510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K261027

B Applicant

Hycor Biomedical

C Proprietary and Established Names

NOVEOS Specific IgE (sIgE), Capture Reagent F014, Soybean (*Glycine max*)
NOVEOS Specific IgE (sIgE), Capture Reagent F017, Hazelnut (*Corylus avellana)*
NOVEOS Specific IgE (sIgE), Capture Reagent F352, Ara h 8 PR-10, Peanut
NOVEOS Specific IgE (sIgE), Capture Reagent F423, Ara h 2, Peanut
NOVEOS Specific IgE (sIgE), Capture Reagent F447, Ara h 6, Peanut

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:

Five new devices

B Measurand:

Allergen specific IgE to Soybean - F014, *Glycine max*)
Allergen specific IgE to Hazelnut - F017, *Corylus avellana*
Allergen specific IgE to Ara h 8 PR-10, Peanut - F352, Ara h 8
Allergen specific IgE to Ara h 2, Peanut - F423, Ara h 2
Allergen specific IgE to Ara h 6, Peanut - F447, Ara h 6

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
  - Soybean - F014, *Glycine max*
  - Hazelnut - F017, *Corylus avellana*
  - Ara h 8 PR-10, Peanut - F352, Ara h 8

- Ara h 2, Peanut - F423, Ara h 2
- Ara h 6, Peanut - F447, Ara h 6

- 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):	K261027 (Candidate Device)	K051218 (Predicate Device)
Device Trade Name	NOVEOS Specific IgE (sIgE)	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.
Traceability	World Health Organization (WHO) reference reagent serum Immunoglobulin E (IgE) 11/234	Same
Assay Type	Quantitative	Same
Calibration Method	Heterologous interpolation based on Total IgE calibration curve	Same
Reaction Temperature	37°C	Same
Limit of Quantification	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 instrument 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 imprecision

   The within-laboratory precision study was conducted per the CLSI EP05-A3 for each of four NOVEOS Specific IgE assays. A panel of four to five human sera (one to two negative and two to three positive patient samples) were tested in at least duplicates per run, two runs per day for a minimum of 20 days using one reagent lot on one or two NOVEOS Immunoassay Analyzers. 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 20-day within-laboratory precision results for each NOVEOS Specific IgE assay are summarized in the following tables:

NOVEOS Specific IgE, F014, Soybean										
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	6.7	0.01	7.3	0.01	5.0	0.02	11.1
2	0.27	82*	0.02	7.7	0.01	3.3	0.01	3.7	0.02	9.1
3	4.06	80	0.13	3.2	0.11	2.7	0.10	2.5	0.20	4.8
4	92.69	80	3.83	4.1	5.51	5.9	3.54	3.8	7.59	8.2

*Sample 2 had two outliers removed on Day 12 and one additional day was added

NOVEOS Specific IgE, F017, Hazelnut										
Sample	Mean (kU/L)	N	Within-Run		Between-Run		Between-Day		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
1	0.23	80	0.01	4.5	0.01	4.4	0.01	5.2	0.02	8.2
2	0.31	80	0.01	3.0	0.03	10.3	0.01	3.6	0.04	11.3
3	1.37	80	0.04	2.8	0.05	3.9	0.08	6.1	0.11	7.8
4	5.48	80	0.17	3.0	0.27	5.0	0.35	6.4	0.47	8.6
5	88.97	82*	7.35	8.3	5.64	6.3	0.00	0.0	9.26	10.4

*An extra day was tested due to two dropped replicates (incorrect sample loading).

NOVEOS Specific IgE, F352, Ara h 8 PR-10, Peanut										
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	5.4	0.00	2.7	0.02	10.5	0.02	12.1
2	0.27	80	0.02	5.8	0.01	4.7	0.02	5.9	0.03	9.5
3	1.60	80	0.07	4.4	0.01	0.9	0.07	4.2	0.10	6.2
4	6.45	80	0.19	2.9	0.13	2.0	0.21	3.2	0.31	4.7
5	81.42	92*	6.32	7.8	5.25	6.4	2.23	2.7	8.52	10.5

*Sample 5 was tested in five replicates in the first run and two replicates in the second run on each day for four days, and in two replicates per run and two runs per day for the remaining 16 days

NOVEOS Specific IgE, F423, Ara h 2, Peanut										
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	9.9	0.01	5.7	0.01	6.0	0.02	12.9
2	0.32	80	0.03	8.0	0.00	0.0	0.00	0.0	0.03	8.0
3	2.75	80	0.15	5.5	0.06	2.0	0.11	4.0	0.19	7.1
4	77.35	80	4.15	5.4	3.29	4.3	2.37	3.1	5.80	7.5

