

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

A. 510(k) Number:

k122197

B. Purpose for Submission:

Addition of 6 new recombinant allergens and 4 purified native allergens to a cleared device

C. Measurand:

Ten new allergen-specific IgE analytes: e101, rCan f 1 (Dog); e102, rCan f 2 (Dog); e221, nCan f 3 (Dog serum albumin); e226, rCan f 5 (Dog); f353, rGly m 4 PR-10 (Soy); f431, nGly m 5 Beta-conglycinin (Soy); f432, nGly m 6 Glycinin (Soy); t224, rOle e 1 (Olive); t227, nOle e 7 LTP (Olive); t240 rOle e 9 (Olive)

D. Type of Test:

Fluoroenzymeimmunoassay, Quantitative

E. Applicant:

Phadia AB

F. Proprietary and Established Names:

ImmunoCAP Specific IgE

ImmunoCAP Allergen e101, Allergen Component rCan f 1, Dog

ImmunoCAP Allergen e102, Allergen Component rCan f 2, Dog

ImmunoCAP Allergen e221, Allergen component nCan f 3, Dog serum albumin

ImmunoCAP Allergen e226, Allergen component rCan f 5, Dog

ImmunoCAP Allergen f353, Allergen component rGly m 4 PR-10, Soy

ImmunoCAP Allergen f431, Allergen component nGly m 5 Beta-conglycinin, Soy

ImmunoCAP Allergen f432, Allergen component nGly m 6 Glycinin, Soy

ImmunoCAP Allergen t224, Allergen component rOle e 1, Olive

ImmunoCAP Allergen t227, Allergen component nOle e 7 LTP, Olive

ImmunoCAP Allergen t240, Allergen component rOle e 9, Olive

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 (EDTA or Na-Heparin). ImmunoCAP Specific IgE is to be used with instruments Phadia 100, Phadia 250, Phadia 1000, Phadia 2500 and Phadia 5000. 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:

Phadia 100, Phadia 250, Phadia 1000, Phadia 2500 and Phadia 5000

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 (EDTA or Na-Heparin) sample. It is comprised of general, test and method specific reagents for Phadia 100, Phadia 250, Phadia 1000, Phadia 2500 and Phadia 5000 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 Predicate 510(k) number(s):

UniCAP[®] Specific IgE Assay and UniCAP[®] Specific IgE Conjugate 100 and 400 (k051218)

UniCAP Specific IgE Assay (k962274)

2. Comparison with predicate:

Similarities		
Item	Device	Predicate
Intended Use	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	Same

Similarities		
Item	Device	Predicate
	clinical diagnosis of IgE mediated allergic disorders in conjunction with other clinical findings and to be used in clinical laboratories.	
Assay type	Quantitative	Same
Basic principle	Fluoroenzymeimmunoassay	Same
Antibody	β -Galactosidase-anti-human IgE (mouse monoclonal antibody) for all ImmunoCAP	Same
Specimen type	Serum and plasma (EDTA and Na Heparin)	Same
Sample volume	40 μ L	Same
Number of calibrators	Six	Same
Process time	Phadia 100: 2 hrs 30 min. Phadia 250, Phadia 1000, Phadia 2500 and Phadia 5000: 1 hour 45 minutes from entering the first sample.	Same
Incubation temperature	37°C - for all Phadia instruments	Same

Differences		
Item	Device	Predicate
Form of allergens	Recombinant proteins and purified whole native proteins	Purified native allergens
Allergens	Individual recombinant proteins: e 101, rCan f 1 (Dog); e102, rCan f 2 (Dog); e226, rCan f 5 (Dog); f353, rGly m 4 PR-10 (Soy); t224, rOle e 1 (Olive); tt240, rOle e 9 (Olive) Whole allergens comprising multiple proteins from purified native allergen source: e221, nCan f 3 (Dog serum albumin); f431, nGly m 5 Beta-conglycinin (Soy); f432, nGly m 6 Glycinin (Soy); t227, nOle e 7 LTP (Olive)	Not included
Sample matrix	Serum and plasma (EDTA or sodium heparin)	Serum and plasma (sodium heparin)
Laboratory settings	Clinical laboratories	Clinical laboratories and physician office

