510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K252493

B Applicant

Hycor Biomedical

C Proprietary and Established Names

NOVEOS Specific IgE (sIgE), Capture Reagent F024, Shrimp (*Shrimp spp.*)
NOVEOS Specific IgE (sIgE), Capture Reagent F207, Clam (*Mercenaria mercenaria*)
NOVEOS Specific IgE (sIgE), Capture Reagent F256, Walnut (*Juglans spp.*)
NOVEOS Specific IgE (sIgE), Capture Reagent I006, German Cockroach (*Blatella germanica*)

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:

Four new devices

B Measurand:

Allergen specific IgE to Shrimp - F024, *Shrimp spp.*
Allergen specific IgE to Clam - F207, *Mercenaria mercenaria*
Allergen specific IgE to Walnut - F256, *Juglans spp.*
Allergen specific IgE to German Cockroach - I006, *Blatella germanica*

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
  - Shrimp - F024, *Shrimp spp.*
  - Clam - F207, *Mercenaria mercenaria*
  - Walnut - F256, *Juglans spp.*
  - German Cockroach - I006, *Blatella germanica*

- 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 use of 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 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 and ImmunoCAP Specific IgE Conjugate 100 and Conjugate 400

B Predicate 510(k) Number(s):

K051218

C Comparison with Predicate(s):

Device & Predicate Device(s):	K252493 (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.
Assay Type	Quantitative	Same
Traceability	World Health Organization (WHO) reference reagent serum Immunoglobulin E (IgE) 11/234	Same
Calibration Method	Heterologous interpolation based on Total IgE calibration curve	Same
Cut-off	0.35 kU/L	Same
Reaction Temperature	37°C	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 45 minutes to 2 hours and 30 minutes depending on model

Detection Limit	F024, Shrimp: LoB: 0.06 kU/L LoD: 0.08 kU/L LoQ: 0.10 kU/L F207, Clam: LoB: 0.04 kU/L LoD: 0.09 kU/L LoQ: 0.10 kU/L F256, Walnut: LoB: 0.07 kU/L LoD: 0.10 kU/L LoQ: 0.10 kU/L I006, German Cockroach: LoB: 0.03 kU/L LoD: 0.06 kU/L LoQ: 0.10 kU/L	LoB: 0.001 kU/L LoD: 0.02 kU/L LoQ: 0.10 kU/L

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 EP12-A2: User Protocol for Evaluation of Qualitative Test Performance; Approved Guideline – Second 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 five NOVEOS Specific IgE assays. A panel of five human sera that include one or two negative samples were tested in duplicate per run, two runs per day for 20 days using one reagent lot on one NOVEOS Immunoassay Analyzer (for a total of 80 measurements per sample except for the highest sample). 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 results for each NOVEOS Specific IgE assay are summarized in the following tables:

NOVEOS Specific IgE, F024, Shrimp										
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	4.0	0.01	4.1	0.01	5.8	0.02	8.1
2	0.29	80	0.01	4.8	0.01	4.6	0.02	5.5	0.03	8.6
3	1.52	80	0.07	4.3	0.06	3.7	0.03	2.0	0.09	6.0
4	6.61	80	0.23	3.4	0.09	1.4	0.33	5.0	0.41	6.2
5	84.11	92*	5.29	6.3	4.98	5.9	3.21	3.8	7.94	9.4

* Sample 5 was tested in five replicates for 1st run and two replicates for 2nd run for four days, and in two replicates/run with two runs per day for 16 days, yielding N=92 datapoints

NOVEOS Specific IgE, F207, Clam										
Sample	**Mean (kU/L)**	**N**	**Within-Run**		**Between Run**		**Between Day**		**Total**	
			SD	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**
1	0.18	80	0.01	8.0	0.03	14.3	0.00	0.0	0.03	16.3
2	0.30	80	0.01	4.8	0.03	9.8	0.01	4.1	0.03	11.6
3	1.65	80	0.08	4.6	0.01	0.6	0.05	2.8	0.09	5.5
4	8.24	80	0.26	3.2	0.16	1.9	0.25	3.0	0.39	4.8
5	82.32	95*	5.81	7.1	5.03	6.1	1.71	2.1	7.87	9.6

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

NOVEOS Specific IgE, F256, Walnut										
Sample	**Mean (kU/L)**	**N**	**Within-Run**		**Between Run**		**Between Day**		**Total**	
			SD	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**
1	0.29	80	0.01	5.1	0.02	6.7	0.01	2.8	0.03	8.9
2	0.32	80	0.02	6.2	0.04	11.7	0.02	6.9	0.05	14.9
3	1.20	80	0.05	4.1	0.05	4.1	0.03	2.1	0.07	6.1
4	3.62	80	0.12	3.4	0.00	0.0	0.12	3.3	0.17	4.8
5	83.90	95*	5.72	6.8	7.55	9.0	0.00	0.0	9.47	11.3

