August 3, 2022

Phadia AB
% Tosha Dave
Regulatory Affairs Specialist III
Phadia US Inc
4169 Commercial Avenue
Portage, Michigan 49002

Re: K212181
Trade/Device Name: ImmunoCAP Allergen f433, Allergen component rTri a 14 LTP, Wheat
ImmunoCAP Allergen f416, Allergen component rTri a 19 Omega-5 Gliadin, Wheat
ImmunoCAP Allergen f449, Allergen component rSes i 1 Sesame seed
Regulation Number: 21 CFR 866.5750
Regulation Name: Radioallergosorbent (RAST) Immunological Test System
Regulatory Class: Class II
Product Code: DHB
Dated: May 4, 2022
Received: May 5, 2022

Dear Sheryl Skinner:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801 and Part 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Ying Mao, Ph.D.
Branch Chief
Division of Immunology
and Hematology Devices
OHT7: Office of In Vitro Diagnostics
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2023
See PRA Statement below.

510(k) Number *(if known)*
K212181

Device Name
ImmunoCAP Specific IgE
ImmunoCAP Allergen f433, Allergen component rTri a 14 LTP, Wheat, ImmunoCAP Allergen f416, Allergen component rTri a 19 Omega-5 Gliadin, Wheat and ImmunoCAP Allergen f449, Allergen component rSes i 1 Sesame seed

Indications for Use *(Describe)*

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). 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.
ImmunoCAP Specific IgE is to be used with the instruments Phadia 250, Phadia 1000, Phadia 2500 and Phadia 5000.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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510(k) Summary

This 510(k) Summary is prepared in accordance with the requirements of 21 CFR Part 807.92.

Premarket Notification 510(k) No: K212181

Date of Summary Preparation: **June 28, 2022**

Manufacturer:

Phadia AB

Rapsgatan 7P
P.O. Box 6460
751 37 Uppsala, Sweden

Distributor:

Phadia US Inc.

4169 Commercial Avenue
Portage, MI 49002

Company Contact Person:

Jane Anthony

Sr. Manager, Quality Systems and Compliance
Phadia US Inc.
4169 Commercial Avenue
(269) 254-6833
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Device Name:

ImmunoCAP Specific IgE

- ImmunoCAP Allergen f433, Allergen Component rTri a 14 LTP, Wheat
- ImmunoCAP Allergen f416, Allergen Component rTri a 19 Omega-5 Gliadin, Wheat
- ImmunoCAP Allergen f449, Allergen Component rSes i 1, Sesame seed

Purpose for Submission:

This submission is for the clearance of three new ImmunoCAP Allergen Components to be added to the previously cleared ImmunoCAP Allergen Specific IgE assay system.

The addition of the new ImmunoCAP Allergen Components does not affect the Intended Use or the Indications for Use. The previously cleared system may be referenced under K051218.

Measurand:

Allergen specific IgE

Type of Test:

Fluoroenzymeimmunoassay, Quantitative

Common Name:

Automated in-vitro quantitative assay for the measurement of allergen specific IgE antibodies.

Regulatory Information:

Product Code	DHB
Class	II
CFR	866.5750 – Radioallergosorbent immunological test system (RAST)
Panel	Immunology (82)

Intended use:

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). 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. ImmunoCAP Specific IgE is to be used with instruments Phadia 250, Phadia 1000, Phadia 2500 and Phadia 5000.

Indications For Use Statement:

Same as intended use.

Special Conditions for Use:

Rx – For Prescription Use Only.

Special instrument requirements:
For use on the instruments Phadia 250, Phadia 1000, Phadia 2500 and Phadia 5000.

Device Description:

Reagents

ImmunoCAP Specific IgE reagents are modular in concept and are available individually. For a complete listing of reagents needed to perform the Phadia ImmunoCAP Specific IgE assay, please consult the ImmunoCAP Specific IgE Conjugate Directions for Use.

