unrelated allergens. Testing was performed using one positive sample with three unrelated allergen extracts.

f. Assay cut-off:

Not applicable

2. Comparison studies:

a. *Method comparison with predicate device:*

Refer to clinical studies.

b. *Matrix comparison:*

Serum, heparin plasma, and EDTA plasma samples were collected from patients with clinical history of known specific allergies. These samples were tested with the ImmunoCap allergen components included in this submission. This resulted in a range of results (negative and positive) within each sample; for example, a sample was negative for f423 (peanut rAra h 2) but was strongly positive for e94 (cat rFel d 1). Recovery of the heparin plasma and EDTA plasma was acceptable in all positive (≥ 0.35 kU_A/L) samples. This study suggests that the three sample matrices are interchangeable.

3. Clinical studies:

a. *Clinical sensitivity and Specificity:*

The performance of all 13 individual allergen components was compared to a clinical diagnosis of allergy. Atopic samples were obtained from individuals with a clinical history of allergy-like symptoms upon exposure to an allergen as diagnosed by a physician and/or clinical symptoms and/or positive skin prick test to a specific allergen. Information about clinical symptoms and manifestations was available for all atopic samples. 100 negative samples (<0.35 kU_A/L) from healthy non-atopic donors were also tested.

House dust mites:

ImmunoCAP Allergen d202, nDer p 1

		Clinical Diagnosis		
		Atopic	Non-atopic	Total
nDer p 1(d202)	Positive	56	0	56
	Negative	1	100	101
	Total	57	100	157

Sensitivity =98% (95% CI: 90.7 – 99.7%)

Specificity =100%

ImmunoCAP Allergen d203, rDer p 2

		Clinical Diagnosis		
		Atopic	Non-atopic	Total
rDer p 2 (d203)	Positive	53	0	53
	Negative	4	100	104
	Total	57	100	157

Sensitivity =93% (95% CI: 83.3 – 97.2%)

Specificity =100%

ImmunoCAP Allergen d205, rDer p 10, Tropomyosin

		Clinical Diagnosis		
		Atopic	Non-atopic	Total
rDer p 10 (d205)	Positive	36	0	36
	Negative	36	100	136
	Total	72	100	172

Sensitivity =50% (95% CI: 38.8 – 61.3%)

Specificity =100%

Cat:

ImmunoCAP Allergen e94, rFel d 1

		Clinical Diagnosis		
		Atopic	Non-atopic	Total
rFel d 1 (e94)	Positive	72	0	72
	Negative	1	100	101
	Total	73	100	173

Sensitivity =99% (95% CI: 92.6 – 99.8%)

Specificity =100%

ImmunoCAP Allergen e220, nFel d 2

		Clinical Diagnosis		
		Atopic	Non-atopic	Total
nFel d 2 (e220)	Positive	34	0	34
	Negative	39	100	139
	Total	73	100	173

Sensitivity =47% (95% CI: 35.6 – 57.9%)

Specificity =100%

Peanut:

ImmunoCAP Allergen f422, rAra h 1

		Clinical Diagnosis		
		Atopic	Non-atopic	Total
rAra h 1 (f422)	Positive	37	0	37
	Negative	56	100	156
	Total	93	100	193

Sensitivity =40% (95% CI: 30.4 – 50.0%)

Specificity =100%

ImmunoCAP Allergen f423, rAra h 2

		Clinical Diagnosis		
		Atopic	Non-atopic	Total
rAra h 2 (f423)	Positive	40	0	40
	Negative	53	100	153

	Total	93	100	193
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Sensitivity =43% (95% CI: 33.4 – 53.2%)

Specificity =100%

ImmunoCAP Allergen f424, rAra h 3

		Clinical Diagnosis		
		Atopic	Non-atopic	Total
rAra h 3 (f424)	Positive	37	0	37
	Negative	56	100	156
	Total	93	100	193

Sensitivity =40% (95% CI: 30.4 – 50.0%)

Specificity =100%

ImmunoCAP Allergen f352, rAra h 8, PR-10

		Clinical Diagnosis		
		Atopic	Non-atopic	Total
rAra h 8 (f352)	Positive	43	0	43
	Negative	50	100	150
	Total	93	100	193

Sensitivity =46% (95% CI: 33.4 – 53.2%)

Specificity =100%

ImmunoCAP Allergen f427, rAra h 9, LTP

		Clinical Diagnosis		
		Atopic	Non-atopic	Total
rAra h 9 (f427)	Positive	52	0	52
	Negative	22	100	141
	Total	74	100	193

Sensitivity =70% 95% CI: 59.1 – 79.5%)

Specificity =100%

Bermuda grass:

ImmunoCAP Allergen g216, nCyn d 1

		Clinical Diagnosis		
		Atopic	Non-atopic	Total
nCyn d 1 (g216)	Positive	31	0	31
	Negative	0	100	100
	Total	31	100	131

