510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K252775

B Applicant

Hycor Biomedical

C Proprietary and Established Names

NOVEOS Specific IgE (sIgE), Capture Reagent F013, Peanut (*Arachis hypogaea*)
NOVEOS Specific IgE (sIgE), Capture Reagent F076, Bos d 4 α-lactalbumin, Milk
NOVEOS Specific IgE (sIgE), Capture Reagent F077, Bos d 5 β-lactoglobulin, Milk
NOVEOS Specific IgE (sIgE), Capture Reagent F232, Gal d 2 Ovalbumin, 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:

Four new devices

B Measurand:

Allergen specific IgE to Peanut - F013, *Arachis hypogaea*
Allergen specific IgE to Bos d 4 α-lactalbumin, Milk - F076, Bos d 4
Allergen specific IgE to Bos d 5 β-lactoglobulin, Milk - F077, Bos d 5
Allergen specific IgE to Gal d 2 Ovalbumin, Egg - F232, Gal d 2

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
  - Peanut - F013, *Arachis hypogaea*
  - Bos d 4 α-lactalbumin, Milk - F076, Bos d 4
  - Bos d 5 β-lactoglobulin, Milk - F077, Bos d 5
  - Gal d 2 Ovalbumin, Egg - F232, Gal d 2

- 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 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):	K252775 (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
Reaction Temperature	37°C	Same
Limit of quantitation (LoQ)	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 eight NOVEOS Specific IgE assays. A panel of four to 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 samples of F013, F077, and F232). 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, F013, Peanut										
Sample	**Mean (kU/L)**	**N**	**Within-Run**		**Between-Run**		**Between-Day**		**Total**	
			SD	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**
1	0.22	80	0.01	6.0	0.01	3.5	0.00	2.2	0.02	7.3
2	0.46	80	0.02	4.5	0.01	2.1	0.01	1.8	0.02	5.3
3	1.61	80	0.06	3.5	0.03	1.6	0.06	3.9	0.09	5.5
4	73.49	95*	4.16	5.7	3.49	4.7	3.89	5.3	6.67	9.1

* Sample 4 was tested in five replicates for Run 1 and two replicates for Run 2 on Days 1,2,4 and 6, in two replicates for Run 1 and five replicates for Run 2 on Day 5, and in two replicates per run with two runs per day for Days 3 and 7-20, yielding N=95 datapoints

NOVEOS Specific IgE, F076, Bos d 4 α-lactalbumin, Milk										
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	5.0	0.01	4.5	0.00	1.4	0.01	6.9
2	0.36	80	0.02	4.7	0.01	2.6	0.01	3.4	0.02	6.4
3	1.19	80	0.05	4.1	0.03	2.8	0.00	0.0	0.06	5.0
4	72.85	80	4.21	5.8	0.59	0.8	2.99	4.1	5.20	7.1

NOVEOS Specific IgE, F077, Bos d 5 β-lactoglobulin, Milk										
Sample	**Mean (kU/L)**	**N**	**Within-Run**		**Between-Run**		**Between-Day**		**Total**	
			SD	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**
1	0.23	80	0.02	6.8	0.00	0.0	0.01	4.1	0.02	7.9
2	0.46	80	0.02	5.3	0.00	0.4	0.01	1.5	0.03	5.5
3	1.23	80	0.04	3.6	0.03	2.4	0.02	1.7	0.06	4.7
4	76.08	97*	3.44	4.5	2.91	3.8	3.32	4.4	5.59	7.4

* Sample 4 was tested in five replicates for Run 1 and two replicates for Run 2 on Days 1,3 and 4, in five replicates for Run 1 and five replicates for Run 2 with an additional Run 3 (two replicates) on Day 2, and in two replicates per run with two runs per day for Days 5-20, yielding N=97 datapoints

NOVEOS Specific IgE, NOVEOS F232, Gal d 2 Ovalbumin, Egg										
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	5.8	0.01	3.6	0.01	5.5	0.01	8.8
2	0.31	80	0.01	3.1	0.01	2.6	0.01	3.8	0.02	5.6
3	1.61	80	0.05	2.9	0.03	1.9	0.04	2.7	0.07	4.4
4	2.41	80	0.07	3.0	0.06	2.5	0.11	4.4	0.14	5.9
5	88.47	101*	5.30	6.0	5.60	6.3	3.06	3.5	8.29	9.4

* Sample 5 was tested in five replicates for Run 1 and two replicates for Run 2 on Days 1-3, 5 and 6, in five replicates for Run 1 and five replicates for Run 2 on Day 4, and in two replicates per run with two runs per day for Days 7-20, yielding N=101 datapoints

b. Lot-to-lot imprecision

A panel of four 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, F013, Peanut										
Sample	**Mean (kU/L)**	**N**	**Within-Run**		**Between-Day**		**Between-Lot**		**Total**	
			SD	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**
1	0.21	75	0.01	6.5	0.01	4.0	0.00	1.1	0.02	7.7
2	0.59	75	0.02	3.9	0.01	2.3	0.01	1.4	0.03	4.7
3	1.60	75	0.06	3.7	0.05	2.8	0.00	0.0	0.07	4.7
4	75.46	75	4.81	6.4	2.64	3.5	0.00	0.0	5.49	7.3