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

NOVEOS Specific IgE, I006, German Cockroach										
Sample	**Mean (kU/L)**	**N**	**Within-Run**		**Between Run**		**Between Day**		**Total**	
			SD	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**
1	0.21	80	0.02	10.4	0.00	0.0	0.02	9.1	0.03	13.8
2	0.43	80	0.02	5.1	0.02	4.1	0.03	7.7	0.04	10.1
3	1.51	80	0.05	3.3	0.08	5.3	0.06	4.1	0.11	7.4
4	21.12	80	0.84	4.0	1.29	6.1	1.12	5.3	1.90	9.0
5	62.86	82*	2.18	3.5	3.42	5.4	2.06	3.3	4.55	7.2

* Sample 5 was tested in two replicates/run with two runs per day for 21 days with exclusion of two outliers for Day 11, yielding N=82 datapoints

b. Lot-to-lot imprecision

A panel of four to five 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 per sample for all three lots. The results are summarized in the following tables:

NOVEOS Specific IgE, F024, Shrimp										
Sample	**Mean (kU/L)**	**N**	**Within-Run**		**Between-Day**		**Between-Lot**		**Total**	
			SD	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**
1	0.19	75	0.01	5.1	0.01	6.1	0.01	6.1	0.01	6.1
2	0.54	75	0.02	3.6	0.03	4.9	0.03	5.7	0.03	5.7
3	1.58	75	0.05	3.0	0.06	3.7	0.06	3.9	0.06	3.9
4	81.84	75	5.32	6.5	6.52	8.0	0.00	0.0	8.42	10.3

NOVEOS Specific IgE, F207, Clam										
Sample	**Mean (kU/L)**	**N**	**Within-Run**		**Between-Day**		**Between-Lot**		**Total**	
			SD	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**
1	0.21	75	0.02	9.2	0.02	8.0	0.00	0.0	0.03	12.1
2	0.54	79*	0.02	4.5	0.04	7.5	0.00	0.0	0.05	8.7
3	1.65	75	0.06	3.7	0.02	1.3	0.01	0.5	0.07	4.0
4	8.27	75	0.34	4.1	0.09	1.1	0.03	0.3	0.35	4.2
5	85.43	75	7.01	8.2	5.99	7.0	0.00	0.0	9.22	10.8

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

NOVEOS Specific IgE, F256, Walnut										
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	10.2	0.00	0.0	0.02	15.6
2	0.46	75	0.03	7.3	0.02	4.6	0.00	0.0	0.04	8.6
3	1.19	75	0.05	4.4	0.04	3.0	0.05	3.8	0.08	6.6
4	21.43	75	0.79	3.7	0.39	1.8	0.30	1.4	0.93	4.4
5	91.83	75	6.28	6.8	3.49	3.8	2.09	2.3	7.48	8.1

NOVEOS Specific IgE, I006, German Cockroach										
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	10.5	0.02	13.6	0.00	0.0	0.02	17.2
2	0.47	75	0.02	4.9	0.02	3.3	0.01	1.5	0.03	6.0
3	1.14	75	0.06	5.0	0.02	2.1	0.10	8.9	0.12	10.4
4	21.32	75	0.69	3.3	0.75	3.5	0.45	2.1	1.11	5.2
5	83.67	75	5.15	6.2	5.41	6.5	0.00	0.0	7.47	8.9

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) diluted with one negative serum sample. Three dilution panels overlapped and created the full dilution panel. 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 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 results for each NOVEOS Specific IgE Assay are shown in the tables below:

NOVEOS Specific IgE, F024, Shrimp					
Dilution Panel	**Range (kU/L)**	**Slope (95% CI)**	**Intercept (95% CI)**	**R^2**	**% Deviation from Linearity**
1	0.03–3.80	0.92 (0.85–0.99)	0.02 (0.01–0.03)	0.996	-4.9%–9.1%
2	1.01–55.93	0.89 (0.80–0.98)	0.18 (-0.04–0.40)	0.992	-3.2%–11.8%*
3	1.95–130.70	0.87 (0.82–0.91)	0.05 (-0.17–0.28)	0.998	-9.5%–9.6%
All	0.03–130.70	0.91 (0.88–0.94)	0.02 (0.01–0.03)	0.995	-9.5%–11.8%