Sensitivity =100%

Specificity =100%

Alternaria alternata:

ImmunoCAP Allergen m229, rAlt a 1

		Clinical Diagnosis		
		Atopic	Non-atopic	Total
rAlt a 1 (m229)	Positive	45	0	45
	Negative	0	100	100
	Total	45	100	145

Sensitivity =100%

Specificity =100%

Ragweed:

ImmunoCAP Allergen w230, nAmb a 1

		Clinical Diagnosis		
		Atopic	Non-atopic	Total
nAmb a 1 (w230)	Positive	34	0	34
	Negative	0	100	100
	Total	34	100	134

Sensitivity =100%

Specificity =100%

All studies described above were performed on the Phadia 250 instrument system. The applicant provided studies to show that the Phadia 100 and Phadia 1000 instrument system performed similarly to the Phadia 250.

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

Specific Allergen Clinical Sensitivity (%)	Allergen Name	Literature Cited	Prevalence Found	Clinical Sensitivity
rDer p 10 d205 (50%)	d1 House dust mite	1) Jaén A et al. European Community Respiratory Health Survey. Specific sensitization to common allergens and pulmonary function in the European Community Respiratory Health Survey. Clin Exp Allergy. 2002 Dec;32(12):1713-9. 2) Weghofer M et al. Variability of IgE reactivity profiles among European mite allergic patients. Eur J Clin Invest 2008;38 (12): 959-65.	1) ECRHS 12687 subjects from 34 centres in 15 countries. Prevalence of sensitization to mite: Women; 16.8% Men; 23.5%	2) Mite allergic patients from Austria (n=56) France N(55) Italy n=(67) Sweden (n=31) Der p 10 positive in 18%, 9%,10% and 18% respectively 3) 90 mite allergic patients in Colombia. Der p 10 positive

Specific Allergen Clinical Sensitivity (%)	Allergen Name	Literature Cited	Prevalence Found	Clinical Sensitivity
		3) Jiménez S. et al. IgE antibody responses to recombinant allergens of <i>Blomia tropicalis</i> and <i>Dermatophagoides pteronyssinus</i> in a tropical environment. Allergy and Clinical Immunology International Volume 19, Issue 6, November 2007, Pages 233-238 4) Boquete M. et al. Seafood hypersensitivity in mite sensitized individuals: is tropomyosin the only responsible allergen? Annals of Allergy, Asthma & Immunology, Volume 106, Issue 3, March 2011, Pages 223-229		16.7% 4) 60 mite allergic patients in Spain; Der p 10 positive in 32% of 30 patients with both mite and seafood symptoms and in 0% of 30 patients with only mite symptoms
n Fel d 2 e220 (47%)	e1 Cat	1) Spitzauer S. et al. IgE cross-reactivities against albumins in patients allergic to animals. J Allergy Clin Immunol 1995;96(6 Pt 1): 951-9 2) Hilger C. et al. Allergic cross-reactions between cat and pig serum albumin. Study at the protein and DNA levels. Allergy 1997;52(2):179-87 3) van Ree R. et al. Purified natural and recombinant Fel d 1 and cat albumin in in vitro diagnostics for cat allergy. J Allergy Clin Immunol 1999;104(6):1223-30 4) Cabanas, R., M. C. Lopez-Serrano, et al. "Importance of albumin in cross-reactivity among cat, dog and horse allergens." Journal of Investigational Allergology & Clinical Immunology 2000; 10(2): 71-77.	1) ECRHS 12687 subjects from 34 centres in 15 countries. Prevalence of sensitization to cat: Women ; 9.3 % Men; 9.5%	1) 200 animal allergic patients; Cat albumin (Fel d 2) positive in 26% of patients 2) 2 groups of cat allergic patients (n=39 and n=39) Fel d 2 positive in 14% and 23% 1 group (n=10) allergic both to cat and pork ; Fel d 2 positive in 100% 3) 509 cat sensitized patients ; Fel d 2 positive in 16.7% 4) 117 cat allergic patients; Fel d 2 positive in 22%