NOVEOS Specific IgE, F447, Ara h 6, Peanut										
Sample	Mean (kU/L)	N	Within-Run		Between-Run		Between-Day		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
1	0.19	80	0.01	6.2	0.01	4.7	0.01	3.5	0.02	8.5
2	0.50	89*	0.02	4.0	0.02	4.2	0.04	8.1	0.05	10.0
3	4.49	83**	0.34	7.6	0.00	0.0	0.14	3.2	0.37	8.2
4	76.23	80	5.03	6.6	3.84	5.0	3.89	5.1	7.43	9.7

* Sample 2 was tested in five replicates in the first run and two replicates in the second run on each day for 3 days, and in two replicates per run and two runs per day for the remaining 17 days

**Sample 3 had one outlier removed on Day 19 and one additional day was added

b. Lot-to-lot precision

A panel of four to six serum samples tested with three different lots of each NOVEOS sIgE allergen. The samples were tested in replicates of five per run, one run per day, for five to six days, to generate a total of 75 replicates per sample unless otherwise indicated for all three lots. The results are summarized in the following tables:

NOVEOS Specific IgE, F014, Soybean										
Sample	**Mean (kU/L)**	**N**	**Within-Run**		**Between-Day**		**Between-Lot**		**Total**	
			SD	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**
1	0.14	75	0.02	11.8	0.01	10.4	0.00	0.0	0.02	15.7
2	0.46	75	0.02	5.3	0.01	3.0	0.00	0.6	0.03	6.2
3	1.35	75	0.04	2.8	0.05	3.4	0.02	1.6	0.06	4.7
4	4.08	75	0.16	3.9	0.11	2.7	0.00	0.0	0.19	4.7
5	72.06	75	2.94	4.1	2.16	3.0	0.00	0.0	3.65	5.1

NOVEOS Specific IgE, F017, Hazelnut										
Sample	**Mean (kU/L)**	**N**	**Within-Run**		**Between-Day**		**Between-Lot**		**Total**	
			SD	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**
1	0.15	75	0.01	8.7	0.02	11.1	0.00	0.0	0.02	14.1
2	0.46	75	0.02	5.2	0.04	8.4	0.00	0.0	0.05	9.9
3	1.49	75	0.06	3.8	0.10	6.8	0.00	0.0	0.12	7.8
4	6.04	75	0.30	4.9	0.43	7.1	0.18	2.9	0.55	9.1
5	60.28	75	2.66	4.4	2.30	3.8	0.00	0.0	3.52	5.8
6	88.21	79*	3.71	4.2	5.92	6.7	0.00	0.0	6.99	7.9

*Sample 6 had one outlier removed on Day 5 and one additional day (1 run with 5 replicates) was added

NOVEOS Specific IgE, F352, Ara h 8 PR-10, Peanut										
Sample	**Mean (kU/L)**	**N**	**Within-Run**		**Between-Day**		**Between-Lot**		**Total**	
			SD	0.15	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**
1	0.18	75	0.01	6.0	0.01	4.6	0.01	2.9	0.01	8.1
2	0.31	75	0.02	5.1	0.02	4.9	0.01	4.3	0.03	8.3
3	0.56	75	0.04	6.5	0.00	0.0	0.04	7.9	0.06	10.2
4	1.51	75	0.05	3.5	0.02	1.4	0.04	2.7	0.07	4.6
5	5.93	75	0.21	3.6	0.08	1.4	0.07	1.1	0.24	4.0
6	78.85	75	4.84	6.1	4.06	5.2	0.00	0.0	6.32	8.0

NOVEOS Specific IgE, F423, Ara h 2, Peanut										
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	5.4	0.01	3.2	0.00	0.0	0.01	6.2
2	0.27	75	0.02	5.8	0.01	4.3	0.00	0.0	0.02	7.2
3	0.52	75	0.02	3.6	0.03	5.5	0.00	0.0	0.03	6.6
4	1.15	75	0.05	4.5	0.06	5.5	0.00	0.0	0.08	7.1
5	93.56	75	3.13	3.3	4.00	4.3	0.00	0.0	5.07	5.4

