

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

A. 510(k) Number:

k111919

B. Purpose for Submission:

Addition of 12 new recombinant allergens to a cleared device

C. Measurand:

Twelve new recombinant allergen-specific IgE analytes: Two Hazel nut: (rCor a 8 and rCor a 1 PR-10), six Timothy (rPhl p1, rPhl p2, rPhl p6, rPhl p7, rPhl p12, rPhl and p5b) and four Birch (rBet v 1 PR-10, rBet v 2 Profilin, rBet v4 and rBet v 6)

D. Type of Test:

Fluoroenzymeimmunoassay, Quantitative and Semi-quantitative

E. Applicant:

Phadia AB

F. Proprietary and Established Names:

ImmunoCAP Allergen f425, Allergen component rCor a 8, Hazel nut
ImmunoCAP Allergen f428, Allergen component rCor a 1, PR-10, Hazel nut
ImmunoCAP Allergen g205, Allergen component rPhl p1, Timothy
ImmunoCAP Allergen g206, Allergen component rPhl p2, Timothy
ImmunoCAP Allergen g209, Allergen component rPhl p6, Timothy
ImmunoCAP Allergen g210, Allergen component rPhl p7, Timothy
ImmunoCAP Allergen g212, Allergen component rPhl p12, Timothy
ImmunoCAP Allergen g215, Allergen component rPhl p5b, Timothy
ImmunoCAP Allergen t215, Allergen component rBet v 1, PR-10, Birch
ImmunoCAP Allergen t216, Allergen component rBet v 2 Profilin, Birch
ImmunoCAP Allergen t220, Allergen component rBet v4, Birch
ImmunoCAP Allergen t225, Allergen component rBet v 6, Birch

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 instruments Phadia 100, Phadia 250 and Phadia

I. Device Description:

The ImmunoCAP system is a fully integrated and automated system for the determination of specific IgE in human blood serum or sodium heparin plasma sample. It is comprised of general, test and method specific reagents for Phadia 100, Phadia 250 and Phadia 1000 test system modules, as well as instrument and data management software.

The general 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. The method specific reagents consist of individual purified allergen (native or recombinant) covalently coupled to a support in a plastic housing.

J. Substantial Equivalence Information:

1. Predicate device name(s) and 510(k) numbers:

UniCAP Specific IgE Assay/ Conjugate 100/ Conjugate 400 (k051218) and UniCAP Specific IgE Assay (k962274)

2. Comparison with predicate:

- 3.

Similarities		
Item	Device	Predicate
Intended Use	ImmunoCAP Specific IgE is an <i>in vitro</i> 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	Same
Number of calibrators	Six	Same
Sample matrix	Serum and plasma (sodium heparin)	Same
Antibody	β -Galactosidase-anti-IgE (mouse monoclonal antibody) for all ImmunoCAP	Same
Basic principle	Fluoroenzymeimmunoassay	Same
Sample volume	40 μ L	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
Allergens	Individual recombinant proteins: <u>Two Hazel nut</u> : rCor a 8 and rCor a 1 PR-10; <u>six Timothy</u> : rPhl p1, rPhl p2, rPhl p6, rPhl p7, rPhl p12, rPhl p5b; and <u>four Birch</u> : rBet v 1 PR-10, rBet v 2 Profilin, rBet v4, rBet v6	Whole allergens comprising multiple proteins from purified native allergen source
Assay type	Quantitative	Semi-Quantitative

Differences		
Item	Device	Predicate
Laboratory settings	Clinical laboratories	Clinical laboratories and physician office laboratories.
Instruments	Phadia 100, Phadia 250 and Phadia 1000	UniCAP 100

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

- CLSI I/LA20-A2: Analytical Performance Characteristics of Immunological Assays for Human Immunoglobulin E (IgE) Antibodies, March 2009
 CLSI EP5-A: Evaluation of Precision Performance of Quantitative Measurement Methods, August 2004
 CEN 13640: 2002 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 was evaluated by using two plasma samples ($0.35 \pm 25\%$ and ≥ 0.7 kU_A/l) tested four times per day, for 20 operating days (a total of 80 replicates per allergen). The study data shown below were performed on a Phadia 250 instrument according to the ImmunoCAP Specific IgE Directions for Use. Similar assay precision was demonstrated on the Phadia 100 and Phadia 1000 instruments.