Differences		
Item	Device	Predicate
		laboratories.
Instruments	Phadia 100, Phadia 250, Phadia 1000, Phadia 2500 and Phadia 5000	UniCAP 100
Built-in Software versions	Phadia 100: 2.34 Phadia 250: 2.20 Phadia 1000: 2.30 Phadia 2500: 1.30 Phadia 5000: 1.30 Phadia Information Data Manager (IDM): 5.34	Not available

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

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

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

CLSI I/LA20-A2: Analytical Performance Characteristics and Clinical Utility of Immunological Assays for Human Immunoglobulin E (IgE) Antibodies and Defined Allergy Specificities; Approved Guidelines – Second Edition.

CEN 13640: 2002 Stability Testing of *in vitro* Diagnostic Reagents

L. Test Principle:

The allergen of interest, covalently coupled to ImmunoCAP solid phase, reacts with the specific IgE in the patient sample. After washing away non-specific IgE, enzyme-labeled anti-IgE antibodies are added to form a complex. After incubation, unbound enzyme-anti-IgE is washed away and the bound complex is then incubated with a developing agent. After stopping the reaction, the fluorescence of the eluate is measured. The higher the response value, the more specific IgE is present in the specimen. To evaluate the test results, the responses 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:*

i) *Within-Lot imprecision:*

Imprecision of the individual allergen components was evaluated by using two positive plasma samples, including a low range sample ($0.35 \pm 25\%$) and a high range sample (≥ 0.7 kU_A/L). Each sample was tested in 4 replicates in 1 assay run per day for a total of 20 operating days (a total of 80 replicates per sample). The assay was performed according to the ImmunoCAP Specific IgE Directions for

Use using Phadia 250. Between-day and within-run coefficients of variance (%CV) were calculated for each component and each sample separately. Results of CV% values for individual allergen components are shown below:

Allergen component	Sample	Number of tests	Mean (kU /l)	CV% Between Run	CV% Within Run	CV% Total
e101, rCan f 1 (Dog)	46441	80	2.33	3.11	2.47	3.97
	62849	80	0.36	4.36	2.10	4.84
e102, rCan f 2 (Dog)	29709	80	2.25	3.50	4.05	5.35
	62850	80	0.37	4.36	2.77	5.16
e221, nCan f 3 Dog serum albumin	37678	80	2.67	3.29	3.58	4.86
	62968	80	0.39	4.42	2.82	5.25
e226, rCan f 5 (Dog)	58563	80	1.70	3.81	3.06	4.89
	62847	80	0.35	3.86	2.57	4.64
f353, rGly m 4 PR-10 (Soy)	43293	80	2.65	3.41	3.08	4.60
	62972	80	0.37	4.55	2.94	5.42
f431, nGly m 5 β -conglycinin (Soy)	35585	80	2.71	3.58	2.66	4.45
	62974	80	0.38	5.17	3.90	6.48
f432, nGly m 6 Glycinin (Soy)	27640	80	2.20	4.11	4.75	6.28
	62969	80	0.35	4.09	2.22	4.65
t224, rOle e 1 (Olive)	44343	80	1.99	4.60	2.55	5.26
	62971	80	0.33	4.68	2.22	5.18
t227, nOle e 7 LTP (Olive)	34243	80	4.58	4.07	3.66	5.47
	62973	80	0.38	4.96	2.55	5.58
t240, rOle e 9 (Olive)	19957	80	1.68	4.59	4.12	6.16
	62975	80	0.39	4.37	2.19	4.89

Results of pooled CV% values for individual allergens:

Test	Number of samples n	CV% Between run	CV% Within run	CV% Total
e101	2	3.78	2.29	4.42
e102	2	3.95	3.47	5.26
e221	2	3.90	3.22	5.06
e226	2	3.84	2.82	4.76
f353	2	4.02	3.01	5.03
f431	2	4.45	3.34	5.56
f432	2	4.10	3.71	5.53
t224	2	4.64	2.39	5.22
t227	2	4.53	3.15	5.52

t240	2	4.48	3.30	5.56
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ii) *Lot-to-lot imprecision:*

For each allergen, three different ImmunoCAP Allergen Component lots were tested using two positive plasma samples ($0.35 \pm 25\%$ and ≥ 0.7 kU_A/L) and one negative plasma 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. The assay was performed according to the ImmunoCAP Specific IgE, Directions for Use using Phadia 250. Mean concentration values, %CV and concentration quotients between lots were calculated for the positive samples.