Instrument System

Phadia 250, Phadia 1000, Phadia 2500 and Phadia 5000 instrument systems, and associated software, processes all steps of the assay and calculates results automatically after the assay is completed. Analytical and clinical validation of these components were performed on the representative instrument Phadia 250 and Phadia 1000.

ImmunoCAP Specific IgE, 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 responses for the patient samples are transformed to concentrations with the use of a calibration curve.

Substantial Equivalence to:

K051218
ImmunoCAP Specific IgE

- ImmunoCAP Allergen f4, Wheat (14-4113-01)
- ImmunoCAP Allergen f10, Sesame (14-4175-01)

Comparison with predicate:

	Proposed Device	**Predicate Device**
	ImmunoCAP Allergen Components	ImmunoCAP Specific IgE (formally UniCAP Specific IgE) ***(K051218)***
Similarities		
Classification	Class II	Class II
Product Code	DHF	DHF
Regulation Number	866.5750	866.5750
Intended Use/Indication for Use	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). 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. ImmunoCAP Specific IgE is to be used with the instrument Phadia 250, Phadia 1000, Phadia 2500 and Phadia 5000.	UniCAP Specific IgE is an in vitro semi-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.
Analyte	Specific IgE	Specific IgE
Type of test	Fluoroenzymeimmunoassay	Fluoroenzymeimmunoassay
Method	Sandwich immunoassay	Sandwich immunoassay
Assay Type	Quantitative	Quantitative

Sample Type	Human serum or plasma (EDTA or Na-Heparin)	Human serum or plasma (EDTA or Na-Heparin)
Assay system reagents	ImmunoCAP Specific IgE Calibrators, Conjugate and Controls	ImmunoCAP Specific IgE Calibrators, Conjugate and Controls
Technology	Immunofluorescence	Immunofluorescence
Software	ImmunoCAP Specific IgE method in Phadia Information Data Manager (IDM) or Phadia Prime	ImmunoCAP Specific IgE method in Phadia Information Data Manager (IDM) or Phadia Prime
Reporting of results	Quantitative, kU_A/L	Quantitative, kU_A/L
Analytical sensitivity (LoD/LoQ)	0.1 kU_A/L	0.1 kU_A/L
Differences		
Allergen raw material coupled to ImmunoCAP solid phase	Individual recombinant allergen component	Extract based allergen comprising of multiple protein components from the allergen source component

Standard/Guidance Document Referenced:

EP25-A, CLSI, 2009, Evaluation of Stability of In Vitro Diagnostic reagents

CLSI EP05-A3: Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline - Third Edition

I/LA20: Analytical Performance Characteristics, Quality Assurance, and Clinical Utility of Immunological Assays for Human Immunoglobulin E Antibodies of Defined Allergen Specificities, 3rd Edition

CLSI EP07-A2: Interference testing in Clinical Chemistry; Approved Guideline – Second Edition.

CLSI EP07 3rd Edition: Interference Testing in Clinical Chemistry.

CLSI EP17-A2: Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline - Second Edition

CLSI EP39, 1st Edition, 2021, A Hierarchical Approach to Selecting Surrogate Samples for the Evaluation of In Vitro Medical Laboratory

Performance Characteristics

The new ImmunoCAP Allergen Components were compared to the extract based predicate device. Positive clinical samples (atopic) and samples from healthy, non-atopic donors were

studied. Analytical performance characteristics for the new ImmunoCAP Allergen Components were established by Precision/reproducibility, Linearity, Limit of Detection, and Stability studies. Inhibition studies verified the analytical specificity of the allergen components.

