510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K260059

B Applicant

Hycor Biomedical

C Proprietary and Established Names

NOVEOS Specific IgE (sIgE), Capture Reagent F018, Brazil Nut (*Bertholletia excelsa*)
NOVEOS Specific IgE (sIgE), Capture Reagent F036, Coconut (*Cocos nucifera*)
NOVEOS Specific IgE (sIgE), Capture Reagent F040, Tuna (*Thunnus sp.*)
NOVEOS Specific IgE (sIgE), Capture Reagent F041, Salmon (*Salmo salar*)
NOVEOS Specific IgE (sIgE), Capture Reagent F075, Egg Yolk (*Gallus gallus*)
NOVEOS Specific IgE (sIgE), Capture Reagent F201, Pecan Nut (*Carya illinoensis*)
NOVEOS Specific IgE (sIgE), Capture Reagent F203, Pistachio Nut (*Pistacia vera*)
NOVEOS Specific IgE (sIgE), Capture Reagent F290, Oyster (*Ostrea edulis*)

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
DHB	Class II	21 CFR 866.5750 - Radioallergosorbent (RAST) Immunological Test System	IM - Immunology

II Submission/Device Overview:

A Purpose for Submission:

Eight new devices

B Measurand:

Allergen specific IgE to Brazil Nut - F018, *Bertholletia excelsa*
Allergen specific IgE to Coconut - F036, *Cocos nucifera*
Allergen specific IgE to Tuna - F040, *Thunnus sp.*
Allergen specific IgE to Salmon - F041, *Salmo salar*

Allergen specific IgE to Egg Yolk - F075, *Gallus gallus*
Allergen specific IgE to Pecan Nut - F201, *Carya illinoensis*
Allergen specific IgE to Pistachio Nut - F203, *Pistacia vera*
Allergen specific IgE to Oyster - F290, *Ostrea edulis*

C Type of Test:

Chemiluminescent, Quantitative

III Intended Use/Indications for Use:

A Intended Use(s):

See Indications for Use below.

B Indication(s) for Use:

The NOVEOS Specific IgE assay is an *in vitro* quantitative assay for the measurement of allergen specific IgE in human serum. NOVEOS Specific IgE assay is to be used with the NOVEOS Immunoassay Analyzer. It is intended for use as an *in vitro* diagnostic aid in the clinical diagnosis of IgE mediated allergic disorders in conjunction with other clinical findings and is to be used in clinical laboratories.

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

D Special Instrument Requirements:

For use on the NOVEOS Immunoassay Analyzer

IV Device/System Characteristics:

A Device Description:

The NOVEOS Specific IgE assay consists of the following reagents:

- IgE Common Kit:
    - Diluent A (human serum albumin in buffer with preservative)
    - Conjugate IgE (horse radish peroxidase labeled mouse monoclonal anti-IgE antibody with preservative)
    - Substrate A
    - Substrate B
    - Fluo Beads (streptavidin coated magnetic particles with preservative)

- Capture Reagent Pack

- Brazil Nut - F018, *Bertholletia excelsa*
- Coconut - F036, *Cocos nucifera*
- Tuna - F040, *Thunnus sp.*
- Salmon - F041, *Salmo salar*
- Egg Yolk - F075, *Gallus gallus*
- Pecan Nut - F201, *Carya illinoensis*
- Pistachio Nut - F203, *Pistacia vera*
- Oyster - F290, *Ostrea edulis*

- IgE Calibrator Set (six levels: 0.07, 0.35, 0.70, 3.5, 17.5, 100 kU/L)
- IgE Calibrator Antibody Pack (mouse monoclonal anti-human IgE with preservative)
- IgE Positive Control Pack (known to be >0.35 kU/L)
- IgE Negative Control Packs (known to be <0.35 kU/L)
- Others:
  - Probe Wash Pack (phosphate buffered citric acid solution with preservative)
  - Wash Buffer Concentrate Pack (10X phosphate buffer saline solution with preservative)
  - Cuvette Wash Pack (citric acid solution with preservative)

B Principle of Operation:

The NOVEOS Specific IgE assay is an immunometric, chemiluminescent procedure for the quantitative determination of IgE of known specificity in human serum samples. It employs fluorescent labelled magnetic, streptavidin coated microparticles which are incubated with a biotinylated allergenic capture reagent, patient sample and monoclonal anti-human IgE antibody labeled with horseradish peroxidase (Conjugate IgE). The beads are collected by using a magnetic field to remove the liquid, and then undergo a wash step to remove unbound biotinylated allergen prior to incubation with the sample. If present in the sample, sIgE binds to the captured biotinylated allergen. After incubation, the beads are washed and subsequently incubated with an horseradish peroxidase (HRP)-labeled anti-IgE monoclonal antibody (Conjugate IgE) to form an antibody-conjugate complex that is bound to the captured biotinylated allergen. After washing away the non-bound conjugate, a chemiluminescent substrate is added to the assay mixture resulting in light generation in proportion to the amount of antibody-conjugate that has been bound to the beads. The fluorescence is used to correct for any bead loss during the assay, and the (corrected) chemiluminescence is compared to a calibration curve to provide quantification of bound sIgE. The higher the value of chemiluminescent signal detected by the instrument, the higher the amount of sIgE detected in the sample tested. The concentration of allergen specific IgE is determined from a standard curve, which is traceable to the World Health Organization (WHO) reference reagent serum Immunoglobulin E (IgE) 11/234.