Lot	Positive 1		Positive 2		Negative	Concentration Quotient		
	Mean (kU _A /L)	CV (%)	Mean (kU _A /L)	CV (%)	Mean (kU _A /L)		Positive 1	Positive 2
ImmunoCAP Allergen, e101, rCan f 1, (Dog)								
1	2.45	1.9	0.37	1.8	<0.1	lot1/lot2	1.04	1.05
2	2.36	2.6	0.35	1.7	<0.1	lot1/lot3	1.13	1.12
3	2.17	5.5	0.33	3.6	<0.1	lot2/lot3	1.09	1.07
ImmunoCAP Allergen, e102, rCan f 2, (Dog)								
1	2.56	2.0	0.46	2.4	<0.1	lot1/lot2	1.04	1.07
2	2.47	1.8	0.43	1.8	<0.1	lot1/lot3	1.10	1.22
3	2.33	5.3	0.37	1.6	<0.1	lot2/lot3	1.06	1.14
ImmunoCAP Allergen, e221, nCan f 3 (Dog serum albumin)								
1	2.64	1.3	0.38	1.9	<0.1	lot1/lot2	0.91	0.92
2	2.90	2.1	0.41	1.3	<0.1	lot1/lot3	1.00	1.00
3	2.65	1.6	0.38	2.2	<0.1	lot2/lot3	1.09	1.09
ImmunoCAP Allergen, e226, rCan f 5 (Dog)								
1	1.75	2.6	0.37	3.3	<0.1	lot1/lot2	0.94	0.94
2	1.85	1.1	0.39	1.4	<0.1	lot1/lot3	0.92	0.94
3	1.90	3.5	0.39	3.4	<0.1	lot2/lot3	0.97	1.01
ImmunoCAP Allergen, f353, rGly m 4 PR-10 (Soy)								
1	2.51	2.9	0.35	2.5	<0.1	lot1/lot2	1.00	0.99
2	2.52	2.5	0.35	2.7	<0.1	lot1/lot3	0.99	0.97
3	2.53	3.7	0.36	2.0	<0.1	lot2/lot3	1.00	0.98
ImmunoCAP Allergen, f431, nGly m 5 Beta-conglycinin (Soy)								
1	2.72	2.7	0.36	1.9	<0.1	lot1/lot2	0.99	0.98
2	2.75	2.9	0.37	6.2	<0.1	lot1/lot3	1.03	0.94
3	2.65	1.7	0.38	1.9	<0.1	lot2/lot3	1.04	0.95
ImmunoCAP Allergen, f432, nGly m 6 Glycinin (Soy)								
1	2.23	1.8	0.37	1.9	<0.1	lot1/lot2	0.99	0.99

Lot	Positive 1		Positive 2		Negative	Concentration Quotient		
	Mean (kU _A /L)	CV (%)	Mean (kU _A /L)	CV (%)	Mean (kU _A /L)		Positive 1	Positive 2
2	2.26	4.9	0.37	1.8	<0.1	lot1/lot3	1.09	1.00
3	2.06	5.1	0.37	3.1	<0.1	lot2/lot3	1.10	1.02
ImmunoCAP Allergen, t224, rOle e 1 (Olive)								
1	0.31	2.2	1.43	1.7	<0.1	lot1/lot2	1.00	1.02
2	0.31	2.7	1.40	2.6	<0.1	lot1/lot3	1.00	1.01
3	0.31	2.9	1.41	2.5	<0.1	lot2/lot3	1.00	1.00
ImmunoCAP Allergen, t227, nOle e 7 LTP (Olive)								
1	0.33	1.5	1.00	1.7	<0.1	lot1/lot2	0.89	0.83
2	0.37	2.4	1.21	2.6	<0.1	lot1/lot3	0.87	0.81
3	0.38	2.4	1.24	2.5	<0.1	lot2/lot3	0.98	0.98
ImmunoCAP Allergen, t240, rOle e 9 (Olive)								
1	0.32	4.9	1.05	1.7	<0.1	lot1/lot2	1.03	0.95
2	0.31	8.2	1.10	1.7	<0.1	lot1/lot3	0.95	0.96
3	0.34	10.3	1.09	2.6	<0.1	lot2/lot3	0.92	1.01

b. Linearity/assay reportable range:

The linearity of the 10 individual allergens was assessed following the CLSI I/LA20-A2 guidelines. For each allergen component, three positive plasma samples were each diluted in negative plasma generating 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. ImmunoCAP Specific Total IgE working range is LoD to 100 kU_A/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:

Allergen Component	Regression Equation	r ²	95% CI Slope	95% CI Intercept	Highest concentration tested (kU _A /L)
e101	y=0.99x+0.01	1.00	0.98-1.00	0.00-0.02	74.1
e102	y=1.01x-0.01	1.00	1.01-1.02	-0.02-(-0.01)	36.5
e221	y=0.99x	1.00	0.98-1.00	-0.01-0.01	77.6
e226	y=1.04x-0.10	1.00	1.03-1.05	-0.01-(-0.09)	92.7
f353	y=1.01x	1.00	1.00-1.01	-0.01-0.00	77.7
f431	y=0.98x+0.03	1.00	0.97-0.99	0.03-0.04	26.4
f432	y=0.98x+0.05	1.00	0.97-0.99	0.04-0.06	82.0
t224	y=0.99x+0.04	1.00	0.98-1.00	0.04-0.05	74.6

Allergen Component	Regression Equation	r ²	95% CI Slope	95% CI Intercept	Highest concentration tested (kU _A /L)
t227	y=1.05x-0.07	1.00	1.05-1.06	-0.07-(-0.07)	36.5
t240	y=0.99x+0.02	1.00	0.98-0.99	0.01-0.02	30.5

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

i) *Traceability:*

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).

ii) *Kit Stability:*

Real-time and Accelerated stability: The stability studies were performed in accordance with EN 13640 (Stability Testing of *In Vitro* Diagnostic Reagents) to demonstrate 24 month unopened shelf-life stability (at recommended storage temperature of 2-8°C) of the ImmunoCAP Allergen e101, rCan f 1 (Dog); e1, rCan f 2 (Dog); e221, nCan f 3 (Dog serum albumin); e226, rCan f 5 (Dog); f353, rGly m 4 PR-10 (Soy); f431, nGly m 5 Beta-conglycinin (Soy); f432, nGly m 6 Glycinin (Soy); t224, rOle e 1 (Olive); t227, nOle e 7 LTP (Olive); t240, rOle e 9 (Olive) by an on-going real time stability study and accelerated stability study. For real time stability study, three lots of each ImmunoCAP Allergen Components were stored at recommended storage temperature, 2-8 °C. Two positive plasma samples and one negative plasma sample were tested at different occasions according to the ImmunoCAP Specific IgE, Directions for Use, using Phadia 250. The study is ongoing. For accelerated study, three lots of ImmunoCAP Allergen Components were stored at 30°C for 8 weeks or 4 weeks at 40°C. The same lots stored at 2-8 °C was used as reference. They were tested after 4 and 8 weeks when stored in 30 °C and after 2 and 4 weeks when stored at 40°C, using two positive plasma samples and one negative plasma sample. The results support the manufacture's claim of 24 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 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: $LoD = LoB + c\beta \cdot SD$ where SD, the standard deviation, was based on 20 determinations of 3 low positive samples, in total 60 determinations. The results are shown in the table below.

Allergen component	LoB	LoD
e101	0.006	0.014
e102	0.003	0.010
e221	0.000	0.009
e226	0.021	0.027
f353	0.000	0.010
f431	0.011	0.022
f432	0.000	0.014
t224	0.010	0.018
t227	0.000	0.004
t240	0.007	0.016

e. *Analytical specificity:*

i) *Inhibition studies:*

Immunological specificity of the allergen components was verified through competitive inhibition. The studies were planned in accordance with CLSI I/LA20-A2. The specific IgE concentration for the positive samples is shown in the table below.