* %Deviation from linearity of 11.8% for sample level with IgE concentration of 1.91 kU/L

NOVEOS Specific IgE, F207, Clam					
Dilution Panel	**Range (kU/L)**	**Slope (95% CI)**	**Intercept (95% CI)**	**R^2**	**% Deviation from Linearity**
1	0.08–3.92	1.02 (0.98–1.06)	-0.01 (-0.02–0.00)	0.999	2%–14%*
2	0.34–24.70	0.95 (0.87–1.04)	-0.06 (-0.11– -0.01)	0.994	-14%**– 3%
3	1.45–95.09	1.08 (0.99–1.17)	-0.43 (-0.80– -0.06)	0.995	-10%–12%***
All	0.08–95.09	0.99 (0.93–1.04)	-0.02 (-0.04–0.01)	0.987	-14%–14%

* % Deviation from linearity of 14% for sample level with IgE concentration of 0.08 kU/L
** % Deviation from linearity of -14% for sample levels with IgE concentrations of 0.34, 0.67, and 1.32 kU/L
*** % Deviation from linearity of 12% for sample level with IgE concentration of 52.74 kU/L

NOVEOS Specific IgE, F256, Walnut					
Dilution Panel	**Range (kU/L)**	**Slope (95% CI)**	**Intercept (95% CI)**	**R^2**	**% Deviation from Linearity**
1	0.06–2.22	0.99 (0.96–1.02)	-0.00 (-0.02–0.02)	0.999	-4%–9%
2	1.06–69.05	0.91 (0.82–1.00)	-0.17 (-0.56–0.21)	0.992	-14%*–4%
3	1.46–88.83	1.00 (0.99–1.02)	-0.03 (-0.12–0.05)	1.000	0%–7%
All	0.06–88.83	0.97 (0.93–1.00)	0.00 (-0.04–0.04)	0.995	-14%–9%

* % Deviation from linearity of -14% for sample level with IgE concentration of 3.65 kU/L

NOVEOS Specific IgE Assay, I006, German Cockroach					
Dilution Panel	**Range (kU/L)**	**Slope (95% CI)**	**Intercept (95% CI)**	**R^2**	**% Deviation from Linearity**
1	0.09–1.02	0.97 (0.91–1.03)	-0.25 (-0.51–0.02)	0.999	-9%–4%
2	0.89–53.98	0.99 (0.96–1.02)	-0.05 (-0.13–0.04)	0.999	-1%–6%
3	1.54–110.48	1.00 (0.97–1.03)	-0.01 (-0.01–0.00)	0.997	-15%*–4%
All	0.09–110.48	0.96 (0.93–0.99)	0.00 (-0.01–0.01)	0.996	-15%–6%

* % Deviation from linearity of -15% for sample level with IgE concentration of 2.88 kU/L

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	Analytical Measuring Range
F024, Shrimp	0.03 – 130.70 kU/L	0.10 – 100.0 kU/L
F207, Clam	0.08 – 95.09 kU/L	0.10 – 95.0 kU/L
F256, Walnut	0.06 – 88.83 kU/L	0.10 – 88.0 kU/L
I006, German Cockroach	0.09 – 110.48 kU/L	0.10 – 100.0 kU/L

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 I/LA20-A3. Positive samples with specific IgE concentration used in the study include: 7.64 kU/L for F024, Shrimp; 13.33 kU/L for F207, Clam; 1.39 kU/L for F256, Walnut; and 1.62 kU/L for I006, German Cockroach.

   The allergen solution (inhibitor) was diluted 1:1 into the positive serum sample to achieve a starting concentration of 50 µg/mL for F024 and for F207, 100 µg/mL for F256 and for I006. The sample solution was serially diluted five times in two-fold increments and each diluted sample was evaluated for dose-dependent inhibition in four replicates using one lot of NOVEOS sIgE for F207, F256, and I006, and two lots for F024. The results of the dose-dependent inhibition study showed that ≥85% inhibition was achieved at a final µg/mL inhibitor concentration of 12.5 µg/mL for F024, 50 µg/mL for F207, 100 µg/mL for F256, and 25 µg/mL for I006.

   For the NOVEOS Specific IgE assays, F024, F207, F256, and I006, the related and unrelated allergens tested were as follows:

   - For F024, Shrimp, the related allergen F202 (Cashew Nut) and the unrelated allergens D070 (*Acarus Siro*), M012 (*Aureobasidium pullulans*), T009 (Olive Pollen), and W006 (Mugwort) were tested as potential inhibitors at a final concentration of at least ten times the concentration of F024 at which ≥85% 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, F024. The results of the single-dose inhibition studies did not show inhibition at a test concentration of 125 µg/mL for the

related allergen and unrelated allergens. The inhibition studies indicate that the NOVEOS Specific IgE, F024 contains the immunologically relevant allergen.

