

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY TEMPLATE**

A. 510(k) Number:

k071913

B. Purpose for Submission:

New allergen

C. Measurand:

Allergen specific IgE

D. Type of Test:

Fluoroenzymeimmunoassay

E. Applicant:

Phadia AB

F. Proprietary and Established Names:

ImmunoCAP Allergen f338, Scallop

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. 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. ImmunoCAP Allergen f338, Scallop is to be used with the ImmunoCAP Instrument System, ImmunoCAP 100, ImmunoCAP 250, and ImmunoCAP 1000.

2. Indication(s) for use:

Same as above

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 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, Allergen ImmunoCAP carriers (Single and Multiple), ImmunoCAP development solution and stop solution.

J. Substantial Equivalence Information:

1. Predicate device name(s):
UniCAP® Specific IgE Assay
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)	Same
Basic principle	Fluorescence immunoassay	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 f338, Scallop	Absence of allergen f338, Scallop

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

Evaluation Methods and Analytical Performance Characteristics of Immunological Assays for Human Immunoglobulin E (IgE) Antibodies of Defined Allergen

Specificities; Approved Guideline (1997) I/LA 20-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 ImmunoCAP Allergen f338, Scallop, three different lots were tested using two positive and one negative control samples. For this study, values below $0.35 \text{ kU}_A/\text{L}$ were reported as negative. The samples were tested in duplicates in one assay run. Mean values were calculated. Specifications were as follows:

Positive sample concentration quotient: 0.7-1.3.

Negative sample response quotient: (compared with calibrator $0.35 \text{ kU}_A/\text{L}$) $n/0.35 < 1.0$.

Results showed specifications are fulfilled; i.e. quotient between lots based on uptake of positive sample is within 0.7-1.3 and the response of the low sample is below calibrator $0.35 \text{ kU}_A/\text{L}$.

b. *Linearity/assay reportable range:*

Not provided

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

24 months real time stability (at recommended storage temperature of $2-8^\circ\text{C}$) of ImmunoCAP Allergen f338, Scallop, was demonstrated by the following:

Three lots of ImmunoCAP Allergen were stored at $2-8^\circ\text{C}$. Two positive and one negative control samples (stored human plasma) were tested in duplicates in one assay at different monthly intervals. For this study values below $0.35 \text{ kU}_A/\text{L}$ were reported as negative. The mean concentrations or response values were calculated for each sample and occasion. Specifications were:

Positive sample concentration quotient: 0.7-1.3

Negative sample response quotient (compared with calibrator $0.35 \text{ kU}_A/\text{L}$): $(n/0.35) < 1.0$.

Results of the real time stability study showed the ImmunoCAP Allergen f338, Scallop is stable for at least 24 months from date of manufacture when stored at $2-8^\circ\text{C}$.

d. *Detection limit:*

- Not provided
- e. *Analytical specificity:*
Not provided
- f. *Assay cut-off:*
Not provided.
- 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:*
Studies to demonstrate the following were provided:
 1. Presence of specific IgE to scallop specific allergens in the serum/plasma samples of patients with suspected scallop and/or food intolerance.
 2. Absence of specific IgE to scallop in the samples from healthy, non-sensitized donors with no reported scallop intolerance

Two hundred and fourteen clinical samples collected in Japan from patients with the suspicion of scallop intolerance were tested for IgE mediated scallop intolerance. Fifty-four patients (Ch1) had a history of allergic reaction after ingestion of scallop. The reactions were urticaria, edema, respiratory and gastro-intestinal symptoms and anaphylaxis. The remaining 160 patients (Ch2) had a history of symptoms with a suspicion of food allergy, where scallop was not specified. Samples from 103 healthy, non-sensitized donors with no reported symptoms of scallop or food intolerance were also tested. Samples were tested, using ImmunoCAP Specific IgE assay, with three lots of ImmunoCAP Allergen f338, Scallop in one replicate on one occasion. For this study values below $0.35 \text{ kU}_A/\text{L}$ were reported as negative. Specifications were as follows:

Samples from healthy, non-sensitized donors (Neg) with no suspicion of IgE mediated allergy to scallop should have undetectable levels ($<0.35 \text{ kU}_A/\text{L}$) of scallop specific IgE.

Samples from patients with suspected IgE mediated allergy should have a rate of detectable IgE antibodies to scallop in line with currently published reports.

Results showed that 44% of Ch1 had a reported detectable level of scallop specific IgE antibodies, 39% of Ch2 had a reported detectable level of scallop specific IgE antibodies and 100% of the Neg had no reported detectable level of scallop specific IgE antibodies. These figures are consistent with literature reports (ref.1-9) of patients who had self reported symptoms of food allergy (see figure 1 for distribution of three patient groups tested for scallop specific IgE antibodies).