Allergen component	kU _A /L
e101, rCan f 1	4.9
e102, rCan f 2	4.2
e221, rCan f 3	7.7
e226, rCan f 5	3.3
f353, rGly m 4	6.1
f431, nGly m 5	7.7
f432, nGly m 6	7.7
t224, rOle e 1	4.4
t227, nOle e 7	9.2
t240, nOle e 9	11.1

The allergen solution was serially diluted with buffer to show an overall dose dependent inhibition. 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:

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

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.

The results of the inhibition with the allergen solution and the unrelated inhibitors indicate that the 10 new allergens contain the immunologically relevant allergen as shown below:

ImmunoCAP Allergen e101, rCan f 1 (Dog)

The e101, rCan f 1 (Dog) allergen Inhibition study showed that >50% inhibition was achieved with related inhibitor (e101, rCan f 1, Dog allergen) at a final inhibitor concentration of 5 µg/mL. The inhibition studies using four unrelated inhibitors, including three from unrelated groups (r Hev b 6.01, Latex; rBet v 2, Birch; and rPru p 1, Peach) and one from the related/same group (rCan f5, Dog) did not show any significant inhibition. The inhibition studies indicate that the ImmunoCAP Allergen e101, rCan f 1 (Dog) solid phase contains the immunologically relevant allergen.

ImmunoCAP Allergen e102, rCan f 2 (Dog)

The e102, rCan f 2 (Dog) allergen Inhibition study showed that >50% inhibition was achieved with related inhibitor (e102, rCan f 2, Dog allergen) at a final inhibitor concentration of 5 µg/mL. The inhibition studies using four unrelated inhibitors, including three from unrelated groups (rHev b 6.01, Latex; rBet v 2, Birch; and rPen a 1, Shrimp) and one from the related/same group (rCan f5, Dog) did not show any significant inhibition. The inhibition studies indicate that the ImmunoCAP Allergen e102, rCan f 2 (Dog) solid phase contains the immunologically relevant allergen.

ImmunoCAP Allergen e221, nCan f 3 (Dog serum albumin)

The e221, rCan f 3 (Dog serum albumin) allergen Inhibition study showed that >50% inhibition was achieved with related inhibitor (e221, rCan f 3, Dog serum albumin allergen) at a final inhibitor concentration of 5 µg/mL. The inhibition studies using four unrelated inhibitors, including three from unrelated groups (rPru p 1, Peach; rPhl 5b, Timothy; and rBet v 2, Birch) and one from the related/same group (rCan f5, Dog) did not show any significant inhibition. The inhibition studies indicate that the ImmunoCAP Allergen e221, nCan f 3 (Dog serum albumin) solid phase contains the immunologically relevant allergen.

ImmunoCAP Allergen e226, rCan f 5 (Dog)

The e226, rCan f 5 (Dog) allergen Inhibition study showed that >50% inhibition was achieved with related inhibitor (e226, rCan f 5 (Dog) allergen) at a final

inhibitor concentration of 5 µg/mL. The inhibition studies using four unrelated inhibitors, including three from unrelated groups (nCyn d 1, Bermuda grass; rBet v 1, Birch; and rDer p 2, House dust mite) and one from the related/same group (rCan f3, Dog) did not show any significant inhibition. The inhibition studies indicate that the ImmunoCAP Allergen e226, rCan f 5 (Dog) solid phase contains the immunologically relevant allergen.

ImmunoCAP Allergen f353, rGly m 4 PR-10 (Soy)

The f353, rGly m 4 PR-10 (Soy) allergen Inhibition study showed that 94% inhibition was achieved with related inhibitor (f353, rGly m 4 PR-10 (Soy)) at a final inhibitor concentration of 500 µg/mL. The inhibition studies using five unrelated inhibitors, including three from unrelated groups (rPhl p 7, Timothy; rFel d 1, Cat; and rHev b 6.01, Latex) and two from the related/same group: f346 (Abalone) and f233 nGal d 1 (Egg) did not show any significant inhibition. The inhibition studies indicate that the ImmunoCAP Allergen f353, rGly m 4 PR-10 (Soy) solid phase contains the immunologically relevant allergen.