Specific Allergen Clinical Sensitivity (%)	Allergen Name	Literature Cited	Prevalence Found	Clinical Sensitivity
rAra h 1 f422 (40%)	f13 Peanut	1) Branum AM, Lukacs SL. Food allergy among children in the United States Pediatrics. 2009 Dec;124(6):1549-55. Epub 2009 Nov 16. 2) Asarnoj A. et al. IgE to peanut allergen components: relation to peanut symptoms and pollen sensitization in 8-year-olds. Allergy 2010;65: 1189-1195 3) Codreanu et al. A Novel Immunoassay using recombinant allergens simplifies peanut allergy diagnosis. Int Arch Allergy Immunol 2011;154:216–226 4) Vereda A. et al. Peanut allergy: Clinical and immunologic differences among patients from 3 different geographic regions (J Allergy Clin Immunol 2011 in press on line; DOI: 10.1016/j.jaci.2010.09.010)	1) NHANES: Prevalence of peanut sensitized children in USA estimated to 9%	2) Peanut allergic children in Sweden (n=58); Positive to: Ara h 1; 48% 3) Peanut allergic patients in France (n=166) Positive to: Ara h 1; 75% 4) Peanut Allergic patients from 3 countries Spain (n=50) USA (n=30), Sweden (n=35) Positive to : Ara h 1; 30%, 80%, 62,9% respectively
r Ar a h 2f423 (43%)	f13 Peanut	1) Branum AM, Lukacs SL. Food allergy among children in the United States Pediatrics. 2009 Dec;124(6):1549-55. Epub 2009 Nov 16. 2) Asarnoj A. et al. IgE to peanut allergen components: relation to peanut symptoms and pollen sensitization in 8-year-olds. Allergy 2010;65: 1189-1195 3) Codreanu et al. A Novel Immunoassay using recombinant allergens simplifies peanut allergy diagnosis. Int Arch Allergy Immunol 2011;154:216–226	1) NHANES: Prevalence of peanut sensitized children in USA estimated to 9%	2) Peanut allergic children in Sweden (n=58); Positive to: Ara h 2; 78% 3) Peanut allergic patients in France (n=166) Positive to: Ara h 2; 96% 4) Peanut Allergic patients from 3 countries Spain (n=50) USA (n=30), Sweden (n=35)

Specific Allergen Clinical Sensitivity (%)	Allergen Name	Literature Cited	Prevalence Found	Clinical Sensitivity
		4) Vereda A. et al. Peanut allergy: Clinical and immunologic differences among patients from 3 different geographic regions (J Allergy Clin Immunol 2011 in press on line ; DOI: 10.1016/j.jaci.2010.09.010)		Positive to : Ara h 2; 42%, 90%, 74,3% respectively
rAra h 3 f424 (40%)	f13 Peanut	1) Branum AM, Lukacs SL. Food allergy among children in the United States Pediatrics. 2009 Dec;124(6):1549-55. Epub 2009 Nov 16. 2) Asarnoj A. et al. IgE to peanut allergen components: relation to peanut symptoms and pollen sensitization in 8-year-olds. Allergy 2010;65: 1189-1195 3) Codreanu et al. A Novel Immunoassay using recombinant allergens simplifies peanut allergy diagnosis. Int Arch Allergy Immunol 2011;154:216–226 4) Vereda A. et al. Peanut allergy: Clinical and immunologic differences among patients from 3 different geographic regions (J Allergy Clin Immunol 2011 in press on line; DOI: 10.1016/j.jaci.2010.09.010)	1) NHANES: Prevalence of peanut sensitized children in USA estimated to 9%	2) Peanut allergic children in Sweden (n=58); Positive to: Ara h 3; 41% 3) Peanut allergic patients in France (n=166) Positive to: Ara h 3; 61% 4) Peanut Allergic patients from 3 countries Spain (n=50) USA (n=30), Sweden (n=35) Positive to : Ara h 3: 16%,56,7%, 37,1% respectively
rAra h 8 f352 (46%)	f13 Peanut	1) Branum AM, Lukacs SL. Food allergy among children in the United States Pediatrics. 2009 Dec;124(6):1549-55. Epub 2009 Nov 16. 2) Mittag D. et al. Ara h 8, a Bet v 1-homologous allergen from peanut, is a major allergen in	1) NHANES: Prevalence of peanut sensitized children in USA estimated to 9%	2) Peanut and birch allergic patients in Germany (n=20) Positive to: Ara h 8; 85 % 3) Peanut allergic children in Sweden (n=58);

Specific Allergen Clinical Sensitivity (%)	Allergen Name	Literature Cited	Prevalence Found	Clinical Sensitivity
		patients with combined birch pollen and peanut allergy. J Allergy Clin Immunol 2004;114:1410-1417 3) Asarnoj A. et al. IgE to peanut allergen components: relation to peanut symptoms and pollen sensitization in 8-year-olds. Allergy 2010;65: 1189-1195 4) Vereda A. et al. Peanut allergy: Clinical and immunologic differences among patients from 3 different geographic regions (J Allergy Clin Immunol 2011 in press on line; DOI: 10.1016/j.jaci.2010.09.010)		Positive to: Ara h 8; 14 % 4) Peanut Allergic patients from 3 countries Spain (n=50) USA (n=30), Sweden (n=35) Positive to : Ara h 8: 2%, 19,1%, 65,7%

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

4. Clinical cut-off:

Not applicable

5. Expected values/Reference range:

The expected value is negative ($< 0.35 \text{ kU}_A/\text{L}$) for a specific allergen in a non-allergic person. The manufacturer recommends a cut-off of $0.35 \text{ kU}_A/\text{L}$. Each laboratory should establish its own expected range of values.

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.