- For F207, Clam, the related allergen F040 (Yellowfin Tuna) and the unrelated allergens M006 (*Alternaria Alternata*), E070 (Goose Feathers), W013 (Cocklebur Pollen), and G010 (Johnson Grass) were tested as potential inhibitors at a final concentration of at least ten times the highest concentration of F207 at which ≥85% 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, F207. The results of the single-dose inhibition studies did not show inhibition at a test concentration of 1335 µg/mL for the related allergen and at 830 µg/mL (M006), 3975 µg/mL (E070), 1080 µg/mL (W013), and 850 µg/ml (G010) for unrelated allergens. The inhibition studies indicate that the NOVEOS Specific IgE, F207 contains the immunologically relevant allergen.

- For F256, Walnut, the related allergen F020 (Almond) and the unrelated allergens D201 (*Blomia tropicalis*), T014 (Eastern Cottonwood Pollen), and W001 (Short Ragweed) were tested as potential inhibitors at a final concentration of at least ten times the final concentration of F256 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, F256. The results of the single-dose inhibition studies did not show inhibition at a test concentration of 2565 µg/mL for the related allergen and at 2850 ug/ml (D201), 1080 ug/ml (T014) and 1150 ug/ml (W001) for unrelated allergens. The inhibition studies indicate that the NOVEOS Specific IgE, F256 contains the immunologically relevant allergen.

- For I006, German Cockroach, the related allergen I070 (Fire Ant) and the unrelated allergens F018 (Brazil Nut), T010 (California Black Walnut), and W006 (Common Mugwort) were tested as potential inhibitors at a final concentration of at least ten times the concentration of I006 at which ≥85% 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, I006. The results of the single-dose inhibition studies did not show inhibition at a test concentration of 250 µg/mL for the related allergen and unrelated allergens. The inhibition studies indicate that the NOVEOS Specific IgE, I006 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, 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 F024 (Shrimp), F207 (Clam), F256 (Walnut), and I006 (German Cockroach). 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 as shown in the table below:

NOVEOS Specific IgE Assay	Assay Reportable Range/ Analytical Measuring Range
F024, Shrimp	0.10 – 100.0 kU/L
F207, Clam	0.10 – 95.0 kU/L
F256, Walnut	0.10 – 88.0 kU/L
I006, German Cockroach	0.10 – 100.0 kU/L

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

a. 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 in accordance with CLSI EP25-A2.

Shelf-life stability: A real-time stability study for the NOVEOS Specific sIgE Capture Reagent Pack of F024, F207, F256, and I006 stored at 2–8°C is ongoing using three lots. The test 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. The result for each NOVEOS Specific sIgE Capture Reagent is summarized in the table below:

	Shelf-life Stability (2–8°C)
Capture Reagent Pack F024*	36 months
Capture Reagent Pack F207*	36 months
Capture Reagent Pack F256*	36 months
Capture Reagent Pack I006**	2 months

* Results based on accelerated stability data, while the real-time stability is on-going

** Results based on ongoing real time stability study

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) on at least one lot of each NOVEOS Specific IgE Capture Reagent Pack F024, F207, F256, and I006 stored on the NOVEOS Immunoassay Analyzer. The test was planned by testing each sample in three replicates at Day 0 and scheduled timepoints of 15, 28, and 29 days. The timepoints were chosen to at minimum have a penultimate (Tn) and ultimate (Tn+1) timepoint. The result supports that the allergen specific capture reagent is stable for 15 days stored on-board. The result supports that the allergen specific capture reagent is stable for 15 days on-board.

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

Open-vial stability: Accelerated open vial stability studies were performed using one lot for F024, F207, F256, and I006 capture reagents. 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 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 sIgE assay, i.e., F024 (Shrimp), F207 (Clam), F256 (Walnut), and I006 (German Cockroach), 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 no more than one run per day, using two lots of each capture reagent on one or two NOVEOS Immunoassay Analyzers. Only the NOVEOS Specific IgE Assay for F256 was evaluated on two NOVEOS Immunoassay Analyzers. The LoB was estimated as the 95th percentile of the 60 measurements for each of the two lots tested.

