



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

I Background Information:

A 510(k) Number

K260280

B Applicant

Hycor Biomedical

C Proprietary and Established Names

NOVEOS Specific IgE (sIgE), Capture Reagent F004, Wheat (*Triticum aestivum*)
NOVEOS Specific IgE (sIgE), Capture Reagent F023, Crab (*Callinectes spp.*)
NOVEOS Specific IgE (sIgE), Capture Reagent F079, Gluten, Wheat
NOVEOS Specific IgE (sIgE), Capture Reagent F202, Cashew Nut (*Anacardium occidentale*)
NOVEOS Specific IgE (sIgE), Capture Reagent F233, Gal d 1 Ovomucoid, Egg

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 Wheat - F004, *Triticum aestivum*
Allergen specific IgE to Crab - F023, *Callinectes spp.*
Allergen specific IgE to Gluten, Wheat - F079
Allergen specific IgE to Cashew Nut - F202, *Anacardium occidentale*
Allergen specific IgE to Gal d 1 Ovomucoid, Egg - F233, Gal d 1

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
 - Wheat - F004, *Triticum aestivum*
 - Crab - F023, *Callinectes spp.*
 - Gluten, Wheat - F079
 - Cashew Nut - F202, *Anacardium occidentale*

- Gal d 1 Ovomucoid, Egg - F233, Gal d 1
- 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 a 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):	<u>K260280</u> (Candidate Device)	<u>K051218</u> (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 <i>in vitro</i> 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 <i>in vitro</i> 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 <i>in vitro</i> 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 <i>in vitro</i> diagnostic use as an aid in the clinical diagnosis of IgE mediated allergic disorders in conjunction with other clinical findings and is to be used in clinical laboratories.
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
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 imprecision

The within-laboratory precision study was conducted per the CLSI EP05-A3 for each of five NOVEOS Specific IgE assays. A panel of four to five human sera that included two negative samples with allergen specific IgE concentrations above the limit of Quantitation (LoQ) 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 measurements per sample except for the highest samples of F079, F202, and F233). 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, F004, Wheat										
Sample	Mean (kU/L)	N	Within-Run		Between-Run		Between-Day		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
1	0.12	80	0.02	12.8	0.01	9.0	0.01	9.6	0.02	18.3
2	0.30	80	0.02	5.8	0.02	5.1	0.01	2.6	0.02	8.2
3	2.68	80	0.11	4.1	0.00	0.0	0.07	2.5	0.13	4.8
4	74.79	80	4.63	6.2	0.00	0.0	4.09	5.5	6.18	8.3

NOVEOS Specific IgE, F023, Crab										
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	7.1	0.01	7.0	0.01	8.1	0.02	12.9
2	0.34	80	0.02	7.2	0.00	0.0	0.02	4.7	0.03	8.6
3	2.53	80	0.08	3.1	0.06	2.4	0.00	0.0	0.10	4.0
4	88.26	80	3.94	4.5	2.52	2.9	2.27	2.6	5.20	5.9

NOVEOS Specific IgE, F079, Gluten, Wheat										
Sample	Mean (kU/L)	N	Within-Run		Between-Run		Between-Day		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
1	0.20	80	0.01	6.4	0.00	0.0	0.02	9.5	0.02	11.5
2	0.32	80	0.02	5.8	0.01	3.3	0.01	2.7	0.02	7.2
3	3.20	80	0.10	3.1	0.07	2.1	0.13	4.0	0.17	5.5
4*	79.21	92*	5.16	6.5	8.47	10.7	0.00	0.0	9.92	12.5

* Sample 4 was tested in five replicates for Run 1 and two replicates for Run 2 on Days 1-5, and in two replicates per run with two runs per day for Days 6-20, and 3 total replicates dropped yielding N=92 datapoints

NOVEOS Specific IgE, F202, Cashew Nut										
Sample	Mean (kU/L)	N	Within-Run		Between-Run		Between-Day		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
1	0.15	80	0.01	9.7	0.00	0.0	0.01	8.6	0.02	12.9
2	0.27	80	0.01	3.8	0.01	5.2	0.02	7.3	0.03	9.7
3	1.24	80	0.04	2.8	0.05	3.6	0.02	1.8	0.06	5.0
4	5.40	80	0.30	5.6	0.08	1.5	0.12	2.2	0.34	6.2
5*	86.68	95*	5.86	6.8	7.19	8.3	7.70	8.9	12.05	13.9