Precision/Reproducibility

i. Within-laboratory imprecision

Imprecision of each ImmunoCAP Allergen Component was evaluated by testing five (f433, rTri a 14) or six (f416, rTri a 19 and f449, rSes i 1) positive-samples (> 0.1 kU_A/L) with concentrations of allergen specific IgE spanning the analytical measuring range (AMR). Each sample was tested in four replicates in one assay run per day for a total of 20 operating days (a total of 80 replicates per sample) except Sample 6 for f416, rTri a 19 that was tested in three replicates in 11 runs over 20 days (a total of 33 replicates). One (1) lot of each ImmunoCAP Allergen component was tested with each sample. The assay was performed according to the ImmunoCAP Specific IgE Directions for Use using a Phadia 250. Mean concentrations of allergen specific IgE, standard deviation (SD), and coefficients of variance (%CV) were calculated for each sample, separately. Results are shown in the table 1 below:

ImmunoCAP Allergen Component	Sample	N	Mean (kUA/L)	Within-run (Repeatability)		Between-run (Repeatability)		Total (Within-Laboratory)	
				SD	%CV	SD	%CV	SD	%CV
f433, rTri a 14 LTP (Wheat)	1	80	0.18	0.01	6.05	0.01	6.10	0.02	8.59
	2	80	0.34	0.03	7.43	0.02	7.14	0.03	10.30
	3	80	2.24	0.08	3.35	0.10	4.41	0.12	5.53
	4	80	14.83	0.48	3.27	0.70	4.75	0.85	5.76
	5	80	82.81	4.91	5.93	5.20	6.27	7.15	8.63
f416, rTri a 19 Omega-5 Gliadin (Wheat)	1	80	0.15	0.01	8.88	0.01	6.63	0.02	11.09
	2	80	0.28	0.02	6.47	0.01	4.94	0.02	8.14
	3	80	2.72	0.09	3.20	0.08	3.06	0.12	4.42
	4	80	18.49	0.53	2.86	0.96	5.17	1.09	5.91
	5	80	37.50	1.00	2.66	2.05	5.46	2.28	6.08
	6	33	71.52	5.56	7.77	3.16	4.42	6.40	8.95
f449, rSes i 1 (Sesame seed)	1	80	0.16	0.01	7.22	0.01	5.42	0.01	9.03
	2	80	0.35	0.01	2.43	0.01	2.36	0.01	3.39
	3	80	2.23	0.06	2.59	0.04	1.69	0.07	3.09
	4	80	14.27	0.38	2.68	0.22	1.53	0.44	3.09
	5	80	56.25	2.58	4.59	2.06	3.67	3.30	5.87
	6	80	71.85	4.95	6.89	2.48	3.45	5.53	7.70

Table 1: Within-Laboratory imprecision

ii. Lot-to-lot imprecision

Three different lots of each ImmunoCAP Allergen Component: f433, rTri a 14 LTP (Wheat); f416, rTri a 19 Omega-5 Gliadin (Wheat); and f449, rSes i 1 (Sesame seed) were tested using four (f433, rTri a 14 and f416, rTri a 19) or five (f449, rSes i 1) positive samples 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. The assay was performed according to the ImmunoCAP Specific IgE, Directions for Use, using the Phadia 250 instrument. Negative samples results were all below 0.1 kU_A/L and only positive results are included in the table below. Mean concentrations of allergen specific IgE and %CV within lot were calculated for the positive samples and are presented in the tables below:

ImmunoCAP Allergen Component f433, rTri a 14 LTP (Wheat)								
Lot	Sample Panel							
	Sample 1		Sample 2		Sample 3		Sample 4	
	Mean (kU_A/L)	%CV	Mean (kU_A/L)	%CV	Mean (kU_A/L)	%CV	Mean (kU_A/L)	%CV
1	0.35	4.03	2.12	2.45	17.30	2.32	78.46	4.29
2	0.33	2.50	2.07	2.33	16.80	3.53	75.30	3.95
3	0.34	2.98	2.10	2.29	17.25	4.15	79.93	6.09