NOVEOS Specific IgE, F447, Ara h 6, Peanut										
Sample	**Mean (kU/L)**	**N**	**Within-Run**		**Between-Day**		**Between-Lot**		**Total**	
			SD	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**
1	0.20	79*	0.01	5.5	0.01	5.9	0.00	0.7	0.02	8.1
2	0.47	75	0.02	4.1	0.03	5.5	0.01	1.7	0.03	7.1
3	9.98	75	0.40	4.0	0.56	5.6	0.00	0.0	0.69	6.9
4	75.92	75	3.98	5.2	2.64	3.5	0.00	0.0	4.78	6.3

*Sample 1 had one outlier removed on Day 5 and one additional day (1 run with 5 replicates) was added

2. Linearity:

Linearity of each NOVEOS Specific IgE assay was evaluated in accordance with the CLSI guideline I/LA20-A3. Three sets of linearity dilution panels including six levels were prepared by using three positive human serum samples (low, mid, and high). The samples were serially diluted with one negative serum sample to create overlapping dilution panels. Testing was performed using one lot 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 guideline 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 the claimed analytical mearing range for each NOVEOS Specific IgE are shown in the table below:

NOVEOS Specific IgE	Tested Linear Range (kU/L)	Analytical Measuring Range (kU/L)	Regression Equation
F014, Soybean	0.07–124.26	0.10 – 100.0	y = 1.02x + 0.01
F017, Hazelnut	0.08–111.87	0.10 – 100.0	y = 0.99x – 0.02
F352, Ara h 8 PR-10, Peanut	0.06–100.93	0.10 – 100.0	y = 0.93x + 0.01
F423, Ara h 2, Peanut	0.09–99.09	0.10 – 99.0	y = 0.97x + 0.00
F447, Ara h 6, Peanut	0.07–118.95	0.10 – 100.0	y = 0.94x – 0.01

3. Analytical Specificity/Interference:

a. Inhibition Study

Immunological specificity of each NOVEOS Specific IgE assay was verified through competitive inhibition study according to the CLSI guideline I/LA20-A3. Positive samples with specific IgE concentration used in the study include: 1.39 kU/L for F014, Soybean; 7.94 kU/L for F017, Hazelnut; 5.77 kU/L for F352, Ara h 8 PR-10, Peanut; 6.48 kU/L for F423, Ara h 2, Peanut; and 6.83 kU/L for F447, Ara h 6, Peanut.

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 four using one lot of NOVEOS Specific IgE assay for F014 (Soybean), F017 (Hazelnut), F352 (Ara h 8 PR-10, Peanut), F423 (Ara h 2, Peanut), and F447 (Ara h 6, Peanut). Greater than 85% inhibition was achieved for F017 (Hazelnut) at 25 µg/mL (87% inhibition) and F447 (Ara h 6, Peanut) at

3.125 µg/mL (88% inhibition). Substantial inhibition was also observed at the following inhibitor concentrations: 84% inhibition for F014 (Soybean) at 25 µg/mL, 83% inhibition for F352 (Ara h 8 PR-10, Peanut) at 50 µg/mL, and 85% inhibition for F423 (Ara h 2, Peanut) at 3.125 µg/mL.

For the NOVEOS Specific IgE Assays F014 (Soybean), F017(Hazelnut), F352 (Ara h 8 PR-10, Peanut), F423 (Ara h 2, Peanut), and F447(Ara h 6, Peanut) the related and unrelated allergens tested were as follows:

- For F014 (Soybean), the related allergen F018 (Brazil Nut) and the unrelated allergens K082 (Latex), M005 (Candida albicans) and W013 (Cocklebur Pollen) were tested as potential inhibitors at a final concentration of at least ten times the highest concentration of F014 at which 84% inhibition was achieved. All allergen inhibitors were spiked into the positive serum sample at a 1:1 dilution and evaluated with one lot of NOVEOS Specific IgE Assay, F014. The results of the single-dose inhibition studies using one related allergen (F018) and three unrelated allergens showed ≤15% inhibition at a test concentration of 2180 µg/mL (F018), 975 µg/mL (K082), 1235 µg/mL (M005) and 1080 µg/mL (W013). The inhibition studies indicate that the NOVEOS Specific IgE Assay, F014 contains the immunologically relevant allergen.