V Substantial Equivalence Information:

A Predicate Device Name(s):

ImmunoCAP Specific IgE Assay

B Predicate 510(k) Number(s):

K051218

C Comparison with Predicate(s):

Device & Predicate Device(s):	K260059 (Candidate Device)	K051218 (Predicate Device)
Device Trade Name	NOVEOS Specific IgE	ImmunoCAP Specific IgE
General Device Characteristic Similarities		
Intended Use/ Indications For Use	The NOVEOS Specific IgE assay is an *in vitro* quantitative assay for the measurement of allergen specific IgE in human serum. NOVEOS Specific IgE assay is to be used with the NOVEOS Immunoassay Analyzer. It is intended for use as an *in vitro* diagnostic 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 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.
Assay Type	Quantitative	Same
Traceability	WHO reference reagent serum Immunoglobulin E (IgE) 11/234	Same
Calibration Method	Heterologous interpolation based on Total IgE calibration curve	Same
Reaction Temperature	37°C	Same
Limit of Quantitation	0.10 kU/L	Same
General Device Characteristic Differences		
Solid Phase	Magnetic microparticles	Cellulose derivative
Assay Principle	Chemiluminescent assay	Fluoroenzyme-immunoassay
Instrument(s)	NOVEOS Immunoassay Analyzer	Phadia 100, Phadia 250/1000/2500/5000
Specimen Type	Serum	Serum or plasma (EDTA, Na-Heparin)
Specimen Volume	4 µL	40 µL
Detection Antibody	HRP-conjugated mouse anti-human IgE monoclonal antibody	β-Galactosidase-anti-human IgE (mouse monoclonal antibody)
Calibrator levels	6 levels: 0.07, 0.35, 0.7, 3.5, 17.5, 100 kU/L	6 levels: 0, 0.35, 0.7, 3.5, 17.5, 100 kU/L
Time to First Result	1 hour and 45 minutes	1 hour and 45 minutes to 2 hours and 30 minutes depending on model

VI Standards/Guidance Documents Referenced:

The following Clinical and Laboratory Standards Institute (CLSI) guidelines were used:

- CLSI I/LA20-A3: Performance Characteristics, Quality Assurance, and Clinical Utility of Immunological Assays for Human Immunoglobulin E Antibodies and Defined Allergen Specificities, Approved Guideline – Third Edition
- CLSI EP05-A3: Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline – Third Edition.
- CLSI EP06, 2nd ed.: Evaluation of Linearity of Quantitative Measurement, Approved Guideline – Second Edition
- CLSI EP07, 3rd ed.: Interference Testing in Clinical Chemistry; Approved Guideline –Third Edition
- CLSI EP17-A2: Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline – Second Edition
- CLSI EP25, 2nd ed: Evaluation of Stability of In Vitro Medical Laboratory Test Reagent Reagents– Second Edition
- CLSI EP28-A3c: Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline – Third Edition
- CLSI EP37, Supplemental Tables for Interference Testing in Clinical Chemistry – First Edition

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

   a. Within-laboratory precision

   The within-laboratory precision study was conducted per CLSI EP05-A3 for each of eight NOVEOS Specific IgE assays. A panel of four to six human sera that include two negative samples were tested in duplicate per run, two runs per day for 20 days using one reagent lot on one to two NOVEOS Immunoassay Analyzers (for a total of 80 replicates per sample except for the highest samples of F018, F036, F041, F075, and F201; the second highest sample of F040; and the lowest sample of F203). The standard deviation (SD) and %CV of the within-run, between-run, between-day, and total within-laboratory imprecision were calculated for each sample. The within-laboratory precision results for each NOVEOS Specific IgE assay are summarized in the following tables:

NOVEOS Specific IgE, F018, Brazil Nut										
Sample	**Mean (kU/L)**	**N**	**Within-Run**		**Between-Run**		**Between-Day**		**Total**	
			SD	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**
1	0.10	80	0.01	14.4	0.00	0.0	0.01	12.3	0.02	19.1
2	0.33	80	0.01	3.9	0.01	2.3	0.01	3.1	0.02	5.5
3	0.85	80	0.03	3.7	0.01	1.1	0.03	3.5	0.04	5.2
4	89.39	95*	6.56	7.3	8.44	9.4	4.25	4.8	11.50	12.9

* Sample 4 was tested in five replicates for Run 1 and two replicates for Run 2 for five days, and in two replicates per run with two runs per day for 15 days, yielding N=95 datapoints

NOVEOS Specific IgE, F036, Coconut										
Sample	**Mean (kU/L)**	**N**	**Within-Run**		**Between-Run**		**Between-Day**		**Total**	
			SD	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**
1	0.14	80	0.01	5.9	0.01	4.5	0.01	8.3	0.02	11.2
2	0.27	80	0.02	8.4	0.00	0.0	0.01	5.0	0.03	9.8
3	1.40	80	0.04	2.5	0.07	5.1	0.00	0.0	0.08	5.7
4	78.78	95*	4.67	5.9	5.61	7.1	4.31	5.5	8.47	10.8

* Sample 4 was tested in five replicates for Run 1 and two replicates for Run 2 for five days, and in two replicates per run with two runs per day for 15 days, yielding N=95 datapoints