Table 2: Lot-to-lot Imprecision - Allergan Component f433, rTri a 14 LTP, Wheat

ImmunoCAP Allergen Component f416, rTri a 19 Omega-5 Gliadin (Wheat)								
Lot	Sample Panel							
	Sample 1		Sample 2		Sample 3		Sample 4	
	Mean (kU_A/L)	%CV	Mean (kU_A/L)	%CV	Mean (kU_A/L)	%CV	Mean (kU_A/L)	%CV
1	0.40	9.20	2.03	2.93	12.78	4.09	55.32	6.10
2	0.34	5.93	2.02	2.02	11.93	2.27	55.89	3.36
3	0.31	9.97	2.03	2.51	12.02	2.08	55.63	6.48

Table 3: Lot-to-lot Imprecision - Allergen Component f416, rTri a 19 Omega-5 Gliadin, Wheat

ImmunoCAP Allergen Component f449, rSes i 1 (Sesame seed)										
Lot	Sample Panel									
	Sample 1		Sample 2		Sample 3		Sample 4		Sample 5	
	Mean (kU_A/L)	%CV	Mean (kU_A/L)	%CV	Mean (kU_A/L)	%CV	Mean (kU_A/L)	%CV	Mean (kU_A/L)	%CV
1	0.38	3.33	2.34	5.77	16.15	3.80	50.56	3.17	95.54	6.46
2	0.37	2.15	2.02	10.06	14.77	4.07	48.40	5.91	100.25	6.30
3	0.35	2.70	1.94	9.50	14.26	5.61	44.32	6.22	90.78	7.90

Table 4: Lot-to-lot Imprecision - Allergen Component f449, rSes i 1, Sesame seed

Linearity

The linearity of each ImmunoCAP Allergen Component: f433, rTri a 14 LTP (Wheat); f416, rTri a 19 Omega-5 Gliadin (Wheat); and f449, rSes i 1 (Sesame seed) was assessed following CLSI guideline I/LA-20 3rd Edition. Three (f449, rSes i 1) or four (f433, rTri a 14 and f416, rTri a 19) positive samples were each diluted in negative sample matrix to generate at least six 2-fold consecutive dilutions. Samples were tested at a minimum of four replicates in one assay run on the Phadia 250 instrument according to the ImmunoCAP Specific IgE, Directions for Use. One (1) lot of each ImmunoCAP Allergen component was tested with each sample. Results were analyzed for Linearity. 'Pooled' sample result indicates combined test results of individual samples to present an estimate of a single regression analysis model for each ImmunoCAP Allergen component. Hence, mean value for each dilution and sample was used instead of single replicate results (as is the case in the regression analysis of individual samples). The concentration range given for the pooled regression analysis is thus the total range covered by any of the individual samples.

Regression statistics comparing the observed results to the expected results are presented below in table 5, 6, and 7:

ImmunoCAP Allergen Component f433, rTri a 14 LTP (Wheat)				
Sample	**Concentration range tested (kU_A/L)**	**r^2**	**Slope (95% CI)**	**Intercept (95% CI)**
1	0.48–30.49	1.00	1.00 (0.99; 1.01)	0.00 (-0.01; 0.01)
2	0.15–9.36	1.00	1.01 (1.00; 1.03)	0.00 (-0.01; 0.01)
3	0.07–75.87	1.00	1.00 (0.99; 1.01)	0.03 (0.02; 0.04)
4	0.05–100	1.00	1.02 (1.01; 1.03)	0.03 (0.02; 0.05)
Pooled	0.05–100	1.00	1.02 (1.00; 1.03)	0.02 (0.01; 0.03)

