

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

A. 510(k) Number:

k092050

B. Purpose for Submission:

New Allergen

C. Measurand:

Allergen specific IgE

D. Type of Test:

Fluoroenzymeimmunoassay, Quantitative and Semi-quantitative

E. Applicant:

Phadia AB

F. Proprietary and Established Names:

ImmunoCAP Allergen d201, House dust mite (*Blomia tropicalis*)

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 Assay 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 the instruments ImmunoCAP 100E, ImmunoCAP 250 and ImmunoCAP 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, as well as physician office laboratories.
2. Indication(s) for use:
Same as Intended Use.
3. Special conditions for use statement(s):
Prescription use only.
4. Special instrument requirements:
ImmunoCAP Specific IgE is to be used with the instrument ImmunoCAP 100, ImmunoCAP 250, and ImmunoCAP 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 ImmunoCAP 100, ImmunoCAP 250 and ImmunoCAP 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, ImmunoCAP Allergen carriers (Single and Multiple), ImmunoCAP Development Solution and Stop Solution.

J. Substantial Equivalence Information:

1. Predicate device name(s):
UniCAP[®] 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
Sample volume	40/μL	Same
Process time	1 hour 45 minutes	Same
Incubation temperature	37°C	Same

Differences		
Item	Device	Predicate
Modification	Addition of new allergen d201, House dust mite (<i>Blomia tropicalis</i>)	Absence of allergen d201, House dust mite (<i>Blomia tropicalis</i>)

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 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 ImmunoCAP, reacts with the specific

IgE in the patient 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 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 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:*

To demonstrate lot-to-lot reproducibility of the ImmunoCAP Allergen d201, House dust mite, three lots of ImmunoCAP Allergen from routine production were tested using two positive and one negative control samples (stored human plasma). The samples were tested in duplicates in one assay run. Mean concentration values, concentration quotients, and %CV were calculated.

The concentration quotients between lots based on uptake of positive sample were between 0.99 – 1.09, the concentrations of the negative samples were <0.35 kU_A/L, and all %CV were less than 4%.

b. *Linearity/assay reportable range:*

Not provided (see k962274)

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

A stability study was performed to demonstrate 24 months real time stability (at recommended storage temperature of 2-8°C) of ImmunoCAP Allergen d201, House dust mite. The study was planned in accordance with CEN 13640, Stability Testing of In Vitro Diagnostic Reagents. Three lots of ImmunoCAP Allergen were stored at 2-8°C. Two positive and one negative control samples (stored human plasma) were tested in duplicates in one assay at monthly intervals. The mean concentrations were calculated for each sample and occasion. Concentration quotients were calculated for the positive samples. The sample concentration at a specific month is divided with the start value, (month x)/(month 0). The concentration quotients ranged from 0.8 – 1.3 kU_A/L of the starting value for the positive samples while the value for the negative sample remained at <0.1 kU_A/L demonstrating at least 24 months stability from the date of manufacture.

d. *Detection limit:*

0.1 kU_A/L (see k051218)

e. *Analytical specificity:*

Not provided (see k051218)

f. *Assay cut-off:*

Not provided (see k051218)

2. Comparison studies:

a. *Method comparison with predicate device:*

Not applicable for this kind of submission.

b. *Matrix comparison:*

Not applicable.

3. Clinical studies:

a. *Clinical Sensitivity/Clinical specificity:*

To demonstrate the presence of specific IgE to *Blomia tropicalis* in the serum/plasma samples of patients with diagnosed or suspected allergy to the allergen and healthy, non-sensitized donors with no reported clinical reaction, 66 positive and 100 negative samples were tested with the ImmunoCAP Allergen d201. The positive samples consisted of 3 clinical, 37 positive, and another 26 patients with allergic asthma and exhibited positive reactions to either conjunctival and/or bronchial challenge with *B. tropicalis*. A clinical sample was defined as a sample from an individual with a clinical history of allergy-like symptoms upon exposure to the specific allergen, as diagnosed by a physician. A positive sample was defined as a sample from an individual with a relevant suspected allergy and with measurable levels of IgE antibodies. Negative samples were collected from healthy non-atopic donors.

The 26 patients were from a published study^a of 42 patients from Spain with allergic asthma and/or rhinoconjunctivitis sensitized to house dust mites. 26 patients had positive reactions to conjunctival and/or bronchial challenge with freeze-dried extracts of *Blomia tropicalis* and *D. pteronyssinus*, 23 of these were positive by ImmunoCAP Allergen d201, House dust mite (*Blomia tropicalis*). For the purposes of the clinical study, the clinical results used to define the subjects were a clinical history, clinical symptoms compatible with mite sensitization, and/or a positive result from either bronchial and/or conjunctival challenge, irrespective of skin prick test results. For this study values below 0.35 kU_A/L were reported as negative.

^aGarcia Robaina J.C., *et al.* Skin Tests and Conjunctival and Bronchial Challenges with Extracts of *Blomia tropicalis* and *Dermatophagoides pteronyssinus* in Patients with Allergic Asthma and/or Rhinoconjunctivitis. *Int Arch Allergy Immunol* 2003;131:182-188.

The results are shown in the table below and are similar to those described in the article from different geographical regions around the world.

Table 1. Sensitivity and Specificity of *B. tropicalis* allergens.