NOVEOS Specific IgE, F040, Tuna										
Sample	**Mean (kU/L)**	**N**	**Within-Run**		**Between-Run**		**Between-Day**		**Total**	
			SD	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**
1	0.14	80	0.02	11.0	0.00	0.0	0.02	11.7	0.02	16.0
2	0.30	80	0.02	5.8	0.01	4.4	0.02	7.0	0.03	10.1
3	2.41	80	0.09	3.6	0.10	4.1	0.05	2.1	0.14	5.9
4	9.97	80	0.46	4.6	0.24	2.4	0.24	2.4	0.57	5.7
5	47.32	95*	2.84	6.0	0.91	1.9	0.51	1.1	3.03	6.4
6	73.33	80	4.92	6.7	3.70	5.0	1.55	2.1	6.35	8.7

* Sample 5 was tested in five replicates for Run 1 and two replicates for Run 2 for five days, and in two replicates per run with two runs per day for 15 days, yielding N=95 datapoints

NOVEOS Specific IgE, F041, Salmon										
Sample	**Mean (kU/L)**	**N**	**Within-Run**		**Between-Run**		**Between-Day**		**Total**	
			SD	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**
1	0.17	80	0.01	6.5	0.01	7.8	0.02	9.5	0.02	13.9
2	0.24	80	0.01	5.2	0.01	4.5	0.01	5.0	0.02	8.5
3	1.25	80	0.04	3.3	0.05	3.7	0.05	4.0	0.08	6.4
4	9.68	80	0.38	3.9	0.23	2.3	0.27	2.8	0.51	5.3
5	86.34	95*	3.55	4.1	3.55	4.1	0.75	0.9	5.07	5.9

* Sample 5 was tested in five replicates for Run 1 and two replicates for Run 2 for five days, and in two replicates per run with two runs per day for 15 days, yielding N=95 datapoints

NOVEOS Specific IgE, F075, Egg Yolk										
Sample	**Mean (kU/L)**	**N**	**Within-Run**		**Between-Run**		**Between-Day**		**Total**	
			SD	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**
1	0.17	80	0.02	8.7	0.00	2.5	0.02	9.7	0.02	13.3
2	0.27	80	0.01	5.0	0.01	3.7	0.01	4.3	0.02	7.6
3	1.44	80	0.08	5.5	0.00	0.0	0.05	3.5	0.09	6.5
4	82.22	95*	4.56	5.5	3.59	4.4	1.85	2.3	6.09	7.4

* Sample 4 was tested in five replicates for Run 1 and two replicates for Run 2 for five days, and in two replicates per run with two runs per day for 15 days, yielding N=95 datapoints

NOVEOS Specific IgE, F201, Pecan Nut										
Sample	**Mean (kU/L)**	**N**	**Within-Run**		**Between-Run**		**Between-Day**		**Total**	
			SD	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**
1	0.17	80	0.01	7.8	0.01	4.8	0.01	6.1	0.02	10.9
2	0.32	80	0.02	5.0	0.01	3.0	0.01	3.9	0.02	6.7
3	1.38	80	0.07	5.1	0.04	3.1	0.06	4.2	0.08	6.1

NOVEOS Specific IgE, F201, Pecan Nut										
Sample	**Mean (kU/L)**	**N**	**Within-Run**		**Between-Run**		**Between-Day**		**Total**	
			SD	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**
4	1.47	80	0.07	4.5	0.05	3.5	0.04	2.8	0.08	5.4
5	97.84	97*	4.72	4.8	7.51	7.7	2.47	2.5	9.20	9.4

* Sample 5 was tested in two replicates for Run 1 and five replicates for Run 2 for five days; in two replicates for Run 1 and four replicates for Run 2 for one day, and in two replicates per run with two runs per day for 14 days, yielding N=97 datapoints

NOVEOS Specific IgE, F203, Pistachio Nut										
Sample	**Mean (kU/L)**	**N**	**Within-Run**		**Between-Run**		**Between-Day**		**Total**	
			SD	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**
1	0.16	83*	0.02	10.7	0.00	1.0	0.02	10.3	0.02	14.8
2	0.32	80	0.02	4.9	0.00	0.7	0.02	6.8	0.03	8.5
3	2.21	80	0.12	5.6	0.00	0.0	0.08	3.7	0.15	6.7
4	89.75	80	3.11	3.5	2.49	2.8	3.54	3.9	5.33	5.9

* Sample 1 was tested in two replicates per run with two runs per day for 21 days, with exclusion of 1 outlier for Day 12, yielding N=83 datapoints

NOVEOS Specific IgE, F290, Oyster										
Sample	**Mean (kU/L)**	**N**	**Within-Run**		**Between-Run**		**Between-Day**		**Total**	
			SD	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**
1	0.16	80	0.01	6.6	0.01	5.0	0.02	9.7	0.02	12.8
2	0.31	80	0.03	8.6	0.01	3.7	0.02	5.6	0.03	10.9
3	1.44	80	0.04	2.9	0.04	2.9	0.02	1.4	0.06	4.3
4	75.65	80	2.99	4.0	2.41	3.2	1.96	2.6	4.31	5.7

b. Lot-to-lot imprecision

A panel of four to six serum samples were tested with three different lots of each NOVEOS Specific IgE assay. The samples were tested in replicates of five per run, one run per day, for five days, to generate a total of 75 replicates (except for a low positive sample for F018) per sample for all three lots. The results are summarized in the following tables:

NOVEOS Specific IgE, F018, Brazil Nut										
Sample	**Mean (kU/L)**	**N**	**Within-Run**		**Between-Day**		**Between-Lot**		**Total**	
			SD	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**
1	0.22	75	0.01	4.4	0.01	5.2	0.00	2.3	0.02	7.2
2	0.55	79*	0.03	5.3	0.02	3.9	0.01	1.2	0.04	6.6
3	0.90	75	0.04	4.0	0.01	1.6	0.01	1.0	0.04	4.4
4	86.39	75	6.29	7.3	5.18	6.0	0.00	0.0	8.15	9.4

* Sample 2 was tested in five replicates per run with one run per day for six days, with exclusion of 1 outlier for Day 5 in Lot 1, yielding N=79 datapoints

NOVEOS Specific IgE, F036, Coconut										
Sample	**Mean (kU/L)**	**N**	**Within-Run**		**Between-Day**		**Between-Lot**		**Total**	
			SD	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**
1	0.18	75	0.01	4.3	0.01	5.6	0.01	6.5	0.01	6.5
2	0.66	75	0.03	4.0	0.04	5.8	0.04	6.1	0.04	6.1
3	1.75	75	0.07	4.2	0.08	4.4	0.13	7.2	0.13	7.2
4	74.80	75	4.23	5.7	1.59	2.1	2.59	3.5	5.21	7.0

NOVEOS Specific IgE, F040, Tuna										
Sample	**Mean (kU/L)**	**N**	**Within-Run**		**Between-Day**		**Between-Lot**		**Total**	
			SD	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**
1	0.13	75	0.02	15.7	0.01	9.1	0.00	0.0	0.02	18.2
2	0.52	75	0.02	4.7	0.02	3.8	0.00	0.0	0.03	6.0
3	2.52	75	0.09	3.4	0.07	2.9	0.03	1.3	0.12	4.7
4	10.48	75	0.33	3.1	0.29	2.7	0.00	0.0	0.44	4.2
5	47.75	75	3.09	6.5	0.94	2.0	0.43	0.9	3.26	6.8
6	87.62	75	5.77	6.6	1.36	1.6	1.00	1.1	6.01	6.9

NOVEOS Specific IgE, F041, Salmon										
Sample	**Mean (kU/L)**	**N**	**Within-Run**		**Between-Day**		**Between-Lot**		**Total**	
			SD	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**
1	0.16	75	0.02	15.5	0.01	5.4	0.01	5.7	0.03	17.4
2	0.46	75	0.02	5.0	0.02	4.6	0.00	0.0	0.03	6.8
3	1.22	75	0.07	6.1	0.06	5.3	0.00	0.0	0.10	8.0
4	9.08	75	0.35	3.8	0.33	3.7	0.02	0.2	0.48	5.3
5	87.89	75	5.01	5.7	1.21	1.3	1.95	2.2	5.49	6.2

NOVEOS Specific IgE, F075, Egg Yolk										
Sample	**Mean (kU/L)**	**N**	**Within-Run**		**Between-Day**		**Between-Lot**		**Total**	
			SD	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**
1	0.23	75	0.02	9.3	0.02	6.5	0.00	0.0	0.03	11.4
2	0.50	75	0.02	4.4	0.02	3.2	0.01	2.4	0.03	6.0
3	1.51	75	0.03	2.1	0.06	3.9	0.05	3.5	0.09	5.7
4	85.74	75	4.02	4.7	2.79	3.2	2.55	3.0	5.52	6.4

NOVEOS Specific IgE, F201, Pecan Nut										
Sample	**Mean (kU/L)**	**N**	**Within-Run**		**Between-Day**		**Between-Lot**		**Total**	
			SD	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**
1	0.12	75	0.01	10.6	0.01	7.5	0.01	7.7%	0.02	15.1
2	0.41	75	0.02	4.2	0.03	7.2	0.00	0.0%	0.03	8.3
3	1.19	75	0.05	4.4	0.03	2.3	0.00	0.0%	0.06	5.0
4	93.39	75	5.04	5.4	6.13	6.6	0.00	0.0%	7.94	8.5

NOVEOS Specific IgE, F203, Pistachio Nut										
Sample	**Mean (kU/L)**	**N**	**Within-Run**		**Between-Day**		**Between-Lot**		**Total**	
			SD	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**
1	0.20	75	0.02	11.5	0.02	12.2	0.00	0.0	0.03	16.8
2	0.52	75	0.02	4.7	0.03	5.1	0.00	0.0	0.04	7.0
3	2.25	75	0.07	3.1	0.07	3.2	0.04	1.6	0.11	4.8
4	87.38	75	3.73	4.3	2.65	3.0	1.08	1.2	4.70	5.4

NOVEOS Specific IgE, F290, Oyster										
Sample	**Mean (kU/L)**	**N**	**Within-Run**		**Between-Day**		**Between-Lot**		**Total**	
			SD	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**
1	0.17	75	0.01	5.9	0.02	11.6	0.00	0.0	0.02	13.0
2	0.55	75	0.02	3.5	0.03	6.2	0.00	0.0	0.04	7.1
3	1.50	75	0.05	3.1	0.05	3.6	0.00	0.0	0.07	4.7
4	79.36	75	2.73	3.4	3.03	3.8	0.00	0.0	4.08	5.1

2. Linearity:

Linearity of each NOVEOS Specific IgE assay was evaluated in accordance with the CLSI guideline I/LA20-A3. Three sets of overlapping linearity dilution panels were prepared to create six concentration levels in each dilution series by using three positive human serum samples (low, mid, and high) diluted with one negative serum sample. Testing was performed using one to two lots of each NOVEOS Specific IgE assay in four replicates of each sample. The linearity data analysis was performed individually for each NOVEOS Specific IgE assay in accordance with the CLSI EP06, 2nd Edition. For each sample level in the dilution panels, the mean value of the measured values, the predicted value and the %deviation from linearity were calculated.