* Sample 5 was tested in five replicates for Run 1 and two replicates for Run 2 on Days 1-5, and in two replicates per run with two runs per day for Days 6-20, yielding N=95 datapoints

NOVEOS Specific IgE, F233, Gal d 1 Ovomucoid, Egg										
Sample	Mean (kU/L)	N	Within-Run		Between-Run		Between-Day		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
1	0.18	80	0.02	10.7	0.00	0.0	0.02	11.4	0.03	15.7
2	0.27	80	0.02	5.7	0.00	1.3	0.01	4.6	0.02	7.4
3	1.71	80	0.10	5.9	0.00	0.0	0.08	4.5	0.13	7.5
4*	93.31	95*	6.16	6.6	2.11	2.3	1.82	1.9	6.76	7.2

* Sample 4 was tested in five replicates for Run 1 and two replicates for Run 2 on Days 1-5, and in two replicates per run with two runs per day for Days 6-20, yielding N=95 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, F004, Wheat										
Sample	Mean (kU/L)	N	Within-Run		Between-Day		Between-Lot		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
1	0.13	75	0.01	9.4	0.01	9.6	0.00	0.0	0.02	13.4
2	0.41	75	0.02	5.1	0.00	0.0	0.01	1.6	0.02	5.3
3	0.56	75	0.02	3.9	0.04	7.3	0.00	0.6	0.05	8.3
4	2.94	75	0.07	2.5	0.10	3.4	0.00	0.0	0.12	4.2
5	77.46	75	2.96	3.8	6.53	8.4	0.00	0.0	7.17	9.3

NOVEOS Specific IgE, F023, Crab										
Sample	Mean (kU/L)	N	Within-Run		Between-Day		Between-Lot		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
1	0.14	79*	0.01	8.4	0.01	5.8	0.01	6.9	0.02	12.3
2	0.42	75	0.02	3.9	0.02	4.4	0.00	0.8	0.03	5.9
3	2.35	75	0.08	3.4	0.04	1.7	0.05	2.2	0.10	4.4
4	81.20	75	3.77	4.6	3.42	4.2	1.48	1.8	5.30	6.5

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

NOVEOS Specific IgE, F079, Gluten, Wheat										
Sample	Mean (kU/L)	N	Within-Run		Between-Day		Between-Lot		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
1	0.27	75	0.02	7.6	0.00	1.5	0.00	0.2	0.02	7.7
2	0.62	75	0.03	4.4	0.06	9.2	0.00	0.0	0.06	10.2
3	3.09	75	0.14	4.5	0.19	6.1	0.00	0.0	0.23	7.6
4	77.20	75	5.14	6.7	7.66	9.9	0.00	0.0	9.22	11.9

NOVEOS Specific IgE, F202, Cashew Nut										
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	6.5	0.01	5.1	0.00	0.0	0.01	8.2
2	0.45	75	0.02	4.8	0.02	5.6	0.00	0.0	0.03	7.3
3	1.22	75	0.03	2.6	0.08	6.7	0.00	0.0	0.09	7.2
4	5.06	75	0.17	3.4	0.14	2.8	0.00	0.0	0.22	4.4
5	80.36	75	5.73	7.1	3.53	4.4	0.00	0.0	6.73	8.4

NOVEOS Specific IgE, F233, Gal d 1 Ovomucoid, Egg										
Sample	Mean (kU/L)	N	Within-Run		Between-Day		Between-Lot		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
1	0.19	75	0.02	8.3	0.01	5.5	0.00	1.4	0.02	10.1
2	0.47	75	0.02	3.9	0.01	2.9	0.00	0.2	0.02	4.9
3	1.59	75	0.07	4.1	0.06	3.8	0.00	0.0	0.09	5.6
4	94.98	75	7.76	8.2	1.99	2.1	0.00	0.0	8.01	8.4

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 linear range and the claimed analytical measuring range for each NOVEOS Specific IgE assay are shown in the table below.