Allergen Group: **Hazel nut**

Allergen	Component Number	Mean (kU _A /l)	Between Days CV%	Within run CV%	Total CV%
f425	rCor a 8	2.37	2.64	3.36	4.28
		0.35	3.08	1.88	3.60
f428	rCor a 1, PR-10	2.23	2.60	2.12	3.36
		0.36	3.41	2.06	3.99

Allergen Group: **Timothy**

Allergen	Component Number	Mean (kU _A /l)	Between Days CV%	Within run CV%	Total CV%
g205	rPhl p1	2.09	4.01	2.15	4.55
		0.34	4.77	2.39	5.34

Allergen	Component Number	Mean (kU _A /l)	Between Days CV%	Within run CV%	Total CV%
g206	rPhl p2	2.71	2.67	3.21	4.18
		0.33	3.55	3.40	4.91
g209	rPhl p6	1.71	2.69	3.65	4.54
		0.31	4.58	3.74	5.92
g210	rPhl p7	5.07	2.19	1.95	2.93
		0.33	3.40	1.92	3.91
g212	rPhl p12	2.26	3.31	2.73	4.29
		0.42	3.80	3.05	4.88
g215	rPhl p5b	2.83	2.36	2.45	3.40
		0.33	4.50	2.19	5.00

Allergen Group: **Birch**

Allergen	Component Number	Mean (kU _A /l)	Between Days CV%	Within run CV%	Total CV%
t215	rBet v 1 PR-10	3.29	3.15	2.85	4.25
		0.32	3.57	2.69	4.47
t216	rBet v 2 Profilin	2.63	3.29	2.60	4.19
		0.40	3.07	2.81	4.16
t220	rBet v4	1.79	4.07	2.31	4.68
		0.43	5.76	3.93	6.98
t225	rBet v6	1.73	3.15	2.29	3.89
		0.34	3.15	5.98	6.76

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: **Hazel nut**

Allergen (Component number)	Lot	Sample				
		Positive 1		Positive 2		Negative
		Mean (kU _A /l)	CV (%)	Mean (kU _A /l)	CV (%)	Mean (kU _A /l)
rCor a 8 (f425)	1	1.83	2.5	0.34	1.6	<0.1
	2	1.97	5.0	0.36	1.3	<0.1
	3	2.14	5.4	0.36	1.9	<0.1
rCor a 1, PR-10 (f428)	1	2.08	2.5	0.36	3.0	<0.1
	2	1.84	2.3	0.33	2.4	<0.1
	3	2.24	3.1	0.38	2.1	<0.1

Allergen Group: **Timothy**

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

Allergen (Component number)	Lot	Sample				
		Positive 1		Positive 2		Negative
		Mean (kU _A /l)	CV (%)	Mean (kU _A /l)	CV (%)	Mean (kU _A /l)
rPhl p1 (g205)	1	2.16	5.4	0.31	5.0	<0.1
	2	1.81	2.5	0.31	2.5	<0.1
	3	1.91	3.0	0.33	2.4	<0.1
rPhl p2 (g206)	1	2.47	1.8	0.35	2.4	<0.1
	2	2.60	3.8	0.35	2.6	<0.1
	3	2.52	4.7	0.33	2.2	<0.1
rPhl p6 (g209)	1	1.71	2.2	0.27	2.8	<0.1
	2	1.84	1.8	0.32	2.6	<0.1
	3	1.70	1.9	0.27	4.1	<0.1
rPhl p7 (g210)	1	2.88	4.4	0.35	3.2	<0.1
	2	2.80	2.4	0.33	2.7	<0.1
	3	2.78	1.4	0.34	1.9	<0.1
rPhl p12, Profilin (g212)	1	1.66	3.2	0.37	2.2	<0.1
	2	1.93	1.8	0.32	2.6	<0.1
	3	2.24	2.3	0.39	4.8	<0.1
rPhl p5b (g215)	1	2.57	3.1	0.38	3.9	<0.1
	2	2.60	1.4	0.35	1.9	<0.1
	3	2.61	3.6	0.35	3.9	<0.1

Allergen Group: **Birch**

Allergen (Component number)	Lot	Sample				
		Positive 1		Positive 2		Negative
		Mean (kU _A /l)	CV (%)	Mean (kU _A /l)	CV (%)	Mean (kU _A /l)
rBet v 1, PR-10 (t215)	1	3.50	1.0	0.36	1.7	<0.1
	2	3.27	2.0	0.33	1.8	<0.1
	3	3.31	1.5	0.33	1.7	<0.1
rBet v2, Profilin (t216)	1	2.36	2.1	0.35	2.4	<0.1
	2	2.51	3.1	0.40	2.0	<0.1
	3	2.42	2.1	0.40	2.0	<0.1
rBet v 4 (t220)	1	1.86	1.7	0.36	3.2	<0.1
	2	1.73	1.6	0.30	6.6	<0.1
	3	1.71	1.9	0.42	3.8	<0.1
rBet v 6 (t225)	1	1.81	2.0	0.35	1.9	<0.1
	2	1.86	0.9	0.36	2.3	<0.1
	3	1.83	1.3	0.36	2.3	<0.1

b. Linearity/assay reportable range:

The linearity of the 12 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 to 100 kUA/l.

