510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

I Background Information:

A 510(k) Number

K200825

B Applicant

Hycor Biomedical

C Proprietary and Established Names

NOVEOS Specific IgE (sIgE), Capture Reagent Cat Dander - E001, *Felis Domesticus*
NOVEOS Specific IgE (sIgE), Capture Reagent Timothy Grass - G006, *Phleum pratense*

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:

Two new devices

B Measurand:

Allergen specific IgE to Cat Dander E001, *Felis domesticus*
Allergen specific IgE to Timothy Grass G006, *Phleum pratense*

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 (sIgE) 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
  - Cat Dander E001, *Felis domesticus*
  - Timothy Grass G006, *Phleum pretense*

- 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)

The NOVEOS Immunoassay Analyzer is a high-throughput, highly automated immunoassay platform that employs magnetic microbeads as the solid phase. The immunoassay reaction takes place in individual reaction chambers in the reaction rotor, with other rotors containing patient samples and reagents. Liquids are moved by robotic pipettors. The reaction is quantitated by a combination of chemiluminescence and fluorescence measurements compared to a calibration curve, all performed by the analyzer with the NOVEOS software.

B Principle of Operation:

The NOVEOS specific IgE (sIgE) Assay is an immunometric, chemiluminescent assay for the quantitative determination of IgE of known specificity in human serum samples. Magnetic beads coated with streptavidin and fluorescent dye are incubated with a biotinylated allergen that binds to the streptavidin molecule on the surface of the beads. 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 chemilumiscent signal detected by the instrument, the higher the amount of sIgE detected in the sample tested.

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):	K200825	K051218
Device Trade Name	NOVEOS sIgE Assay	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 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
Allergen	Whole extract of allergen material: • Cat Dander E001, *Felis domesticus* • Timothy Grass G006, *Phleum pratense*	Same
Traceability	World Health Organization (WHO) reference reagent serum Immunoglobulin E (IgE) 11/234	Same
Number of Calibrators	Six	Same
Reaction Temperature	37 ºC	Same
General Device Characteristic Differences		
Specimen Type	Serum	Serum and Plasma (EDTA, Na-Heparin)
Solid Phase	Magnetic microparticles	Cellulose derivative
Instrument(s)	NOVEOS Immunoassay Analyzer	Phadia 100, Phadia 250/1000/2500/5000

Assay Principle	Chemiluminescent assay	Fluoroenzyme-immunoassay
General Device Characteristic Differences		
Detection Antibody	HRP conjugated mouse anti-human IgE monoclonal antibody	β-Galactosidase conjugated mouse anti-human IgE monoclonal antibody
Sample Volume	4 µL	40 µL
Detection Limit	E001: LoB: 0.02 kU/L LoD: 0.06 kU/L LoQ: 0.14 kU/L G006: LoB: 0.03 kU/L LoD: 0.06 kU/L LoQ: 0.14 kU/L	LoB: 0.001 kU/L LoD: 0.02 kU/L LoQ: 0.10 kU/L
Assay Range	0.17 – 100 kU/L	0.10 – 100 kU/L
Assay Duration	1 hour and 45 minutes	Phadia 100: 2 hours and 30 minutes Phadia 250/1000/2500/5000: 1 hour and 45 minutes from entering the first sample

VI Standards/Guidance Documents Referenced:

- 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 EP17-A2, Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline – Second Edition
- CLSI EP6-A, Evaluation of Linearity of Quantitative Measurement, Approved Guideline
- CLSI EP25-A, Evaluation of Stability of In Vitro Diagnostic Reagents, Approved Guideline – Second Edition
- CLSI EP07-A2, Interference Testing in Clinical Chemistry; Approved Guideline – Second Edition
- CLSI EP15-A3, User Verification of Precision and Estimation of Bias; Approved Guideline - Third Edition
- CLSI EP28-A3c, Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline – Third Edition

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

All results presented below met the manufacturer's pre-determined acceptance criteria**.**

1. Precision/Reproducibility:

   i) Within-laboratory imprecision

   A study was conducted per CLSI guideline EP05-A3 to evaluate the imprecision of the NOVEOS sIgE Assay, E001 and the NOVEOS sIgE Assay, G006. Two separate panels, one consisting of five samples (one negative and two positive human serum samples for E001 plus two controls) and the other consisting of six samples (one negative and three positive human serum samples for G006 plus two controls), were tested at one site, in two replicates 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). The standard deviation (SD) and %CV of the within-run, between-run, between-day, and total imprecision were calculated for each sample and results are summarized in the following tables:

NOVEOS sIgE Assay, E001									
Sample	**Mean (kU/L)**	**Within-Run**		**Between-Run**		**Between-Day**		**Total**	
		SD (kU/L)	**CV (%)**	**SD (kU/L)**	**CV (%)**	**SD (kU/L)**	**CV (%)**	**SD (kU/L)**	**CV (%)**
LoQ18	0.26	0.02	7.1	0.01	5.0	0.02	5.9	0.03	10.5
PP46	8.63	0.31	3.6	0.18	2.1	0.49	5.7	0.61	7.0
LYP	12.59	0.45	3.6	0.63	5.0	0.67	5.3	1.02	8.1
NOV	13.62	0.59	4.3	0.68	5.0	0.82	6.0	1.22	8.9
PP28	40.81	1.37	3.4	1.67	4.1	2.47	6.0	3.28	8.0
LYP: Lyphochek Positive Control Sample NOV: NOVEOS Positive Control Sample									