NOVEOS Specific IgE	Tested Linear Range	Analytical Measuring Range	Regression Equation*
F004, Wheat	0.09 – 101.30 kU/L	0.10 – 100.0 kU/L	$y = 0.96x - 0.02$
F023, Crab	0.09 – 103.71 kU/L	0.10 – 100.0 kU/L	$y = 0.92x + 0.03$
F079, Gluten, Wheat	0.06 – 108.94 kU/L	0.10 – 100.0 kU/L	$y = 0.92x - 0.02$
F202, Cashew Nut	0.08 – 110.21 kU/L	0.10 – 100.0 kU/L	$y = 0.94x + 0.01$
F233, Gal d 1 Ovomucoid, Egg	0.08 – 118.50 kU/L	0.10 – 100.0 kU/L	$y = 1.08x - 0.03$

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. The allergen specific IgE concentration in the positive samples used in the study are: 2.14 kU/L for F004 (Wheat), 4.37 kU/L for F023 (Crab), 12.70 kU/L for F079 (Gluten, Wheat), 4.46 kU/L for F202 (Cashew Nut), and 2.42 kU/L for F233 (Gal d 1 Ovomucoid, Egg).

The allergen solution (inhibitor) was diluted 1:1 into the positive serum sample to achieve a starting concentration of 50 µg/mL for F004 (Wheat) and F023 (Crab), 100 µg/mL for F079 (Gluten, Wheat) and F202 (Cashew Nut), and 3.125 µg/mL for F233 (Gal d 1 Ovomucoid, Egg). The sample solution was serially diluted in two-fold increments, and each diluted sample was evaluated for dose-dependent inhibition in four replicates using one lot of NOVEOS Specific IgE assay for F004 (Wheat), F023 (Crab), F079 (Gluten, Wheat), and F233 (Gal d 1 Ovomucoid, Egg). 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: 83% inhibition for F004 (Wheat) at 50 µg/mL, 84% inhibition for F023 (Crab) at 50 µg/mL, 62% inhibition for F079 (Gluten, Wheat) at 100 µg/mL which is near the beginning of the observed plateau in the dose-response curve, 89% inhibition for F202 (Cashew Nut) at 100 µg/mL, and 92% inhibition for F233 (Gal d 1 Ovomucoid, Egg) at 3.125 µg/mL.

For the NOVEOS Specific IgE assays F004 (Wheat), F023 (Crab), F079 (Gluten, Wheat), F202 (Cashew Nut), and F233 (Gal d 1 Ovomucoid, Egg), the related and unrelated allergens tested were as follows:

- For F004 (Wheat), the related allergen F040 (Yellowfin Tuna) and the unrelated allergens G001 (Grass Pollen Sweet Vernal), K082 (Latex), and T218 (Virginia Live Oak Pollen) were tested as potential inhibitors at a final concentration of at least ten times the concentration of F004 at which 83% 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, F004. The results of the single-dose inhibition studies using one related allergen (F040) and three unrelated allergens showed ≤15% inhibition at test concentrations of 1335 µg/mL (F040), 970 µg/mL (G001), 975 µg/mL (K082), and 1325 µg/mL (T218). The inhibition studies indicate that the NOVEOS Specific IgE assay, F004 contains the immunologically relevant allergen.
- For F023 (Crab), the related allergen F003 (Atlantic Cod) and the unrelated allergens E003 (Horse Epithelia), K082 (Latex), and M006 (*Alternaria alternata*) were tested as potential inhibitors at a final concentration of at least ten times the highest concentration of F023 that achieved 84% 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, F023. The results of the single-dose inhibition studies using one related allergen (F003) and three unrelated allergens showed ≤15% inhibition at test concentrations of 550 µg/mL (F003), 510 µg/mL (E003), 975 µg/mL (K082), and 830 µg/mL (M006). The inhibition studies indicate that the NOVEOS Specific IgE assay, F023 contains the immunologically relevant allergen.
- For F079 (Gluten Wheat), the related allergen F023 (Bos d 4, α-lactalbumin, Milk) and the unrelated allergens E221 (Can f 3 Dog, Serum Albumin, Dog), M220 (Asp f 3, *A. 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 F079 that achieved 62% 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, F079. The results of the single-dose inhibition studies using one related allergen (F076) and three unrelated allergens showed $\leq 15\%$ inhibition at test concentrations of 1460 $\mu\text{g/mL}$ (F076), 1970 $\mu\text{g/mL}$ (E221), 1220 $\mu\text{g/mL}$ (M220), and 1200 $\mu\text{g/mL}$ (T215). The inhibition studies indicate that the NOVEOS Specific IgE assay, F079 contains the immunologically relevant allergen.