LoD: The LoD was determined by testing protocol summarized in the table below:

NOVEOS sIgE	No. of Samples	No. of Lots	No. of Analyzers	Testing Protocol
F024	4	2	1	4 samples x 5 replicates/run x 3 runs = 60/Lot
F207	5	2	1	5 samples x 5 replicates/run x 3 runs = 75/Lot
F256*	5	2	2	5 samples x 5 replicates/run x 3 runs = 75/Lot
I006	4	2	1	4 samples x 5 replicates/run x 3 runs = 60/Lot

* LoD study was evaluated on two NOVEOS Immunoassay Analyzers.

The LoD was calculated and determined to be the highest value across two lots tested for each NOVEOS sIgE assay.

LoQ: The LoQ was determined by testing four low IgE samples with three replicates per run over three testing days using two lots of each capture reagent on one NOVEOS Immunoassay Analyzer resulting in a total of 36 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)
F024, Shrimp	0.06	0.08	0.10
F207, Clam	0.04	0.09	0.10
F256, Walnut	0.07	0.10	0.10
I006, German Cockroach	0.03	0.06	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 skin prick testing (SPT results with certificate of analysis), 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, F024, Shrimp	**Positive**	26	0	26
	Negative	11	122	133
	Total	37	122	159
	Sensitivity: 70.3% (26/37) (95% CI: 54.2% to 82.5%) Specificity: 100.0% (122/122) (95% CI: 96.9% to 100.0%)			

		Clinical Diagnosis		
		Atopic	**Non-atopic**	**Total**
NOVEOS Specific IgE, F207, Clam	**Positive**	30	0	28
	Negative	14	120	147
	Total	44	120	175
	Sensitivity: 68.2% (30/44) (95% CI: 53.4% to 80.0%) Specificity: 100.0% (120/120) (95% CI: 96.9% to 100.0%)			

		Clinical Diagnosis		
		Atopic	**Non-atopic**	**Total**
NOVEOS Specific IgE, F256, Walnut	**Positive**	37	1	32
	Negative	3	121	125
	Total	40	122	157
	Sensitivity: 92.5% (37/40) (95% CI: 80.1% to 97.4%) Specificity: 99.2% (121/122) (95% CI: 95.5% to 99.9%)			

		Clinical Diagnosis		
		Atopic	**Non-atopic**	**Total**
NOVEOS Specific IgE, I006, German Cockroach*	**Positive**	12	0	12
	Negative	22	129	151
	Total	34	129	163
	Sensitivity: 35.3% (12/34) (95% CI: 21.5% to 52.1%) Specificity: 100.0% (129/129) (95% CI: 97.1% to 100.0%)			

* All atopic samples are only SPT positive

The following literature was published related to the observed low performance:

NOVEOS sIgE	Literature Citation(s)	Prevalence	Reported Performance
F024, Shrimp Sensitivity: 70.3% Specificity: 100.0%	Ye, YM, *et al.* Allergy Asthma Immunol Res. 2025;17:359–370	Not reported	Serum IgE Test (Shrimp Extract) - concordance of 67.1%.
F207, Clam Sensitivity: 68.2% Specificity: 100.0%	Maldonado, S. *et al*. Journal of Allergy and Clinical Immunology, Volume 125, Issue 2, AB203 (2010)	0.05–0.15%	An overall agreement of 86% with clinical diagnosis (atopic and non-atopic)
F256, Walnut Sensitivity: 92.5% Specificity: 99.2%	• Weinberger T and Sicherer S. J Asthma Allergy. 2018;11:41–51. • Fleischer DM, et al. J Allergy Clin Immunol. 2005;116(5):1087–1093	~0.5%	OFC: Sensitivity: 87% to 95% Specificity:60% to 75%

I006, Cockroach Sensitivity: 35.3% Specificity: 100.0%	• Sohn MH, Kim K-E. Allergy Asthma Immunol Res. 2012;4(5):264-269 • Alimuddin S *et al.* Acta Medica Indonesiana. 2018;50:125–131	~17–41%	SPT: Sensitivity: 24% Specificity: 98%

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

The reference range of NOVEOS Specific IgE Assay for F024 (Shrimp), F207 (Clam), F256 (Walnut), and I006 (German Cockroach), in the normal population was evaluated based on the data collected in clinical studies which were used to test samples from apparently healthy subjects including: 122 non-atopic samples for F024; 120 non-atopic samples for F207; 122 non-atopic samples for F256; and 129 non-atopic samples for I006, tested by corresponding NOVEOS Specific IgE Assay. All samples tested with the NOVEOS Specific IgE Assay for F024 (Shrimp), F207 (Clam), and I006 (German Cockroach) were below <0.35 kU/L. Of the 122 non-atopic samples, one tested positive (IgE =0.40 kU/L) with the NOVEOS Specific IgE Assay for F256 (Walnut).

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.