The linear range and claimed analytical mearing range for each NOVEOS Specific IgE assay are shown in the table below:

NOVEOS Specific IgE	Tested Linear Range	Analytical Measuring Range
F018, Brazil Nut	0.08 – 93.96 kU/L	0.10 – 93 kU/L
F036, Coconut	0.06 – 108.26 kU/L	0.10 – 100 kU/L
F040, Tuna	0.08 – 99.32 kU/L	0.10 – 99 kU/L
F041, Salmon	0.07 – 90.06 kU/L	0.10 – 90 kU/L
F075, Egg Yolk	0.06 – 110.79 kU/L	0.10 – 100 kU/L
F201, Pecan Nut	0.08 – 121.37 kU/L	0.10 – 100 kU/L
F203, Pistachio Nut	0.09 – 93.41 kU/L	0.10 – 93 kU/L
F290, Oyster	0.07 – 109.86 kU/L	0.10 – 100 kU/L

3. Analytical Specificity/Interference:

a. Inhibition study:

Immunological specificity of each NOVEOS Specific IgE assay was verified through competitive inhibition study in accordance with CLSI I/LA20-A3. Positive samples with specific IgE concentrations used in the study include: 6.13 kU/L for F018, Brazil Nut;

0.84 kU/L for F036, Coconut; 2.12 kU/L and 2.22 kU/L for F040, Tuna (tested on two separate occasions); 4.05 kU/L for F041, Salmon; 4.68 kU/L for F075, Egg Yolk; 15.27 kU/L for F201, Pecan Nut; 5.14 kU/L for F203, Pistachio Nut; and 2.31 kU/L for F290, Oyster.

The allergen solution (inhibitor) was diluted 1:1 into the positive sample and subsequently serially diluted five times in two-fold increments. Each diluted sample was evaluated for dose-dependent inhibition in replicates of five using one lot of each NOVEOS Specific IgE assay. The results of the dose-dependent inhibition study demonstrated concentration-dependent inhibition for all allergens tested, with substantial inhibition observed at the following inhibitor concentrations: 91% inhibition for F018 at 1.56 µg/mL, 87% inhibition for F036 at 50 µg/mL, 68% inhibition for F040 at 200 µg/mL, which is near the beginning of the observed plateau in the dose-response curve, 88% inhibition for F041 at 3.125 µg/mL, 97% inhibition for F075 at 1.56 µg/mL, 84% inhibition for F201 at 50 µg/mL, 86% inhibition for F203 at 12.5 µg/mL, and 86% inhibition for F290 at 1.56 µg/mL.

For each NOVEOS Specific IgE assay, except F040, related and unrelated allergen inhibitors were tested in a single-dose competitive inhibition study at a concentration at least 10 times the final concentration that achieved ≥85% inhibition for the allergen under evaluation. The related and unrelated allergens tested for each assay were as follows:

- For F018, Brazil Nut, the related allergen F040 (Yellowfin Tuna) and the unrelated allergens E003 (Horse Epithelia), I006 (German Cockroach), and M006 (*Alternaria alternata*) were tested as potential inhibitors. All inhibitors were spiked into the positive serum sample at a 1:1 dilution at a final concentration of 15.63 µg/mL and evaluated with one lot of NOVEOS Specific IgE assay, F018. The results of the single-dose inhibition studies showed ≤15% inhibition for the related and unrelated allergen inhibitors. The inhibition studies indicate that the NOVEOS Specific IgE assay, F018 contains the immunologically relevant allergen.

- For F036, Coconut, the related allergen F041 (Atlantic Salmon) and the unrelated allergens E003 (Horse Epithelia), I006 (German Cockroach), and M006 (*Alternaria alternata*) were tested as potential inhibitors at a final concentration of 500 µg/mL and evaluated with one lot of NOVEOS Specific IgE assay, F036. The results of the single-dose inhibition studies showed ≤15% inhibition for the related and unrelated allergen inhibitors. The inhibition studies indicate that the NOVEOS Specific IgE assay, F036 contains the immunologically relevant allergen.

- For F040, Tuna, the related allergen F020 (Almond) and the unrelated allergens E070 (Goose Feathers/Skin), I006 (German Cockroach), and W013 (Cocklebur Pollen) were tested as potential inhibitors. The related inhibitor F020 and the unrelated inhibitors were tested with one lot of NOVEOS Specific IgE assay, F040. The results of the single-dose inhibition studies showed ≤15% inhibition for the related and unrelated allergen inhibitors. The inhibition studies indicate that the NOVEOS Specific IgE assay, F040 contains the immunologically relevant allergen.

- For F041, Salmon, the related allergen F014 (Soybean) and the unrelated allergens D201 (*Blomia tropicalis*), I006 (German Cockroach), and M005 (*Candida albicans*) were tested as potential inhibitors at a final concentration of 31.25 µg/mL and evaluated with one lot of NOVEOS Specific IgE assay, F041. The results of the single-dose inhibition studies showed ≤15% inhibition for the related and unrelated allergen inhibitors. The inhibition studies indicate that the NOVEOS Specific IgE assay, F041 contains the immunologically relevant allergen.