For each allergen, results of 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:

ImmunoCAP Allergen Component	Regression Equation	r ²	95% CI Slope	95% CI Intercept
f425, rCor a 8	y = 0.99x + 0.01	0.98	0.96 – 1.02	-0.01 – 0.03
f428, rCor a 1	y = 1.01x + (-0.03)	1.00	1.01 – 1.02	-0.04 – (-0.02)
g205, rPhl p 1	y = 1.00x + 0.02	1.00	0.99 – 1.00	0.01 – 0.02
g206, rPhl p 2	y = 0.99x + 0.04	1.00	0.98 – 0.99	0.03 – 0.04
g209, rPhl p 6	y = 1.02x + (-0.01)	1.00	1.01 – 1.03	-0.02 – 0.00
g210, rPhl p 7	y = 1.00x + 0.02	0.99	0.99 – 1.02	0.00 – 0.03
g212, rPhl p 12	y = 0.95x + 0.08	1.00	0.94 – 0.96	0.07 – 0.09
g215, rPhl p 5b	y = 1.01x + (-0.03)	1.00	1.01 – 1.02	-0.04 – (-0.02)
t215, rBet v 1	y = 0.99x + 0.02	1.00	0.99 – 1.00	0.02 – 0.03
t216, rBet v 2	y = 0.94x + 0.07	1.00	0.94 – 0.95	0.07 – 0.08
t220, rBet v 4	y = 0.99x + 0.04	1.00	0.97 – 1.00	0.03 – 0.05
t225, rBet v 6	y = 1.01x	1.00	1.00 – 1.01	-0.01 – 0.00

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).

Stability

Real-time stability - study results were available for Hazel Nut (f425, f428); Timothy (g205, g206, g209, g210, g212, g215) and Birch allergens (t215, t216, t220, t225) 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, three lots of each component allergen were stored at 2-8°C. At different time intervals (0, 3, 6, 13 months), a positive and a negative human 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. The study is on-going.

Accelerated stability - studies performed on allergen components Hazel Nut (f425, f428); Timothy (g205, g206, g209, g210, g212, g215) and Birch allergens (t215, t216, t220, t225) 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 for 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) and 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.

Allergen Group	Allergen component	LoB	LoD
Hazel Nut	f425	0.029	0.039
	f428	0.023	0.043
Timothy	g205	0.008	0.025
	g206	0.004	0.015
	g209	0.008	0.019
	g210	0.004	0.010
	g212	0.017	0.026
	g215	0.015	0.026
Birch	t215	0.013	0.022
	t216	0.014	0.024
	t220	0.013	0.021
	t225	0.008	0.013

e. *Analytical specificity:*

Specificity of each allergen was verified through competitive inhibition studies in accordance with CLSI I/LA20-A2. 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.

The allergen solution was serially diluted with buffer to show an overall dose dependent inhibition. The unrelated allergen solutions are not further diluted.

Equal volumes of a positive sample and varying dilutions of allergen solution (inhibitor) were premixed. The mixture was incubated in a sample tube at room temperature for 1 hour before being analyzed with the corresponding ImmunoCAP Allergen Component on ImmunoCAP instrument according to the manufacturer's instructions. The testing was performed in duplicates in one assay run. Mean values were calculated.

The inhibition test was evaluated with inhibition values in %, calculated according to the formula below:

$$\left(1 - \left(\frac{r - b}{t - b}\right)\right) \times 100 = i\%$$

r = response [RU]

b = background response (100% inhibition) [RU]

t = total response (0% inhibition) [RU]

i = inhibition

Any negative inhibition %-values are shown as 0% inhibition.

Inhibition studies should show an overall dose dependent decrease of free specific IgE antibodies available to bind to the ImmunoCAP Allergen Component resulting in a decrease in measured response, resulting in at least a 50% decrease of the measured response. At a much higher concentration (about 10 fold), the unrelated inhibitors should not show any appreciable inhibition.