NOVEOS Specific IgE, F076, Bos d 4 α-lactalbumin, Milk										
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	6.1	0.01	4.5	0.00	2.2	0.01	7.9
2	0.51	75	0.02	4.5	0.02	4.4	0.02	4.0	0.04	7.4
3	1.12	75	0.05	4.6	0.02	2.1	0.05	4.6	0.08	6.9
4	74.84	75	2.51	3.3	5.77	7.7	0.00	0.0	6.29	8.4

NOVEOS Specific IgE, F077, Bos d 5 β-lactoglobulin, Milk										
Sample	**Mean (kU/L)**	**N**	**Within-Run**		**Between-Day**		**Between-Lot**		**Total**	
			SD	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**
1	0.20	75	0.01	5.2	0.02	8.7	0.00	0.0	0.02	10.2
2	0.55	75	0.02	4.1	0.02	3.4	0.00	0.0	0.03	5.3
3	1.13	75	0.04	3.9	0.04	3.3	0.00	0.0	0.06	5.1
4	80.09	75	4.53	5.7	7.62	9.5	0.00	0.0	8.86	11.1

NOVEOS Specific IgE, F232, Gal d 2 Ovalbumin, Egg										
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	9.3	0.02	11.8	0.00	0.0	0.02	15.1
2	0.53	75	0.02	4.1	0.02	2.8	0.01	1.3	0.03	5.2
3	1.58	75	0.06	3.6	0.02	1.2	0.01	0.7	0.06	3.8
4	85.61	75	4.01	4.7	3.99	4.7	0.00	0.0	5.65	6.6

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 mearing range for each NOVEOS Specific IgE are shown in the table below:

NOVEOS Specific IgE	Tested Linear Range	Analytical Measuring Range
F013, Peanut	0.05 – 103.76 kU/L	0.10 – 100.0 kU/L
F076, Bos d 4 α-lactalbumin, Milk	0.09 – 98.91 kU/L	0.10 – 98.0 kU/L
F077, Bos d 5, β-lactoglobulin, Milk	0.05 – 132.05 kU/L	0.10 – 100.0 kU/L
F232, Gal d 2 Ovalbumin, Egg	0.08 – 128.31 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 guideline I/LA20-A3. Positive samples with specific IgE concentration used in the study include: 1.64 kU/L for F013, Peanut; 5.39 kU/L for F076, Bos d 4 α-lactalbumin, Milk; 2.39 kU/L for F077, Bos d 4 α-lactalbumin, Milk and 2.21 kU/L for F232, Gal d 2 Ovalbumin, Egg.

The allergen solution (inhibitor) was diluted 1:1 into the positive serum sample to achieve a starting concentration of 50 µg/mL for F013, F076, F077, and F232. 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 sIgE Assay for F076, F077, and F232, and two lots for F013. 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: 86% inhibition for F013 at 40 µg/mL, 87% inhibition for F076 at 50 µg/mL, 92% inhibition for F077 at 50 µg/mL, and 90% inhibition for F232 at 1.5625 µg/mL.

For the NOVEOS Specific IgE Assays F013, F076, F077, and F232 the related and unrelated allergens tested were as follows:

- For F013, Peanut, the related allergen F202 (Cashew Nut) and the unrelated allergens D072 (*Tyrophagus putrescentiae*), D201 (*Blomia tropicalis*), I006 (German Cockroach), and M012 (*Aureobasidium pullulans*) were tested as potential inhibitors at a final concentration of at least ten times the concentration of F013 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 Assay, F013. The results of the single-dose inhibition studies using one related allergen (F202) and four unrelated allergens showed ≤15% inhibition at a test concentration of 400 µg/mL. The inhibition studies indicate that the NOVEOS Specific IgE Assay, F013 contains the immunologically relevant allergen.

- For F076, Bos d 4 α-lactalbumin, Milk, the related allergen F422 (Ara h 1, 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 F076 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, F076. The results of the single-dose inhibition studies using one related allergen (F422) and three unrelated allergens showed ≤15% inhibition at test concentrations of 600 µg/mL for F422, 1970 µg/mL for E221, 660 µg/mL for M218, and 1200 µg/mL for T215. The inhibition studies indicate that the NOVEOS Specific IgE Assay, F076 contains the immunologically relevant allergen.

- For F077, Bos d 4 α-lactalbumin, Milk, the related allergen F422 (Ara h 1, 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 F077 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, F077. The results of the single-dose inhibition studies using one related allergen (F422) and three unrelated allergens showed ≤15% inhibition at test concentrations of 600 µg/mL for F422, 1970 µg/mL for E221, 660 µg/mL for M218, and 1200 µg/mL for T215. The inhibition studies indicate that the NOVEOS Specific IgE Assay, F077 contains the immunologically relevant allergen.