ImmunoCAP Allergen d201, House dust mite	Samples			
	Clinical (positive)	Positive	Negative	Total
ImmunoCAP (+)	26	37	0	63
result (-)	3	0	100	103
Total	66		100	166

Sensitivity: 95.5% (63/33)
 Specificity: 100% (100/100)

b. *Other clinical supportive data:*

The study was designed to verify the immunological specificity of *Blomia tropicalis* allergen solution as bound to ImmunoCAP Allergen d201, House dust mite. The study was planned in accordance with appendix D (“Specificity Analysis of Allergen-Containing Reagents”) in the CLSI standard I/LA20-A2, “Analytical Performance Characteristics and Clinical Utility of Immunological Assays for Human Immunoglobulin E (IgE) Antibodies and Defined Allergen Specificities.” To establish the theoretical response level for 100% inhibition, (“100%”), 90 µL of negative sample was premixed with 90 µl of buffer. This is done to mimic the state where all IgE antibodies are bound by the added soluble inhibitor (allergen) and thus leaving no available IgE antibodies that may be bound to the ImmunoCAP Allergen d201, House dust mite solid phase.

To establish the maximum response level for 0% inhibition, (“0%”), 90 µL of positive sample was premixed with 90 µL buffer. To show an overall dose dependent inhibition, 90 µL of positive sample was premixed with varying dilutions of allergen solution (inhibitor). The allergen solution was serially diluted with buffer in a 1/10-dilution sequence. The initial allergen solution dilution factor is dependent on the concentration of the allergen solution at hand. Subsequent dilutions were then adjusted to the 1/10-dilution sequence. The unrelated allergen solutions were not further diluted. Only concentrated solutions are used for the inhibition studies. The mixture was incubated in a sample tube at 2-8°C for 16-24 hours before being analyzed with ImmunoCAP Allergen d201, House dust mite on ImmunoCAP 100E instrument according to the manufacturer’s instructions. The testing was performed in duplicates in one assay run. Mean values were calculated. The results are shown in Table 2 and Figures 1 and 2, below.

Table 2. Inhibition with *Blomia tropicalis* and unrelated allergens.

Inhibitor	Dilution factor (1/x, w/v)	Response (RU)	Inhibition (%)
100%	-	25	100
0%	-	2745	0
<i>Blomia tropicalis</i> allergen	100,000	2160	22
	10,000	922	67
	1,000	291	90
	100	91	98
	20	46	99
Mouse epithelium allergen	1000	2762	0
Chicken dropping allergen	1000	2669	3
Parrot feathers allergen	1000	2588	6

Figure 1. Inhibition with *Blomia tropicalis* allergen.

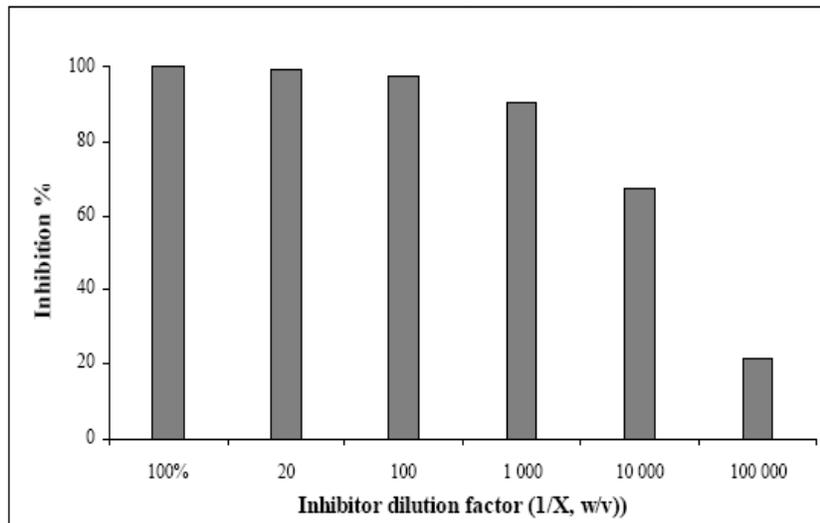
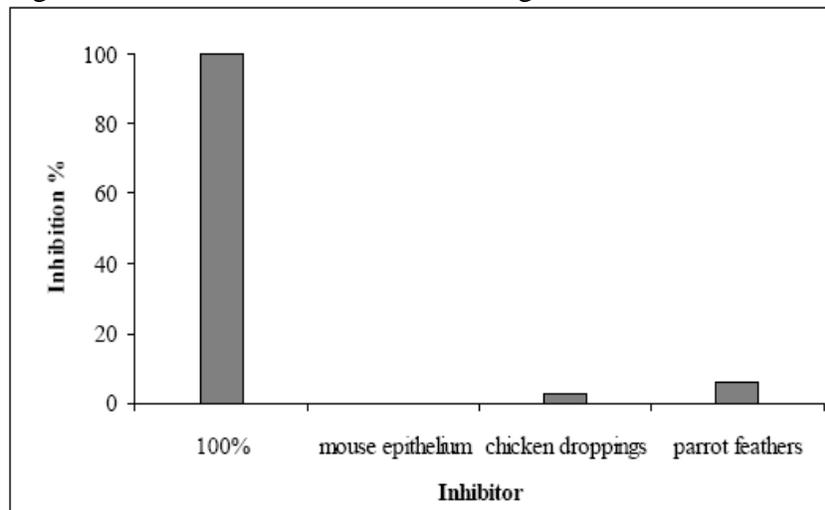


Figure 2. Inhibition with unrelated allergens.



4. Clinical cut-off:

Not provided (see k051218)

5. Expected values/Reference range:

The established clinical cut-off has historically been set at 0.35 kU/L.

Sensitization may be inferred at values above the limit of detection at 0.1 kU_A/L, though the clinical significance of values between 0.1 kU_A/L and 0.35 kU_A/l has not been established. 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 substantial equivalence decision.