The results of the inhibition with the allergen solution and the unrelated inhibitors indicate that the 12 new allergens contain the immunologically relevant allergen as shown below:

Allergen Group: Hazel nut

rCor a 8 (f425), Hazel nut

The rCor a 8 allergen Inhibition study showed that 50% inhibition was achieved with related inhibitor (rCor a 8 allergen) at final inhibitor concentration ~5 µg/mL. The three unrelated inhibitor did not show any significant inhibition at 500 µg/mL.

rCor a 1, PR-10 (f428), Hazel nut

The rCor a 1, PR-10 allergen Inhibition study showed that 50% inhibition was achieved with related inhibitor (rCor a 1, PR-10) at final inhibitor concentration ~50 ng/mL. The three unrelated inhibitor did not show any significant inhibition at 500 µg/mL.

Allergen Group: Timothy

rPhl p 1 (g205), Timothy

The rPhl p 1 allergen Inhibition study showed that 50% inhibition was achieved with related inhibitor (rPhl p 1) at final inhibitor concentration ~50 ng/mL. The three unrelated inhibitor did not show any significant inhibition at 140 µg/mL.

rPhl p 2 (g206), Timothy

The rPhl p 2 allergen Inhibition study showed that 50% inhibition was achieved with related inhibitor (rPhl p 2) at final inhibitor concentration ~50 ng/mL. The three unrelated inhibitor did not show any significant inhibition at 500 µg/mL.

rPhl p 6 (g209), Timothy

The rPhl p 6 allergen Inhibition study showed that 50% inhibition was achieved with related inhibitor (rPhl p 6 allergen) at final inhibitor concentration ~5 µg/mL. The three unrelated inhibitor did not show any significant inhibition at 140 µg/mL.

rPhl p 7 (g210), Timothy

The rPhl p 7 allergen Inhibition study showed that 50% inhibition was achieved with related inhibitor (rPhl p 7 allergen) at final inhibitor concentration ~50 ng/mL. The three unrelated inhibitor did not show any significant inhibition at 500 µg/mL.

rPhl p 12, Profilin (g212), Timothy

The rPhl p 12, Profilin allergen Inhibition study showed that 50% inhibition was achieved with related inhibitor (rPhl p 12, Profilin allergen) at final inhibitor concentration ~5 µg/mL. The three unrelated inhibitor did not show any significant inhibition at 500 µg/mL.

rPhl p 5b (g215), Timothy

The rPhl p 5b allergen Inhibition study showed that 50% inhibition was achieved with related inhibitor (rPhl p 5b_ allergen) at final inhibitor concentration ~50 ng/mL. The three unrelated inhibitor did not show any significant inhibition at 140 µg/mL.

Allergen Group: Birch

rBet v 1, PR-10 (t215), Birch

The rBet v 1, PR-10 allergen Inhibition study showed that 50% inhibition was achieved with related inhibitor (rBet v 1, PR-10_ allergen) at final inhibitor concentration ~50 ng/mL. The three unrelated inhibitor did not show any significant inhibition at 500 µg/mL.

rBet v 2, Profilin (t216), Birch

The rBet v 2, Profilin allergen Inhibition study showed that 50% inhibition was achieved with related inhibitor (rBet v 2, Profilin allergen) at final inhibitor concentration ~5 µg/mL. The three unrelated inhibitor did not show any significant inhibition at 140 µg/mL.

rBet v 4 (t220), Birch

The rBet v 4 allergen Inhibition study showed that 50% inhibition was achieved with related inhibitor (rBet v 4_ allergen) at final inhibitor concentration ~50 ng/mL. The three unrelated inhibitor did not show any significant inhibition at 220 µg/mL.

rBet v 6 (t225), Birch

The rBet v 6 allergen Inhibition study showed that 50% inhibition was achieved with related inhibitor (rBet v 6 allergen) at final inhibitor concentration ~50 ng/mL. The three unrelated inhibitor did not show any significant inhibition at 220 µg/mL.

- f. *Assay cut-off:*
Not applicable
2. Comparison studies:
 - a. *Method comparison with predicate device:*
Refer to clinical studies.
 - b. *Matrix comparison:*
Serum, sodium heparin plasma, and EDTA plasma samples were collected from four patients with clinical history of known specific allergies and four nonatopic patients. These samples were tested with the ImmunoCap allergen components. This resulted in a range of results (negative and positive) within each sample. All positive heparin plasma and EDTA plasma samples (≥ 0.35 kU_A/L) demonstrated acceptable %recovery with the relevant allergens. This study suggests that the three sample matrices are interchangeable.
3. Clinical studies:
 - a. *Clinical sensitivity and Specificity:*
The performance of all 12 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.