- For F075, Egg Yolk, the related allergen F083 (Chicken Meat) and the unrelated allergens K082 (Latex), M006 (*Alternaria alternata*), and T218 (Virginia Live Oak) were tested as potential inhibitors at a final concentration of 15.63 µg/mL and evaluated with one lot of NOVEOS Specific IgE assay, F075. The results of the single-dose inhibition studies showed ≤15% inhibition for the related and unrelated allergen inhibitors. The inhibition studies indicate that the NOVEOS Specific IgE assay, F075 contains the immunologically relevant allergen.

- For F201, Pecan Nut, the related allergen F003 (Atlantic Cod) and the unrelated allergens E003 (Horse Epithelia), I006 (German Cockroach), and M006 (*Alternaria alternata*) were tested as potential inhibitors. The related inhibitor F003 was tested at a final concentration of 555 µg/mL and the unrelated inhibitors were tested at final concentrations ranging from 510 to 830 µg/mL, evaluated with one lot of NOVEOS Specific IgE assay, F201. The results of the single-dose inhibition studies showed ≤15% inhibition for the related and unrelated allergen inhibitors. The inhibition studies indicate that the NOVEOS Specific IgE assay, F201 contains the immunologically relevant allergen.

- For F203, Pistachio Nut, the related allergen F020 (Almond) and the unrelated allergens D201 (*Blomia tropicalis*), E070 (Goose Feathers/Skin), and M005 (*Candida albicans*) were tested as potential inhibitors at a final concentration of 125 µg/mL and evaluated with one lot of NOVEOS Specific IgE assay, F203. The results of the single-dose inhibition studies showed ≤15% inhibition for the related and unrelated allergen inhibitors. The inhibition studies indicate that the NOVEOS Specific IgE assay, F203 contains the immunologically relevant allergen.

- For F290, Oyster, the related allergen F003 (Atlantic Cod) and the unrelated allergens E003 (Horse Epithelia), K082 (Latex), and M005 (*Candida albicans*) were tested as potential inhibitors at a final concentration of 15.63 µg/mL and evaluated with one lot of NOVEOS Specific IgE assay, F290. The results of the single-dose inhibition studies showed ≤15% inhibition for the related and unrelated allergen inhibitors. The inhibition studies indicate that the NOVEOS Specific IgE assay, F290 contains the immunologically relevant allergen.

b. Interference:

i. Endogenous Substance Interference:

The effect of the presence of elevated levels of human serum albumin, hemoglobin, triglyceride, conjugated bilirubin, and unconjugated bilirubin in serum samples was

evaluated by testing three serum sample pools (one negative, one near the cut-off, and one positive) spiked with varying levels of each interferent. Testing was conducted with seven replicates in one assay run using one lot each of the NOVEOS Specific IgE assays for F018 (Brazil Nut), F036 (Coconut), F040 (Tuna), F041 (Salmon), F075 (Egg Yolk), F201 (Pecan Nut), F203 (Pistachio Nut), and F290 (Oyster). The % Interference for each sample spiked with the potential interfering substance was calculated by comparing its result to that of the corresponding control sample spiked with an equal volume of the solvent without the interfering substance. No interference was noted for samples containing human serum albumin up to 120 g/L, hemoglobin up to 200 mg/dL, intralipid up to 3000 mg/dL, conjugated bilirubin up to 30 mg/dL, and unconjugated bilirubin up to 20 mg/dL.

ii. Exogenous Substance Interference:

Refer to K200825.

c. Cross-reactivity:

The potential cross-reactivity of non-IgE (IgA, IgD, IgG, and IgM) to the NOVEOS sIgE assays was evaluated in K200825.

4. Assay Reportable Range:

The assay reportable range is the same as the claimed analytical measuring range for each NOVEOS Specific IgE assay as shown in the table below:

NOVEOS Specific IgE	Assay Reportable Range/ Analytical Measuring Range
F018, Brazil Nut	0.10 – 93 kU/L
F036, Coconut	0.10 – 100 kU/L
F040, Tuna	0.10 – 99 kU/L
F041, Salmon	0.10 – 90 kU/L
F075, Egg Yolk	0.10 – 100 kU/L
F201, Pecan Nut	0.10 – 100 kU/L
F203, Pistachio Nut	0.10 – 93 kU/L
F290, Oyster	0.10 – 100 kU/L

5. Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):

a. Traceability:

The IgE calibrators are traceable to the World Health Organization (WHO) third International Standard 11/234 of Human Serum Immunoglobulin E.

b. Kit stability:

The stability study was conducted in accordance with CLSI EP25-A2.

Shelf-life stability: A real-time stability study for the NOVEOS Specific sIgE Capture Reagent Pack of F018 (Brazil Nut), F036 (Coconut), F040 (Tuna), F041 (Salmon), F075 (Egg Yolk), F201 (Pecan Nut), F203 (Pistachio Nut), and F290 (Oyster) stored at 2–8°C is ongoing using three lots. The study was planned by testing two positive samples and one negative sample. An accelerated stability study was conducted with two positive samples and one negative sample using three lots of each capture reagent stored at 37°C to predict shelf-life stability of 36 months for these capture reagents if stored at 2–8°C.

All other reagents required to perform specific IgE testing on the NOVEOS system are not allergen-specific and the shelf-life stability of these reagents has been previously established per K182479 and K191510 (for the Fluo Beads reagent).