- For F202 (Cashew Nut), the related allergen F040 (Yellowfin Tuna) and the unrelated allergens D201 (*Blomia tropicalis*), E070 (Goose Feathers/Skin), and M012 (*Aureobasidium pullulans*) were tested as potential inhibitors at a final concentration of at least ten times the concentration of F202 at which $\geq 85\%$ 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 assay, F202. The results of the single-dose inhibition studies using one related allergen (F040) and three unrelated allergens (D201, E070, and M012) showed $\leq 15\%$ inhibition at test concentrations of 1000 $\mu\text{g/mL}$. The inhibition studies indicate that the NOVEOS Specific IgE assay, F202 contains the immunologically relevant allergen.
- For F233 (Gal d 1 Ovomuroid, Egg), the related allergen F076 (Bos d 4, α -lactalbumin, Milk) and the unrelated allergens E221 (Can f 3, Dog Serum Albumin, Dog), M218 (Asp f 1, *A. fumigatus*), and T215 (Bet v 1 PR-10, Birch) were tested as potential inhibitors at a final concentration of at least ten times the lowest concentration of F233 that achieved $\geq 85\%$ 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, F233. The results of the single-dose inhibition studies using one related allergen (F076) and three unrelated allergens (E221, M218 and T215) showed $\leq 15\%$ inhibition at test concentrations of 31.25 $\mu\text{g/mL}$. The inhibition studies indicate that the NOVEOS Specific IgE assay, F233 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 Specific IgE assays for F004 (Wheat), F023 (Crab), F079 (Gluten, Wheat), F202 (Cashew Nut), and F233 (Gal d 1 Ovomuroid, Egg). 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 Substance 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 assay as shown in the table below:

NOVEOS Specific IgE	Assay Reportable Range/ Analytical Measuring Range
F004, Wheat	0.10 – 100.0 kU/L
F023, Crab	0.10 – 100.0 kU/L
F079, Gluten, Wheat	0.10 – 100.0 kU/L
F202, Cashew Nut	0.10 – 100.0 kU/L
F233, Gal d 1 Ovomucoid, Egg	0.10 – 100.0 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 IgE Capture Reagent Pack of F004 (Wheat), F023 (Crab), F079 (Gluten, Wheat), F202 (Cashew Nut), and F233 (Gal d 1 Ovomucoid, Egg) 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 Pack stored at 37°C to predict shelf-life stability of 36 months stability of these allergen specific Capture Reagent Packs if 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 at least one lot of each NOVEOS Specific IgE Capture Reagent Pack of F004 (Wheat), F023 (Crab), F079 (Gluten, Wheat), F202 (Cashew Nut), and F233 (Gal d 1 Ovomucoid, Egg) 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 Packs stored on-board are stable for 28 days. The result also supports that the allergen specific Capture Reagent Packs once opened and stored at 2-8°C are stable for 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 F004 (Wheat), F023 (Crab), F079 (Gluten, Wheat), F202 (Cashew Nut), and F233 (Gal d 1 Ovomucoid, Egg). 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., F004 (Wheat), F023 (Crab), F079 (Gluten, Wheat), F202 (Cashew Nut), and F233 (Gal d 1 Ovomucoid, Egg) on the NOVEOS Immunoassay Analyzer were determined according to CLSI guideline 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 Specific IgE	No. of Samples	No. of Lots	No. of Analyzers	Testing Protocol
F004	5	2	1	5 samples x 5 replicates/run x 3 runs (N=75 replicates/lot)
F023	4	2	1	4 samples x 5 replicates/run x 3 runs (N= 60 replicates/lot)
F079	4	2	1	4 samples x 5 replicates/run x 3 runs (N= 60 replicates/lot)
F202*	5	2	1	5 samples x 5 replicates/run x 3 or 5 runs (N=95 replicates/lot)
F233	4	2	1	4 samples x 5 replicates/run x 3 runs (N= 60 replicates/lot)