Table 5: Regression Statistic - Allergen Component f433, rTri a 14 LTP, Wheat

ImmunoCAP Allergen Component f416, rTri a 19 Omega-5 Gliadin (Wheat)				
Sample	**Concentration range tested (kU_A/L)**	**r^2**	**Slope (95% CI)**	**Intercept (95% CI)**
1	0.20 - 6.36	1.00	1.08 (1.06; 1.10)	–0.06 (-0.07; -0.05)
2	0.19 - 23.76	1.00	1.01 (1.00; 1.03)	0.00 (-0.01; 0.01)
3	0.06 - 62.47	1.00	1.02 (1.01; 1.03)	-0.01 (-0.03; 0.00)
4	0.07 - 68.44	1.00	1.00 (0.99; 1.01)	0.01 (0.00; 0.02)
Pooled	0.06 – 68.44	1.00	1.02 (1.01; 1.04)	-0.01 (-0.03; 0.00)

Table 6: Regression Statistic - Allergen Component f416, rTri a 19 Omega-5 Gliadin, Wheat

ImmunoCAP Allergen Component f449, rSes i 1 (Sesame seed)				
Sample	**Concentration range tested (kU_A/L)**	**r^2**	**Slope (95% CI)**	**Intercept (95% CI)**
1	0.08–85.59	1.00	1.05 (1.04; 1.05)	–0.06 (-0.07; -0.05)
2	0.17–43.10	1.00	1.04 (1.03; 1.05)	–0.06 (-0.07; -0.05)
3	0.24–7.83	1.00	1.09 (1.08; 1.11)	-0.08 (-0.09; -0.07)
Pooled	0.08–85.59	1.00	1.06 (1.04; 1.07)	–0.06 (-0.08; -0.05)

Table 7: Regression Statistic - Allergen Component f449, rSes i 1, Sesame seed

The claimed assay ranges claims are summarized in the table 8 below:

ImmunoCAP Allergen Component	Claimed assay range (kU_A/L)
f433, rTri a 14 LTP (Wheat)	0.10-100.00
f416, rTri a 19 Omega-5 Gliadin (Wheat)	0.10-68.44
f449, rSes i 1 (Sesame seed)	0.10-85.59

Table 8: Assay ranges for ImmunoCAP Allergen Components

Detection limit

The Limit of Blank (LoB) and Limit of Detection (LoD) were determined on the Phadia 250 in alignment with CLSI guideline EP17-A2 using two lots of each ImmunoCAP Allergen Component. The LoB was based on determinations of five blank samples in three runs with five replicates per run and was estimated as the 95%percentile of the distribution.

LoD was calculated according to the equation: LoD = LoB + cß • SDLoD, where SDLoD is the pooled SD for each of five low positive samples measured in 15 replicates. Results from maximum LoD of the two lots were used in the calculation of LoQ. The results support the LoQ claim of 0.1 kU_A/L and are shown in table 9 below.

ImmunoCAP Allergen Component	LoB (kUA/L)	LoD (kUA/L)	LoQ (kUA/L)
f433, rTri a 14 LTP Wheat	0.014	0.019	0.058
f416, rTri a 19 Omega-5 Gliadin Wheat	0.007	0.029	0.068
f449, rSes i 1 Sesame seed	0.000	0.014	0.041

Table 9: Detection Limit - LoB, LoD, LoQ

Analytical specificity

Inhibition studies
Immunological specificity of each ImmunoCAP Allergen Component was verified through competitive inhibition. The studies were conducted in accordance with I/LA-20 3rd Edition. For each ImmunoCAP Allergen component, a positive sample was tested and the specific IgE concentration is shown in table 10 below.

ImmunoCAP Allergen Component	Sample level (kU_A/L)
f433, rTri a 14 LTP Wheat	2.94
f416, rTri a 19 Omega-5 Gliadin Wheat	1.55
f449, rSes i 1 Sesame seed	2.17

Table 10: Specific IgE concentration

For each ImmunoCAP Allergen component, three unrelated inhibitors and one related inhibitor were included in the study as controls (as listed in table 11 below) that should not give a significant inhibition. The specific inhibitor was added at serial dilution and should result in > 50% inhibition to show analytical specificity.