On-board stability: A study was performed on one instrument using three samples (two positive and one negative or low-level sample) using at least one lot of each NOVEOS Specific IgE Capture Reagent Pack F018 (Brazil Nut), F036 (Coconut), F040 (Tuna), F041 (Salmon), F075 (Egg Yolk), F201 (Pecan Nut), F203 (Pistachio Nut), and F290 (Oyster) stored on the NOVEOS Immunoassay Analyzer. The test was done by testing each sample in three replicates at Day 0 and scheduled timepoints of 15, 28, and 29 days. The result supports that the allergen-specific capture reagent is stable for 28 days stored on-board. The result supports that the allergen-specific capture reagent is stable for 28 days once opened and stored at 2–8°C.

The on-board stability for all the other assay components has been previously established per K182479.

Open-vial stability: Both an ongoing real-time stability study and an accelerated stability study were performed for NOVEOS sIgE allergens F018 (Brazil Nut), F036 (Coconut), F040 (Tuna), F041 (Salmon), F075 (Egg Yolk), F201 (Pecan Nut), F203 (Pistachio Nut), and F290 (Oyster). The allergen-specific capture reagent is stable for 15 days once opened and stored at 2–8°C.

6. Detection Limit:

The limit of blank (LoB), limit of detection (LoD), and limit of quantitation (LoQ) of each NOVEOS Specific IgE assay, i.e., F018 (Brazil Nut), F036 (Coconut), F040 (Tuna), F041 (Salmon), F075 (Egg Yolk), F201 (Pecan Nut), F203 (Pistachio Nut), and F290 (Oyster) on the NOVEOS Immunoassay Analyzer were determined according to CLSI guideline EP17-A2.

LoB:
The LoB was determined by testing four analyte-free human serum samples in replicates of five per run, over three runs, with one run per day, using two lots on one NOVEOS Immunoassay Analyzer, for a total of 60 replicates per lot of F018, F036, F040, F041, F075, F201, and F203. For F290, four analyte-free human serum samples were tested in replicates of five per run for two runs, and ten replicates per run for one run, with one run per day, for a total of 80 replicates per lot. The LoB was estimated as the 95th percentile of the 60 to 80 measurements for each of the two lots tested.

LoD:
The LoD was determined by the testing protocol summarized in the table below and calculated based on CLSI EP17-A2:

NOVEOS Specific IgE	No. of Samples	No. of Lots	No. of Analyzers	Testing Protocol
F018	5	2	1	5 samples x 5 replicates/run x 3 runs (n=75/Lot)
F036	4	2	1	4 samples x 5 replicates/run x 3 runs (n= 60/Lot)
F040	5	2	1	Lot 1: 5 samples x 5 replicates/run x 3 runs (n=80*) Lot 2: 5 samples x 5 replicates/run x 3 runs (n= 95**) ** One sample had 1 additional replicate, and one sample had 4 additional replicates, for a total of 5 additional replicates.* ***Three samples had 5 additional replicates, one sample had 4 additional replicates, and one sample had 1 additional replicate, for a total of 20 additional replicates.*
F041	5	2	1	5 samples x 5 replicates/run x 3 runs (n=75/Lot)
F075	4	2	1	Lot 1: 4 samples x 5 replicates/run x 3 runs (n= 62*) Lot 2: 4 samples x 5 replicates/run x 3 runs (n= 60) ** Two samples had one additional replicate.*
F201	5	2	1	5 samples x 5 replicates/run x 3 runs (n=75/Lot)
F203	5	2	1	5 samples x 5 replicates/run x 3 runs (n=75/Lot)
F290	6	2	1	6 samples x 5 replicates/run x 3 runs (n=90/Lot)

LoQ:
The LoQ was determined by testing four to six low IgE samples with one to ten replicates per run over three to four testing days, with one run per day using two lots of each capture reagent on one NOVEOS Immunoassay Analyzer, resulting in a total of 60 to 95 replicates across all samples per lot. Data analysis was performed according to the precision profile method using within-lab precision results. The LoQ is defined as the mean value of the lowest sample which fulfills the specification for the total within-laboratory imprecision <20%CV.

The claimed LoB, LoD, and LoQ are based on the highest value obtained from the two lots tested and are summarized in the table below.

NOVEOS Specific IgE	LoB (kU/L)	LoD (kU/L)	LoQ (kU/L)
F018, Brazil Nut	0.07	0.10	0.10
F036, Coconut	0.07	0.09	0.10
F040, Tuna	0.07	0.08	0.10
F041, Salmon	0.07	0.08	0.10
F075, Egg Yolk	0.07	0.08	0.10
F201, Pecan Nut	0.07	0.09	0.10
F203, Pistachio Nut	0.07	0.09	0.10
F290, Oyster	0.07	0.09	0.10

7. Assay Cut-Off:

See clinical cut-off

B Comparison Studies:

1. Method Comparison with Predicate Device:

   Refer to clinical study section below.