- For F017 (Hazelnut), the related allergen F338 (Sea Scallops) and the unrelated allergens D201 (Blomia tropicalis), E070 (Goose Feathers), I006 (German Cockroach), I070 (Fire Ant), M003 (Aspergillus fumigatus), and M012 (Aureobasidium pullulans) were tested as potential inhibitors at a final concentration of at least ten times the highest concentration of F017 that achieved 87% inhibition. All allergen inhibitors were spiked into the positive serum sample at a 1:1 dilution and evaluated with one lot of NOVEOS Specific IgE Assay, F017. The results of the single-dose inhibition studies using one related allergen (F338) and six unrelated allergens showed ≤15% inhibition at test concentrations of 250 µg/mL (F338, D201, E070, I006, I070, M003, M012). The inhibition studies indicate that the NOVEOS Specific IgE Assay, F017 contains the immunologically relevant allergen.

- For F352 (Ara h 8 PR-10, Peanut), the related allergen F077 (Bos d 5 β-lactoglobulin, Milk) and the unrelated allergens E221 (Can f 3 Dog Serum Albumin, Dog), M218 (Asp f 1, Aspergillus fumigatus), and T215 (Bet v 1 PR-10, Birch) were tested as potential inhibitors at a final concentration of at least ten times the highest concentration of F352 that achieved 83% inhibition. All allergen inhibitors were spiked into the positive serum sample at a 1:1 dilution and evaluated with one lot of NOVEOS Specific IgE Assay, F352. The results of the single-dose inhibition studies using one related allergen (F077) and three unrelated allergens showed ≤15% inhibition at test concentrations of 3520 µg/mL (F077), 1970 µg/mL (E221), 660 µg/mL (M218) and 1200 µg/mL (T215). The inhibition studies indicate that the NOVEOS Specific IgE Assay, F352 contains the immunologically relevant allergen.

- For F423 (Ara h 2, Peanut), the related allergen F427 (Ara h 9 LTP, Peanut) and the unrelated allergens E221 (Can f 3 Dog Serum Albumin), M218 (Asp f 1, Aspergillus fumigatus), and T215 (Bet v 1 PR-10, Birch) were tested as potential inhibitors at a final concentration of at least ten times the highest concentration of F423 that

achieved 85% inhibition. All allergen inhibitors were spiked into the positive serum sample at a 1:1 dilution and evaluated with one lot of NOVEOS Specific IgE Assay, F423. The results of the single-dose inhibition studies using one related allergen (F427) and three unrelated allergens showed ≤15% inhibition at test concentrations of 31.25 µg/mL (F427, E221, M218 and T215). The inhibition studies indicate that the NOVEOS Specific IgE Assay, F423 contains the immunologically relevant allergen.

- For F447 (Ara h 1, Peanut), the related allergen F076 (Bos d 4, α-lactoglobulin, Milk) and the unrelated allergens E221 (Can f 3, Dog Serum Albumin), G215 (Phl p 5b, Timothy Grass), and M220 (Asp f 3, Aspergillus fumigatus) were tested as potential inhibitors at a final concentration of at least ten times the concentration of F447 at which 88% inhibition was achieved. All allergen inhibitors were spiked into the positive serum sample at a 1:1 dilution and evaluated with one lot of NOVEOS Specific IgE Assay, F447. The results of the single-dose inhibition studies using one related allergen (F076, Bos d 4, α-lactoglobulin, Milk) and three unrelated allergens showed ≤15% inhibition at test concentrations of 1460 µg/mL (F076), 1970 µg/mL (E221), 1500 µg/mL (G215) and 1220 µg/mL (M220). The inhibition studies indicate that the NOVEOS Specific IgE Assay, F447 contains the immunologically relevant allergen.

b. Interference:

i. Endogenous Substance Interference:

The effect of the presence of elevated levels of human serum albumin, hemoglobin, triglycerides, conjugated bilirubin, and unconjugated bilirubin in serum samples was evaluated by testing three serum sample pools (one negative above LoQ, 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 sIgE assays for F014 (Soybean), F017 (Hazelnut), F352 (Ara h 8 PR-10, Peanut), F423 (Ara h 2, Peanut), and F447 (Ara h 6, Peanut). 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 121 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. Interference testing with rheumatoid factor (RF) was previously performed for NOVEOS sIgE allergens and found no significant interference at 513 IU/mL (refer to K200825).

ii. Exogenous Interference:

Refer to K200825

c. Cross-reactivity:

The potential cross-reactivity of non-IgE (IgA, IgD, IgG, and IgM) to the NOVEOS Specific IgE 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 as shown in the table below:

NOVEOS Specific IgE Assay	Assay Reportable Range/ Analytical Measuring Range
F014, Soyabean	0.10 – 100.00 kU/L
F017, Hazelnut	0.10 – 100.00 kU/L
F352, Ara h 8 PR-10, Peanut	0.10 – 100.00 kU/L
F423, Ara h 2, Peanut	0.10 – 99.00 kU/L
F447, Ara h 6, Peanut	0.10 – 100.00 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 F014 (Soybean), F017 (Hazelnut), F352 (Ara h 8 PR-10, Peanut), F423 (Ara h 2, Peanut), and F447 (Ara h 6, Peanut) stored at 2–8°C is ongoing using three lots. The testing was performed using two positive samples and one negative sample. In addition, 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 a shelf-life stability of 36 months when stored as 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 one lot of each NOVEOS Specific IgE Capture Reagent Pack of F014 (Soybean), F017 (Hazelnut), F352 (Ara h 8 PR-10, Peanut), F423 (Ara h 2, Peanut), and F447 (Ara h 6, Peanut). The testing was performed for 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 also supports that the allergen specific Capture Reagent Packs once opened and stored at 2-8°C are stable up to 28 days. The on-board stability for all the other assay components has been previously established per K182479.

Open Vial Stability: Both an on-going real-time stability study and an accelerated stability study were performed using one lot NOVEOS Specific IgE Capture Reagent Pack of F014 (Soybean), F017 (Hazelnut), F352 (Ara h 8 PR-10, Peanut), F423 (Ara h 2, Peanut), and F447 (Ara h 6, Peanut). The studies evaluated opened capture reagent vials filled to 100% and 50% fill volume, stored at 37°C for up to 10 days to simulate the stress of real-time aging. The allergen specific Capture Reagent Packs are 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., F014 (Soybean), F017(Hazelnut), F352 (Ara h 8 PR-10, Peanut), F423 (Ara h 2, Peanut), and F447(Ara h 6, Peanut) on the NOVEOS Immunoassay Analyzer were determined according to CLSI EP17-A2.

The LoB was determined by testing four analyte-free human serum samples in replicates of five per run, over three runs, with no more than one run per day, using two lots of each capture reagent on one NOVEOS Immunoassay Analyzer. The LoB was estimated as the 95th percentile of the 60 measurements for each of the two lots tested.

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

NOVEOS sIgE	No. of Samples	No. of Lots	No. of Analyzers	Testing Protocol
F014	5	2	1	5 samples x 5 replicates/run x 3 runs = 75 replicates/lot
F017	6	2	1	4 samples x 5 replicates/run x 6 runs + 2 samples x 5 replicates/run x 3 runs = 150 replicates/lot
F352	4	2	1	4 samples x 5 replicates/run x 3 runs = 60 replicates/lot
F423	4	2	1	4 samples x 5 replicates/run x 3 runs = 60 replicates/lot
F447	4	2	1	4 samples x 5 replicates/run x 3 runs = 60 replicates/lot

The LoQ was determined by testing four to six low IgE samples with five replicates per run over three to six testing days using two lots of each capture reagent on one NOVEOS Immunoassay Analyzer resulting in a total of 60 to 150 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)
F014, Soybean	0.07	0.09	0.10
F017, Hazelnut	0.07	0.08	0.10
F352, Ara h 8 PR-10, Peanut	0.07	0.08	0.10
F423, Ara h 2, Peanut	0.07	0.09	0.10
F447, Ara h 6, Peanut	0.07	0.08	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 sIgE 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, F014, Soybean	**Positive**	35	0	35
	Negative	4	131	135
	Total	39	131	170
Clinical Sensitivity: 89.7% (35/39) (95% CI: 76.4 – 95.9%) Clinical Specificity: 100.0% (131/131) (95% CI: 97.2 – 100.0%)				

		Clinical Diagnosis		
		Atopic	**Non-atopic**	**Total**
NOVEOS Specific IgE, F017, Hazelnut	**Positive**	47	2	49
	Negative	3	124	127
	Total	50	126	176
Clinical Sensitivity: 94.0% (47/50) (95% CI: 83.8 – 97.9%) Clinical Specificity: 98.4% (124/126) (95% CI: 94.4 – 99.6%)				

		Clinical Diagnosis		
		Atopic	**Non-atopic**	**Total**
NOVEOS Specific IgE, F352, Ara h 8 PR-10, Peanut	**Positive**	18	0	18
	Negative	36	132	168
	Total	54	132	186
Clinical Sensitivity: 33.3% (18/54) (95% CI: 22.2 – 46.6%) Clinical Specificity: 100.0% (132/132) (95% CI: 97.2 – 100.0%)				