ImmunoCAP Allergen f431, nGly m 5 Beta-conglycinin (Soy)

The f431, nGly m 5 Beta-conglycinin (Soy) allergen Inhibition study showed that >50% inhibition was achieved with related inhibitor (f431, nGly m 5 Beta-conglycinin (Soy)) at a final inhibitor concentration of 5 µg/mL. The inhibition studies using four unrelated inhibitors, including three from unrelated groups (rFel d 1, Cat; rPhl p1, Timothy; and nGal d 4, Egg) and one from the related/same group (rGly m4, Soy) did not show any significant inhibition. The inhibition studies indicate that the ImmunoCAP Allergen f431, nGly m 5 Beta-conglycinin (Soy) solid phase contains the immunologically relevant allergen.

ImmunoCAP Allergen f432, nGly m 6 Glycinin (Soy)

The f432, nGly m 6 Glycinin (Soy) allergen Inhibition study showed that 86% inhibition was achieved with related inhibitor (f432, nGly m 6 Glycinin (Soy)) at a final inhibitor concentration of 500 µg/mL. The inhibition studies using five unrelated inhibitors, including three from unrelated groups (rFel d 1, Cat; rPhl p1, Timothy; and d74, Storage mite) and two from the related/same group: f346 (Abalone) and f233 nGal d 1 (Egg) did not show any significant inhibition. The inhibition studies indicate that the ImmunoCAP Allergen f432, nGly m 6 Glycinin (Soy) solid phase contains the immunologically relevant allergen.

ImmunoCAP Allergen t224, rOle e 1 (Olive)

The t224, rOle e 1 (Olive) allergen Inhibition study showed that >50% inhibition was achieved with related inhibitor (t224, rOle e 1 (Olive) allergen) at a final inhibitor concentration of 5 µg/mL. The inhibition studies using four unrelated inhibitors, including three from unrelated groups (rCan f 1, Dog; nCyn d 1, Bermuda grass; and rDer p 2, House dust mite) and one from the related/same group (rOle e 9, Olive) did not show any significant inhibition. The inhibition studies indicate that the ImmunoCAP Allergen t224, rOle e 1 (Olive) solid phase contains the immunologically relevant allergen.

ImmunoCAP Allergen t227, nOle e 7 LTP (Olive)

The t227, nOle e 7 LTP (Olive) allergen Inhibition study showed that >50%

inhibition was achieved with related inhibitor (t227, nOle e 7 LTP (Olive) allergen) at a final inhibitor concentration of 5 µg/mL. The inhibition studies using four unrelated inhibitors, including three from unrelated groups (nGal d 3, Egg, r Hev b 6.01, Latex, and rDer p 2, House dust mite) and one from the related/same group (rOle e 1, Olive) did not show any significant inhibition. The inhibition studies indicate that the ImmunoCAP Allergen t227, nOle e 7 LTP (Olive) solid phase contains the immunologically relevant allergen.

ImmunoCAP Allergen t240, rOle e 9 (Olive)

The t240, rOle e 9 (Olive) allergen Inhibition study showed that >50% inhibition was achieved with related inhibitor (t240, rOle e 9 (Olive) allergen) at a final inhibitor concentration of 5 µg/mL. The inhibition studies using four unrelated inhibitors, including three from unrelated groups (nGal d 3, Egg; r Hev b 6.01, Latex; and rDer p 2, House dust mite) and one from the related/same group (rOle e 1, Olive) did not show any significant inhibition. The inhibition studies indicate that the ImmunoCAP Allergen t240, rOle e 9 (Olive) solid phase contains the immunologically relevant allergen.