Testing was performed with the respective ImmunoCAP Allergen component on the Phadia 250 according to the ImmunoCAP Specific IgE, Directions for Use. Mean values and % Inhibition were calculated.

The three unrelated control inhibitors and the one related control inhibitor for each ImmunoCAP Allergen component, are shown in table 11 below.

ImmunoCAP Allergen Component	Unrelated inhibitors
f433, rTri a 14 LTP Wheat	Unrelated: rFel d 2, rOle e 1 and rVes v 5 Related: rAra h 6
f416, rTri a 19 Omega-5 Gliadin Wheat	Unrelated: rCan f 4, rVes v 5 and rAsp f 1 Related: rPru p 1
f449, rSes i 1 Sesame seed	Unrelated: rCan f 4, rAsp f 1 and rOle e 1, Related: rCor a 8

Table 11: unrelated inhibitors for allergen components

All results met the specifications and analytical specificity for the ImmunoCAP Allergen Components rTri a 19, Wheat (f416); rTri a 14, Wheat (f433); and Ses i 1, Sesame (f449), was verified.

Interference

Endogenous Substance Interference:
A study was conducted to evaluate if icteric, haemolytic or lipemic samples, or samples containing Rheumatoid Factor, can adversely affect the results of the ImmunoCAP Allergen components rTri a 19, Wheat (f416); rTri a 14, Wheat (f433); and Ses i 1, Sesame (f449) in the ImmunoCAP Specific IgE assay.

Three samples (two positive and one negative) were spiked with Bilirubin F, Bilirubin C, Chyle, Hemoglobin and Rheumatoid Factor. The spiked samples were tested with one (1)

lot of each ImmunoCAP Allergen component to evaluate assay interference. The results demonstrate that icteric, hemolytic or lipemic samples do not adversely affect the results in ImmunoCAP Specific IgE assay using ImmunoCAP Allergen components rTri a 19, Wheat (f416); rTri a 14, Wheat (f433); and Ses i 1, Sesame (f449). In addition, the results show that Rheumatoid Factor do not adversely affect the results in the evaluated assays. Concentrations of interferent that can be tolerated are shown in table 12 below.

Interferant	Tolerated concentration		
	rTri a 14	rTri a 19	rSes i 1
Bilirubin F (mg/dL)	18.5	18.6	39.8
Bilirubin C (mg/dL)	20.8	20.2	42.2
Chyle (FTU)	1640	1630	16300
Hemoglobin (mg/dL)	490	490	500
Rheumatoid Factor (IU/mL)	500	550	550

Table 12: Interference study results, tolerated concentrations of Endogenous interferants

Stability studies

Stability studies were performed in accordance with CLSI EP25-A using three lots of each ImmunoCAP Allergen component. The real-time stability study for ImmunoCAP Allergen components rTri a 19 Omega-5 Gliadin, Wheat (f416); rTri a 14 LTP, Wheat (f433), met the specifications and showed 19 months unopened shelf-life stability.

The real-time stability data for ImmunoCAP Allergen component rSes i 1 (f449), supports unopened shelf-life stability of 6 months. The real-time stability study is ongoing for Allergen component rSes i 1 (f449). An accelerated stability study was performed with two positive and one negative samples and three lots of ImmunoCAP Allergen component rSes i 1 (f449). The accelerated stability data supports the claim of 6 months unopened shelf-life stability for f449, rSes i 1 (Sesame seed).

Method Comparison study

To demonstrate the relationship between specific IgE antibodies to ImmunoCAP Allergen component and the corresponding extract based ImmunoCAP Allergen (predicate device), 43-62 selected samples from; *(i)* individuals with a clinical history of allergy-like symptoms upon exposure to the allergen (32-33 positive clinical samples), *(ii)* samples from sensitized individuals without documented clinical history (10-30 positive non-clinical samples), and *(iii)* samples from healthy non-atopic donors with no history of allergy (100 negative samples) were used.