		Clinical Diagnosis		
		Atopic	**Non-atopic**	**Total**
NOVEOS Specific IgE, F423, Ara h 2, Peanut	**Positive**	42	0	43
	Negative	14	129	143
	Total	56	129	185
Clinical Sensitivity: 75.0% (42/56) (95% CI: 62.3 – 84.5%) Clinical Specificity: 100.0% (129/129) (95% CI: 97.1 – 100.0%)				

		Clinical Diagnosis		
		Atopic	**Non-atopic**	**Total**
NOVEOS Specific IgE, F447, Ara h 6, Peanut	**Positive**	40	0	40
	Negative	16	126	142
	Total	56	126	182
Clinical Sensitivity: 71.4% (40/56) (95% CI: 58.5 – 81.6%) Clinical Specificity: 100.0% (126/126) (95% CI: 97.0 – 100.0%)				

The following literature that supports the observed sensitivity of the NOVEOS Specific IgE assays F352 (Ara h 8 PR-10, Peanut), F423 (Ara h 2, Peanut), and F447 (Ara h 6, Peanut)are presented in the table below.

NOVEOS sIgE	**Literature Citation(s)**	**Prevalence**	**Reported Performance**
F422, Ara h 1, Peanut Sensitivity: 33.3% Specificity: 100.0 %	Warren C., *et al*. J Allergy Clin Immunol. 2021;147(6):2263-2270.e5	1.3% - 2.9% of U.S. adults have a reported peanut allergy	not reported
	Calamelli E., *et al.* BioMed Research International. 2013, Article ID 170452,	Among children sensitized to peanut, only 35% had IgE reactivity to Ara h 8.	
	Vereda A., *et al.* J Allergy Clin Immunol. 2011;127:603-7.	Among patients with peanut allergy, only 25% had IgE reactivity to Ara h 8.	

NOVEOS sIgE	Literature Citation(s)	Prevalence	Reported Performance
F423, Ara h 2, Peanut Sensitivity: 75.0% Specificity: 100.0%	Warren C., *et al.* J Allergy Clin Immunol. 2021;147(6):2263-2270.e5	1.3% - 2.9% of U.S. adults have a reported peanut allergy	
	Calamelli E., *et al.* BioMed Research International. 2013, Article ID 170452,	Among children sensitized to peanut, only 27% had IgE reactivity to Ara h 2.	
	Vereda A., et al. J Allergy Clin Immunol. 2011;127:603-7.	Among patients with peanut allergy, only 64% had IgE reactivity to Ara h 2.	
F423, Ara h 2, Peanut Sensitivity: 75.0% Specificity: 100.0%	Warren C., *et al.* J Allergy Clin Immunol. 2021;147(6):2263-2270.e5	1.3% - 2.9% of U.S. adults have a reported peanut allergy	
	Calamelli E., *et al.* BioMed Research International. 2013, Article ID 170452,	Among children sensitized to peanut, only 27% had IgE reactivity to Ara h 2.	
	Vereda A., et al. J Allergy Clin Immunol. 2011;127:603-7.	Among patients with peanut allergy, only 64% had IgE reactivity to Ara h 2.	
F447, Ara h 6, Peanut Sensitivity: 71.4% Specificity: 100.0%	Warren C., *et al.* J Allergy Clin Immunol. 2021;147(6):2263-2270.e5	1.3% - 2.9% of U.S. adults have a reported peanut allergy	
	Kaur N., *et al.* J Allergy Clin Immunol Pract. 2021;9(1):245-53.	Among children referred for peanut OFC, 37% had IgE reactivity to Ara h 6. Among children found to be allergic to peanut by OFC, 75% had IgE reactivity to Ara h 6.	

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 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) individual. Each laboratory should establish its own expected value/reference range.

The reference range of NOVEOS Specific IgE assay for F014 (Soybean), F017 (Hazelnut), F352 (Ara h 8, PR-10, Peanut), F423 (Ara h 2, Peanut), and F447 (Ara h 6, Peanut) in the normal population was evaluated based on the data collected in clinical studies which tested samples from apparently healthy subjects including: 131 non-atopic samples for F014; 126 non-atopic samples for F017; 132 non-atopic samples for F352; 129 non-atopic samples for F423; and 126 non-atopic samples for F447. Except for two out of 126 samples evaluated with F017 (Hazelnut), 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.