ii) *Interference:*

a) *Endogenous Substance Interference:*

In order to show that icteric, hemolytic or lipemic samples do not adversely affects the results in ImmunoCAP Specific IgE assay using representative allergens, Bilirubin C [final concentration (fc) 20 mg/dL], Bilirubin F (fc 19 mg/dL), Hemoglobin (fc 489 mg/dL) and Chyle (fc 1,440 Formazine Turbidity Units) were spiked into 2 samples per allergen. The allergens tested were e228 rFel d 4, Cat; f351 rPen a 1, Tropomyosin Shrimp; f354 rBer e 1, Brazil nut; f420 rPru p 3, LTP Peach; and w231 nArt v 1, Mugwort. The design of the studies was in general alignment with CLSI EP7-A2 Guideline. The results demonstrate that icteric, hemolytic or lipemic samples do not adversely affects the results in ImmunoCAP Specific IgE.

b) *Exogenous Substance Interference:*

Two literature references were provided supporting that commonly prescribed "allergy medications" do not interfere with ImmunoCAP Specific IgE. The references included (i) Robert G. Hamilton, Accuracy of US Food and Drug Administration-cleared IgE antibody assays in the presence of anti-IgE (omalizumab), J. Allergy Clin. Immunol. 2006; 759-766, and (ii) Linda Cox et al., Pearls and pitfalls of allergy diagnostic testing: report from the American College of Allergy, Asthma and Immunology/American Academy of Allergy, Asthma and Immunology Specific IgE Test Task Force, Annals of Allergy, Asthma & Immunology, 2008; 101:580-592.

f. *Assay cut-off:*

Limit of Quantitation for ImmunoCAP Specific IgE is 0.1 kU_A/L. All results >0.1 kU_A/L are interpreted as being analytically positive.

2. Comparison studies:

a. *Method comparison with predicate device:*

Refer to clinical studies.

b. *Matrix comparison:*

The "*Proof of Principle*" study that different matrix samples (heparin plasma, EDTA plasma and serum) are interchangeable for ImmunoCAP Allergen Components was provided in k101251. Serum, sodium heparin plasma, and EDTA plasma samples were collected from four patients with clinical history of known specific allergies and four nonatopic patients. The samples contained specific IgE antibodies for one or more of the allergen components tested. All sample matrices (heparin plasma, EDTA plasma and serum) from each patient were tested with ImmunoCAP Allergen Components in 2 replicates in one assay run. Mean concentration values for each sample matrix were calculated. Mean logarithmic ratios for 17 results were -0.022 (Plasma heparin/Serum) and 0.054 (Plasma EDTA/Serum). The results from the study show that samples of different matrices (heparin plasma, EDTA plasma and serum) are interchangeable for ImmunoCAP Allergen Components.

3. Clinical studies:

a. *Clinical Sensitivity and specificity:*

The performance of the ten new individual allergen components was compared to a clinical diagnosis of allergy. The objective of this study was, (i) to show the linkage between specific IgE antibodies to ImmunoCAP Allergen Component and the corresponding extract based ImmunoCAP Allergen, using clinical samples, and (ii) to demonstrate that samples from healthy, non-atopic donors with no reported clinical reaction to the allergen have undetectable or very low levels of specific IgE to the individual ImmunoCAP Allergen Component. Fifty one clinical serum samples from individuals with a clinical history of allergy-like symptoms upon exposure to the allergen, as diagnosed by a physician were used in the study. Information about clinical symptoms and manifestations was available for all clinical samples. 100 negative samples (<0.35 kU_A/L) from healthy non-atopic donors were also tested.

ImmunoCAP Allergen e101, rCan f 1 (Dog)

		Clinical Diagnosis		
		Atopic	Non-atopic	Total
Allergen e101, rCan f 1 (Dog)	Positive	69	0	69
	Negative	0	100	100
	Total	69	100	169

Sensitivity =100% (69/69) (95% CI: 94.8 - 100%)

Specificity =100% (100/100) (95% CI: 96.4 - 100%)

ImmunoCAP Allergen e102, rCan f 2 (Dog)

		Clinical Diagnosis		
		Atopic	Non-atopic	Total
Allergen e102, rCan f 2 (Dog)	Positive	40	0	40
	Negative	0	100	100
	Total	40	100	140

Sensitivity =100% (40/40) (95% CI: 91.2 - 100%)

Specificity =100% (100/100) (95% CI: 96.4 - 100%)

ImmunoCAP Allergen e221, nCan f 3 (Dog serum albumin)