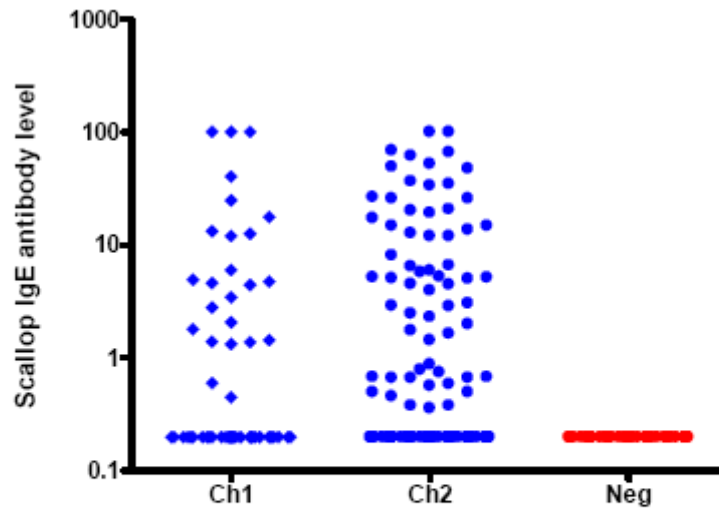


Figure 1. Distribution of three patient groups tested for scallop specific IgE antibodies. Group Ch1 (n=54) are patients with case history of allergic reaction (symptom) after ingestion of scallop, Ch2 (n=160) are patients having symptoms with a suspicion of food allergy (scallop not specified) and Neg (n=103) are healthy, non-sensitized donors with no reports of any kind of clinical reaction to scallop.

- c. Other clinical supportive data (when a. and b. are not applicable):
Inhibition studies were performed to verify immunological specificity of scallop specific IgE antibody binding. One lot of ImmunoCAP Allergen f338, Scallop was tested on the ImmunoCAP 100, Testing materials included scallop-specific allergen raw material extract, a positive sample with specific IgE antibodies to scallop allergen, a negative sample below 0.35 kU_A/L and negative buffer control: PBS with 0,02% NaN₃.

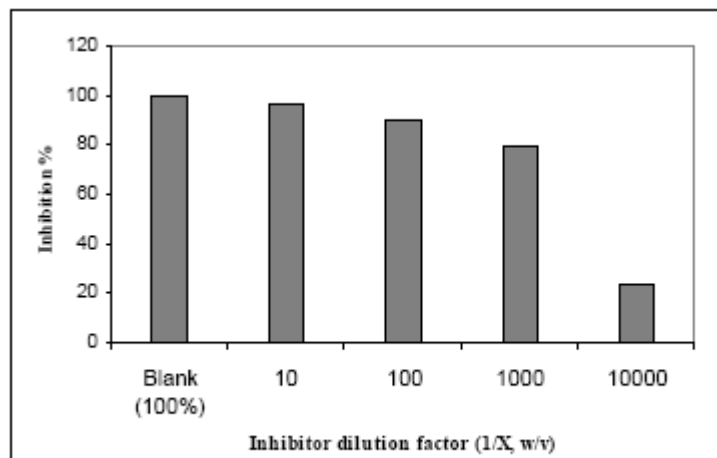
Background response level (blank, 100% inhibition) was determined by using 90 µL of the negative sample premixed with 90 µL of buffer. The maximum uptake response level (positive, % inhibition) was established by using 90 µL of the positive sample premixed with 90 µL buffer. The allergen extract was serially diluted with buffer in a 1/10-dilution sequence. The initial allergen extract dilution factor was dependent on the concentration of the allergen extract at hand. Subsequent dilutions were then adjusted to the 1/10-dilution sequence. To show inhibition, 90 µL of positive sample was premixed with varying dilutions of allergen extract (inhibitor). The mixture was incubated in a sample tube at 2-8°C for 16-24 hours before adding to the ImmunoCAP Allergen f338, Scallop and was then analyzed with ImmunoCAP 100 according to the manufacturer's instructions. The testing was performed in duplicates in one assay run.

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

$$\text{Inhibition \% at inhibition dilution factor } x = \frac{\text{Response}_{(\text{Positive 0\% inhibition})} - \text{Response}_{(x)}}{\text{Response}_{(\text{Positive 0\% inhibition})} - \text{Response}_{(\text{Blank 100\% inhibition})}} \times 100$$

Any negative inhibition %-values are shown as 0 % - inhibition.
The inhibition study results are presented below.

Inhibitor	Dilution factor (1/x, w/v)	Response (RU)	Inhibition (%)
blank (100%)	-	28	100
positive (0%)	-	841	0
scallop allergen extract	10 000	648	24
scallop allergen extract	1000	199	79
scallop allergen extract	100	107	90
scallop allergen extract	10	59	96



Results showed that the binding of specific IgE by the ImmunoCAP Allergen f338, Scallop was inhibited in a dose dependant fashion by increasing amounts of the specific allergen extract. This indicates that the tested ImmunoCAP Allergen solid phase contains the immunologically relevant allergen.

4. Clinical cut-off:

Not provided

5. Expected values/Reference range:

0.35 kU_A/L is the recommended cut-off. 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.