Hazel nut:

ImmunoCAP Allergen f425, rCor a 8

		Clinical Diagnosis		
		Atopic	Non-atopic	Total
rCor a 8 (f425)	Positive	55	0	55
	Negative	0	100	100
	Total	55	100	155

Sensitivity =100% (95% CI: 93.5 – 100%)

Specificity =100%

ImmunoCAP Allergen f428, rCor a 1, PR-10

		Clinical Diagnosis		
		Atopic	Non-atopic	Total
<i>rCor a 1,</i> <i>PR-10</i> <i>(f428)</i>	Positive	70	0	70
	Negative	0	100	100
	Total	70	100	170

Sensitivity =100% (95% CI: 94.9 – 100%)

Specificity =100%

Timothy:

ImmunoCAP Allergen g205, rPhl p 1

		Clinical Diagnosis		
		Atopic	Non-atopic	Total
<i>rPhl p 1</i> <i>(g205)</i>	Positive	85	0	85
	Negative	0	100	100
	Total	85	100	185

Sensitivity =100% (95% CI: 95.8 – 100%)

Specificity =100%

ImmunoCAP Allergen g206, rPhl p 2

		Clinical Diagnosis		
		Atopic	Non-atopic	Total
<i>rPhl p 2</i> (g206)	Positive	47	0	47
	Negative	0	100	100
	Total	47	100	147

Sensitivity =100% (95% CI: 92.5 – 100%)

Specificity =100%

ImmunoCAP Allergen g209, rPhl p 6

		Clinical Diagnosis		
		Atopic	Non-atopic	Total
<i>rPhl p 6</i> (g209)	Positive	61	0	61
	Negative	0	100	100
	Total	61	100	161

Sensitivity =100% (95% CI: 94.1 – 100%)

Specificity =100%

ImmunoCAP Allergen g210, rPhl p 7

		Clinical Diagnosis		
		Atopic	Non-atopic	Total
<i>rPhl p 7</i> (g210)	Positive	21	0	21
	Negative	9	100	109
	Total	30	100	130

Sensitivity = 70% (95% CI: 50.6 – 85.3%)

Specificity =100%

ImmunoCAP Allergen g212, rPhl p 12, Profilin

		Clinical Diagnosis		
		Atopic	Non-atopic	Total
<i>rPhl p 12,</i> <i>Profilin</i> (g212)	Positive	34	0	34
	Negative	0	100	100
	Total	34	100	134

Sensitivity =100% (95% CI: 89.7 – 100%)

Specificity =100%

ImmunoCAP Allergen g215, rPhl p 5b

		Clinical Diagnosis		
		Atopic	Non-atopic	Total
<i>rPhl p 5b</i> (g215)	Positive	67	0	67
	Negative	0	100	100
	Total	67	100	167

Sensitivity =100% (95% CI: 94.6 – 100%)

Specificity =100%

Birch:

ImmunoCAP Allergen t215, rBet v 1, PR-10

		Clinical Diagnosis		
		Atopic	Non-atopic	Total
<i>rBet v 1, PR-10 (t215)</i>	Positive	94	0	94
	Negative	0	100	100
	Total	94	100	194

Sensitivity =100% (95% CI: 96.2 – 100.0%)

Specificity =100%

ImmunoCAP Allergen t216, rBet v 2, Profilin

		Clinical Diagnosis		
		Atopic	Non-atopic	Total
<i>rBet v 2, Profilin (t216)</i>	Positive	39	0	39
	Negative	0	100	100
	Total	39	100	139

Sensitivity =100% (95% CI: 06.2 – 100%)

Specificity =100%

ImmunoCAP Allergen t220, rBet v 4

		Clinical Diagnosis		
		Atopic	Non-atopic	Total
<i>rBet v 4 (t220)</i>	Positive	28	0	28
	Negative	2	100	102
	Total	30	100	130

Sensitivity =93% (95% CI: 77.9 – 99.2%)

Specificity =100%

ImmunoCAP Allergen t225, rBet v 6

		Clinical Diagnosis		
		Atopic	Non-atopic	Total
<i>rBet v 6 (t225)</i>	Positive	24	0	24
	Negative	6	100	106
	Total	30	100	130

Sensitivity =80% (95% CI: 61.4 – 92.3%)

Specificity =100%

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

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

Not applicable

4. Clinical cut-off:

Not applicable

5. Expected values/Reference range:

The expected value is negative (< 0.35 kU_A/L) for a specific allergen in a non-allergic person.

The manufacturer recommends a cut-off of 0.35 kU_A/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.