		Clinical Diagnosis		
		Atopic	Non-atopic	Total
Allergen e221, nCan f 3 (Dog serum albumin)	Positive	41	0	41
	Negative	0	100	100
	Total	41	100	141

Sensitivity =100% (41/41) (95% CI: 91.4 - 100%)

Specificity =100% (100/100) (95% CI: 96.4 - 100%)

ImmunoCAP Allergen e226, rCan f 5 (Dog)

		Clinical Diagnosis		
		Atopic	Non-atopic	Total
Allergen e226, rCan f 5 (Dog)	Positive	40	0	40
	Negative	0	100	100
	Total	40	100	140

Sensitivity =100% (40/40) (95% CI: 91.2 - 100%)

Specificity =100% (100/100) (95% CI: 96.4 - 100%)

ImmunoCAP Allergen f353, rGly m 4 PR-10 (Soy)

		Clinical Diagnosis		
		Atopic	Non-atopic	Total
Allergen f353, rGly m 4 PR-10 (Soy)	Positive	30	0	30
	Negative	0	100	100
	Total	30	100	130

Sensitivity =100% (30/30) (95% CI: 88.4 - 100%)

Specificity =100% (100/100) (95% CI: 96.4 - 100.0%)

ImmunoCAP Allergen f431, nGly m 5 Beta-conglycinin (Soy)

		Clinical Diagnosis		
		Atopic	Non-atopic	Total
Allergen f431, nGly m 5 Beta- conglycinin (Soy)	Positive	31	0	31
	Negative	0	100	100
	Total	31	100	131

Sensitivity =100% (31/31) (95% CI: 88.8 - 100%)

Specificity =100% (100/100) (95% CI: 96.4 - 100%)

ImmunoCAP Allergen f432, nGly m 6 Glycinin (Soy)

		Clinical Diagnosis		
		Atopic	Non-atopic	Total
Allergen f432, nGly m 6 Glycinin (Soy)	Positive	35	0	35
	Negative	0	100	100
	Total	35	100	135

Sensitivity =100% (35/35) (95% CI: 90.0 - 100%)

Specificity =100% (100/100) (95% CI: 96.4 - 100%)

ImmunoCAP Allergen t224, rOle e 1 (Olive)

		Clinical Diagnosis		
		Atopic	Non-atopic	Total
Allergen t224, rOle e 1 (Olive)	Positive	34	0	34
	Negative	0	100	100
	Total	34	100	134

Sensitivity =100% (34/34) (95% CI: 89.7 - 100%)

Specificity =100% (100/100) (95% CI: 96.4-100.0%)

ImmunoCAP Allergen t227, nOle e 7 LTP (Olive)

		Clinical Diagnosis		
		Atopic	Non-atopic	Total
Allergen t227, nOle e 7 LTP (Olive)	Positive	31	0	31
	Negative	0	100	100
	Total	31	100	131

Sensitivity =100% (31/31) (95% CI: 88.8 - 100%)

Specificity =100% (100/100) (95% CI: 96.4 - 100%)

ImmunoCAP Allergen t240, rOle e 9 (Olive)

		Clinical Diagnosis		
		Atopic	Non-atopic	Total
Allergen t240, rOle e 9 (Olive)	Positive	36	0	36
	Negative	0	100	100
	Total	36	100	136

Sensitivity =100% (36/36) (95% CI: 90.3 - 100%)

Specificity =100% (100/100) (95% CI: 96.4 - 100%)

All negative samples showed undetectable level (<0.1 kU_A/L) of allergen specific IgE. Studies described above were performed on the Phadia 1000 instrument system.

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. Instrument Name:

Phadia 100, Phadia 250, Phadia 1000, Phadia 2500 and Phadia 5000 instrument system.

O. System Descriptions:

1. Software:

FDA has reviewed applicant's Hazard Analysis and software development processes for this line of product types:

Yes X or No

P. Other Supportive Instrument Performance Characteristics Data Not Covered In The "Performance Characteristics" Section above:

Refer to k101251 for assay Precision study of ImmunoCAP Allergen Components on Phadia 100, Phadia 250 and Phadia 1000.

Q. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

R. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.