For all three components undetectable levels of specific IgE antibodies (<0.1 kU_A/L) were demonstrated in 100% (100/100) of the negative samples.

In comparison with the extract based ImmunoCAP Allergen f4, Wheat, specific IgE antibodies ≥ 0.1 kU_A/L were demonstrated in 33/33 of the clinical samples and 10/10 of the

non-clinical samples when analyzed with ImmunoCAP Allergen f433, Allergen component rTri a 14 LTP.
In comparison with the extract based ImmunoCAP Allergen f4, Wheat, specific IgE antibodies ≥ 0.1 kU_A/L were demonstrated in 34/34 clinical samples and 14/14 non-clinical samples when analyzed with ImmunoCAP Allergen f416, rTri a 19.

In comparison with the extract based ImmunoCAP Allergen f10, Sesame seed specific IgE antibodies ≥ 0.1 kU_A/L were demonstrated in 32/32 clinical samples and 30/30 non-clinical samples when analyzed with ImmunoCAP Allergen f449, rSes i 1.

Clinical studies

Clinical sensitivity and specificity:

The performance of each ImmunoCAP Allergen Component rTri a 14, Wheat (f433); rTri a 19, Wheat (f416) and Ses i 1, Sesame (f449) was compared to a clinical diagnosis of allergy. The objective of this study was to show the agreement between the specific IgE antibodies to ImmunoCAP Allergen component and clinical diagnosis to wheat, using clinical samples. Selected samples from individuals with a clinical history of allergy-like symptoms upon exposure to wheat, as diagnosed by a physician and samples from healthy subjects with no reported clinical reaction to the allergen (non-atopic subjects; n=100) were used in the study. The samples were tested with the ImmunoCAP Allergen component using one replicate in the ImmunoCAP Specific IgE assay. Clinical sensitivity and specificity in this sample cohort are summarized in the tables 13, 14 and 15. Test results ≥0.35 kU_A/L are considered positive.

ImmunoCAP Allergen Component		Clinical Diagnosis to Wheat		
		Atopic	**Non-atopic**	**Total**
f433, rTri a 14	**Positive**	25	0	25
	Negative	108	100	208
	Total	133	100	233

Sensitivity = 19 % (25/133) 95% CI: 12.5%–26.5%
Specificity =100% (100/100) 95% CI: 96.4%–100%
Table 13:Clinical Sensitivity and Specificity - Allergen Component f433, rTri a 14 LTP, Wheat

ImmunoCAP Allergen Component		Clinical Diagnosis to Wheat		
		Atopic	**Non-atopic**	**Total**
f416, rTri a 19	**Positive**	41	0	41
	Negative	88	100	188
	Total	129	100	229

Sensitivity = 32 % (41/129) 95% CI: 23.9 – 40.6%
Specificity = 100% (100/100) 95% CI: 96.4%–100%

Table 14:Clinical Sensitivity and Specificity - Allergen Component, f416, rTri a 19 Omega-5 Gliadin, Wheat

ImmunoCAP Allergen Component		Clinical Diagnosis to Sesame		
		Atopic	**Non-atopic**	**Total**
f449, rSes i 1	**Positive**	28	0	28
	Negative	7	100	107
	Total	35	100	135

Sensitivity = 80% (28/35) 95% CI: 63.1 – 91.6%
Specificity =100% (100/100) 95% CI: 96.4%–100%
Table 15:Clinical Sensitivity and Specificity - Allergen Component, f449, rSes i 1, Sesame Seed

Conclusion

The safety and effectiveness of the cleared device ImmunoCAP Specific IgE for the determination of specific IgE antibodies have been established in previous 510(k) submissions. This submission covers the addition of three new ImmunoCAP Allergen Component to the existing ImmunoCAP Specific IgE assay. The addition of the new ImmunoCAP Allergen Components does not affect the Intended Use / Indications for Use Statements.