*Two samples had two additional runs

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)
F004, Wheat	0.07	0.10	0.10
F023, Crab	0.07	0.09	0.10
F079, Gluten, Wheat	0.07	0.08	0.10
F202, Cashew Nut	0.07	0.09	0.10
F233, Gal d 1 Ovomucoid, Egg	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 allergen 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, F004, Wheat	Positive	44	0	44
	Negative	4	124	128
	Total	48	124	172
Clinical sensitivity: 91.7% (44/48) (95% CI: 80.4 – 96.7%)				
Clinical specificity: 100.0% (124/124) (95% CI: 97.0 – 100.0%)				

		Clinical Diagnosis		
		Atopic	Non-atopic	Total
NOVEOS Specific IgE, F023, Crab	Positive	38	0	38
	Negative	9	120	129
	Total	47	120	167
Clinical sensitivity: 80.9% (38/47) (95% CI: 67.5 – 89.6%) Clinical specificity: 100.0% (120/120) (95% CI: 96.9 – 100.0%)				

The samples used to evaluate the clinical performance of NOVEOS Specific IgE, F023 (Crab) were also tested with the corresponding predicate device, ImmunoCAP Specific IgE. Clinical specificity of both assays showed 100%, and clinical sensitivity for the two assays are shown in the table below:

	Clinical Sensitivity	
	NOVEOS Specific IgE	ImmunoCAP Specific IgE
F023, Crab	80.9% (38/47)	87.0% (40/46*)

*One patient sample could not be located for testing with ImmunoCAP Specific IgE

		Clinical Diagnosis		
		Atopic	Non-atopic	Total
NOVEOS Specific IgE, F079, Gluten, Wheat	Positive	37	0	37
	Negative	7	126	133
	Total	44	126	170
Clinical sensitivity: 84.1% (37/44) (95% CI: 70.6 – 92.1%) Clinical specificity: 100.0% (126/126) (95% CI: 97.0 – 100.0%)				

		Clinical Diagnosis		
		Atopic	Non-atopic	Total
NOVEOS Specific IgE, F202, Cashew Nut	Positive	52	0	52
	Negative	1	127	128
	Total	53	127	180
Clinical sensitivity: 98.1% (52/53) (95% CI: 90.1 – 99.7%) Clinical specificity: 100.0% (127/127) (95% CI: 97.1 – 100.0%)				

		Clinical Diagnosis		
		Atopic	Non-atopic	Total
NOVEOS Specific IgE, F233, Gal d 1 Ovomucoid, Egg	Positive	24	0	24
	Negative	10	126	136
	Total	34	126	160
Clinical sensitivity: 70.6% (24/34) (95% CI: 53.8 – 83.2%) Clinical specificity: 100.0% (126/126) (95% CI: 97.0 – 100.0%)				

The following literature that supports the observed clinical sensitivity of the NOVEOS Specific IgE assay, F233, Gal d 1 Ovomucoid, Egg is presented in the table below.

NOVEOS Specific IgE assay	Literature Citation(s)	Prevalence	Reported Performance
F233, Gal d 1 Ovomucoid, Egg	Gupta RS, <i>et al.</i> JAMA Network Open. 2019;2(1):e185630	0.8% egg allergy among US adults	Not reported
Clinical sensitivity: 70.6% Clinical specificity: 100.0%	Bartnikas LM, <i>et al.</i> J Allergy Clin Immunol Pract. 2013;1(4):354-360.	n/a	Clinical sensitivity: 66.7% Clinical specificity: 61.3%

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 allergen specific IgE 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 F004 (Wheat), F023 (Crab), F079 (Gluten, Wheat), F202 (Cashew Nut), and F233 (Gal d 1 Ovomucoid, Egg) in the normal population was evaluated based on the data collected in clinical studies which tested samples from apparently healthy subjects including: 124 non-atopic samples for F004; 120 non-atopic samples for F023; 126 non-atopic samples for F079; 127 non-atopic samples for F202; and 126 non-atopic samples for F233. 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.