2. Matrix Comparison:

   Not Applicable

C Clinical Studies:

1. Clinical Sensitivity and Specificity:

   For each NOVEOS Specific IgE assay, the clinical performance was evaluated by comparing the test results from a cohort of atopic and non-atopic samples to the clinical diagnosis of allergy. The atopic samples were from different U.S. and EU vendors with a clinical history of allergy-like symptoms and identified as positive by oral food challenge (OFC) or diagnosed positive by a physician. The non-atopic samples were from donors with no reported allergy and were deemed negative by ImmunoCAP testing (<0.35 kU/L). The specific IgE test results are expressed as positive or negative using a cut-off of 0.35 kU/L. The clinical sensitivity and clinical specificity for each NOVEOS Specific IgE assay are summarized in the following tables:

		Clinical Diagnosis		
		Atopic	**Non-atopic**	**Total**
NOVEOS Specific IgE, F018, Brazil Nut	**Positive**	31	0	31
	Negative	3	126	129
	Total	34	126	160
Clinical Sensitivity: 91.2% (31/34) (95% CI: 77.0 – 97.0%) Clinical Specificity: 100.0% (126/126) (95% CI: 97.0 – 100.0%)				

		Clinical Diagnosis		
		Atopic	**Non-atopic**	**Total**
NOVEOS Specific IgE, F036, Coconut	**Positive**	33	0	33
	Negative	7	125	132
	Total	40	125	165
Clinical Sensitivity: 82.5% (33/40) (95% CI: 68.1 – 91.3%) Clinical Specificity: 100.0% (125/125) (95% CI: 97.0 – 100.0%)				

		Clinical Diagnosis		
		Atopic	**Non-atopic**	**Total**
NOVEOS Specific IgE, F040, Tuna	**Positive**	35	0	35
	Negative	15	121	136
	Total	50	121	171
Clinical Sensitivity: 70.0%* (35/50) (95% CI: 56.2 – 80.9%) Clinical Specificity: 100.0% (121/121) (95% CI: 96.9 – 100.0%)				

* For the observed low sensitivity, the literature from Schulkes KJG *et al*. Clinical and Translational Allergy. 2014,4:27 reported clinical sensitivity of 67% and clinical specificity of 43% analyzed by ImmunoCAP.

		Clinical Diagnosis		
		Atopic	**Non-atopic**	**Total**
NOVEOS Specific IgE, F041, Salmon	**Positive**	35	0	35
	Negative	7	125	132
	Total	42	125	167
Clinical Sensitivity: 83.3% (35/42) (95% CI: 69.4 – 91.7%) Clinical Specificity: 100.0% (125/125) (95% CI: 97.0 – 100.0%)				

		Clinical Diagnosis		
		Atopic	**Non-atopic**	**Total**
NOVEOS Specific IgE, F075, Egg Yolk	**Positive**	28	0	28
	Negative	3	126	129
	Total	31	126	157
Clinical Sensitivity: 90.3% (28/31) (95% CI: 75.1 – 96.7%) Clinical Specificity: 100.0% (126/126) (95% CI: 97.0 – 100.0%)				

		Clinical Diagnosis		
		Atopic	**Non-atopic**	**Total**
NOVEOS Specific IgE, F201, Pecan Nut	**Positive**	30	0	30
	Negative	5	126	131
	Total	35	126	161
Clinical Sensitivity: 85.7% (30/35) (95% CI: 70.6 – 93.7%) Clinical Specificity: 100.0% (126/126) (95% CI: 97.0 – 100.0%)				

		Clinical Diagnosis		
		Atopic	**Non-atopic**	**Total**
NOVEOS Specific IgE, F203, Pistachio Nut	**Positive**	34	0	34
	Negative	2	121	123
	Total	36	121	157
Clinical Sensitivity: 94.4% (34/36) (95% CI: 81.9 – 98.5%) Clinical Specificity: 100.0% (121/121) (95% CI: 96.9 – 100.0%)				

		Clinical Diagnosis		
		Atopic	**Non-atopic**	**Total**
NOVEOS Specific IgE, F290, Oyster	**Positive**	29	1	30
	Negative	9	124	133
	Total	38	125	163
Clinical Sensitivity: 76.3% *(29/38) (95% CI: 60.8 – 87.0%) Clinical Specificity: 99.2% (124/125) (95% CI: 95.6 – 99.9%)				

* For NOVEOS Specific IgE, F290, Oyster, all samples were also tested with the corresponding predicate device, ImmunoCAP Specific IgE. The clinical sensitivity is 76.3% (95% CI: 60.8 – 87.0%) and clinical specificity 100.0% (95% CI: 97.0 – 100.0%) with ImmunoCAP Specific IgE.

2. Other Clinical Supportive Data (When 1. and 2. Are Not Applicable):

Not Applicable

D Clinical Cut-Off:

The clinical cut-off of the assay is 0.35 kU/L. The interpretation of results of the Specific IgE assay uses the following classification system:

Class	Concentration (kU/L)	Interpretation
0	<0.35	Negative
I	0.35 to <0.70	Positive with increasing sIgE concentration
II	0.70 to <3.50	
III	3.50 to <17.50	
IV	17.50 to <50.00	
V	50.00 to <100.00	
VI	≥100	

E Expected Values/Reference Range:

The expected value is <0.35 kU/L (negative) for a specific allergen in an apparently healthy (non-atopic) person. Each laboratory should establish its own expected value/reference range.

The reference range of NOVEOS Specific IgE assay for F018 (Brazil Nut), F036 (Coconut), F040 (Tuna), F041 (Salmon), F075 (Egg Yolk), F201 (Pecan Nut), F203 (Pistachio Nut), and F290 (Oyster) in the normal population was evaluated based on the data collected in clinical studies which tested samples from apparently healthy subjects including 120 to 126 non-atopic samples per NOVEOS Specific IgE assay. All samples tested with the NOVEOS Specific IgE assays were below 0.35 kU/L.

VIII Proposed Labeling:

The labeling supports the finding of substantial equivalence for this device.

IX Conclusion:

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