- For F232, Gal d 2 Ovalbumin, Egg, the related allergen F076 (Bos d 4, α-lactalbumin, Milk) 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 lowest concentration of F232 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, F232. The results of the single-dose inhibition studies using one related allergen (F076) and three unrelated allergens showed ≤15% inhibition at a test concentration of 15.625 µg/mL. The inhibition studies indicate that the NOVEOS Specific IgE Assay, F232 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 F013 (Peanut), F076 (Bos d 4 α-lactalbumin, Milk), F077 (Bos d 5 β-lactoglobulin, Milk), and F232 (Gal d 2 Ovalbumin, 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 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 sIgE as shown in the table below:

NOVEOS Specific IgE	Assay Reportable Range/ Analytical Measuring Range
F013, Peanut	0.10 – 100.0 kU/L
F076, Bos d 4 α-lactalbumin, Milk	0.10 – 98.0 kU/L
F077, Bos d 5, β-lactoglobulin, Milk	0.10 – 100.0 kU/L
F232, Gal d 2 Ovalbumin, 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 sIgE Capture Reagent Pack of F013, F076, F077, and F232 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 to show potential 36 months stability of these Capture Reagent 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 F013, F076, F077, and F232 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 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 28 days stored on-board. The result supports that the allergen specific capture reagent is stable for 28 days once opened and stored at 2-8°C.

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

Open-vial stability: Accelerated open vial stability studies were performed using one lot for F013, F076, F077, and F232 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., F013, F076, F077, and F232 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 sIgE	No. of Samples	No. of Lots	No. of Analyzers	Testing Protocol
F013	4	2	1	4 samples x 5 replicates/run x 3 runs (n= 60)
F076	4	2	1	Lot 1: 4 samples x 5 replicates/run x 3 runs (n= 60) Lot 2: 4 samples x 5 replicates/run x 3 runs (n= 64*)
F077	4-5	2	1	Lot 1: 5 samples x 5 replicates/run x 3 runs (n=75) Lot 2: 4 samples x 5 replicates/run x 3 runs (n= 60**)
F232	5	2	1	5 samples x 5 replicates/run x 3 runs (n= 75)

* A single replicate for a sample dropped on a run so an additional run was performed for lot 2
** One sample was excluded due to carryover

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)
F013, Peanut	0.07	0.08	0.10
F076, Bos d 4, α-lactalbumin, Milk	0.07	0.08	0.10
F077, Bos d 5 β-lactoglobulin, Milk	0.07	0.08	0.10
F232, Gal d 2 Ovalbumin, Egg	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, F013, Peanut	**Positive**	49	0	49
	Negative	5	121	126
	Total	54	121	175
Sensitivity: 90.7% (49/54) (95% CI: 80.1 – 96.0%) Specificity: 100.0% (121/121) (95% CI: 96.9 – 100.0%)				

		Clinical Diagnosis		
		Atopic	**Non-atopic**	**Total**
NOVEOS Specific IgE, F076, Bos d 4, α-lactalbumin, Milk	**Positive**	24	0	24
	Negative	5	132	137
	Total	29	132	161
Sensitivity: 82.8% (24/29) (95% CI: 65.5 – 92.4%) Specificity: 100.0% (132/132) (95% CI: 97.2 – 100.0%)				

		Clinical Diagnosis		
		Atopic	**Non-atopic**	**Total**
NOVEOS Specific IgE, F077, Bos d 5 β-lactoglobulin, Milk	**Positive**	23	0	23
	Negative	6	132	138
	Total	29	132	161
Sensitivity: 79.3% (23/29) (95% CI: 61.6 – 90.2%) Specificity: 100.0% (132/132) (95% CI: 97.2 – 100.0%)				

		Clinical Diagnosis		
		Atopic	**Non-atopic**	**Total**
NOVEOS Specific IgE, F232, Gal d 2 Ovalbumin, Egg	**Positive**	34	0	34
	Negative	0	126	126
	Total	34	126	160
Sensitivity: 100.0% (34/34) (95% CI: 89.8 – 100.0%) Specificity: 100.0% (126/126) (95% CI: 97.0 – 100.0%)				

All samples used to evaluate the clinical performance of each of the above NOVEOS Specific IgE assays were also tested with the corresponding predicate device, ImmunoCAP specific IgE. Clinical specificity of both assays showed 100%, and clinical sensitivity for two assays are shown in the following table:

	Clinical Sensitivity	
	NOVEOS Specific IgE	**ImmunoCAP Specific IgE**
F013, Peanut	90.7%	100.0%
F076, Bos d 4 α-lactalbumin, Milk	82.8%	89.7%
F077, Bos d 5, β-lactoglobulin, Milk	79.3%	79.3%
F232, Gal d 2 Ovalbumin, Egg	100.0%	100.0%

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 F013 (Peanut), F076 (α-lactalbumin), F077 (β-lactoglobulin), and F232 (Ovalbumin) in the normal population was evaluated based on the data collected in clinical studies which tested samples from apparently healthy subjects including: 121 non-atopic samples for F013; 132 non-atopic samples for F076; 132 non-atopic samples for F077; and 126 non-atopic samples for F232 tested by corresponding NOVEOS Specific IgE assay. All samples tested with the NOVEOS Specific IgE assays were below 0.35 kU/L.

VIII Proposed Labeling:

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

IX Conclusion:

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