NOVEOS sIgE Assay, G006									
Sample	**Mean (kU/L)**	**Within-Run**		**Between-Run**		**Between-Day**		**Total**	
		SD (kU/L)	**CV (%)**	**SD (kU/L)**	**CV (%)**	**SD (kU/L)**	**CV (%)**	**SD (kU/L)**	**CV (%)**
LoQ50	0.19	0.01	7.0	0.01	7.1	0.01	3.2	0.02	10.4
PP48	0.37	0.01	4.0	0.01	3.9	0.01	3.1	0.02	6.4
PP25	6.36	0.19	3.0	0.21	3.3	0.15	2.4	0.32	5.0
LYP	8.86	0.24	2.7	0.40	4.5	0.38	4.3	0.60	6.8
NOV	27.50	1.15	4.2	1.86	6.8	2.13	7.7	3.05	11.1
PP06	44.04	2.01	4.6	2.19	5.0	3.72	8.4	4.76	10.8
LYP: Lyphochek Positive Control Sample NOV: NOVEOS Positive Control Sample									

ii) Lot-to-lot imprecision:

The same two sample panels used in the within-laboratory precision study were also tested on two additional different lots of the respective NOVEOS sIgE Assay for a total of three reagent lots. Each sample was tested in two replicates per run, two runs per day for 20 days. The lot-to-lot imprecision was evaluated based on a total of 240 measurements per sample. The results are summarized in the following tables:

NOVEOS sIgE Assay, E001									
Sample	Mean (kU/L)	Within-Run		Between-Day		Between-Lot		Total	
		SD (kU/L)	CV (%)	SD (kU/L)	CV (%)	SD (kU/L)	CV (%)	SD (kU/L)	CV (%)
LoQ18	0.26	0.02	6.5	0.01	5.2	0.00	0.0	0.03	9.5
PP46	8.51	0.30	3.5	0.51	5.9	0.10	1.2	0.65	7.6
LYP	12.66	0.47	3.7	0.79	6.3	0.15	1.2	1.12	8.8
NOV	13.65	0.54	4.0	0.78	5.7	0.00	0.0	1.26	9.2
PP28	41.07	1.53	3.7	2.56	6.2	0.48	1.2	3.35	8.2
LYP: Lyphochek Positive Control Sample NOV: NOVEOS Positive Control Sample									

NOVEOS sIgE Assay, G006									
Sample	Mean (kU/L)	Within-Run		Between-Day		Between-Lot		Total	
		SD (kU/L)	CV (%)	SD (kU/L)	CV (%)	SD (kU/L)	CV (%)	SD (kU/L)	CV (%)
LoQ50	0.20	0.01	7.2	0.01	3.6	0.00	1.9	0.02	10.6
PP48	0.37	0.02	4.1	0.01	3.7	0.01	2.8	0.03	7.2
PP25	6.32	0.21	3.3	0.06	1.0	0.06	1.0	0.33	5.2
LYP	8.83	0.29	3.3	0.48	5.4	0.14	1.6	0.69	7.8
NOV	28.05	1.21	4.3	2.08	7.4	0.08	0.3	3.14	11.2
PP06	45.34	1.95	4.3	3.47	7.7	1.88	4.2	4.94	10.9
LYP: Lyphochek Positive Control Sample NOV: NOVEOS Positive Control Sample									

iii) Site-to-site reproducibility:

Reproducibility of the NOVEOS sIgE Assay, E001 and the NOVEOS sIgE Assay, G006 was evaluated by testing two separate six-member panels, one consisting of one negative and three positive human serum samples for E001 plus two controls and another consisting of one positive and three negative serum samples for G006 plus two controls, at three sites using the same lot of reagent. Each sample was tested in five replicates per run, one run per day for five days on one NOVEOS Immunoassay Analyzer at each site (for a total of 75 measurements per sample at all three sites). The results are summarized in the following tables:

NOVEOS sIgE Assay, E001									
Sample	Mean (kU/L)	Within-Run		Between-Day		Between-Site		Total	
		SD (kU/L)	CV (%)	SD (kU/L)	CV (%)	SD (kU/L)	CV (%)	SD (kU/L)	CV (%)
PP61	0.27	0.02	7.4	0.01	3.7	0.03	11.1	0.03	11.1
PP62	0.50	0.03	6.0	0.01	2.0	0.06	11.9	0.07	13.9
PP63	1.15	0.07	6.1	0.02	1.7	0.11	9.6	0.13	11.3
NOV	10.64	0.56	5.3	0.22	2.1	0.46	4.3	0.76	7.1
LYP	12.58	0.52	4.1	0.22	1.7	0.32	2.5	0.65	5.2
PP64	69.93	4.90	7.0	2.01	2.9	1.83	2.6	5.60	8.0

LYP: Lyphochek Positive Control Sample
NOV: NOVEOS Positive Control Sample

NOVEOS sIgE Assay, G006									
Sample	Mean (kU/L)	Within-Run		Between-Day		Between-Site		Total	
		SD (kU/L)	CV (%)	SD (kU/L)	CV (%)	SD (kU/L)	CV (%)	SD (kU/L)	CV (%)
PP65*	0.18	0.02	11.1	0.00	0.0	0.00	0.0	0.02	11.1
PP66	0.42	0.03	7.1	0.00	0.0	0.02	4.7	0.04	9.5
PP67	2.16	0.10	4.6	0.06	2.8	0.14	6.5	0.18	8.3
LYP	8.46	0.36	4.3	0.25	3.0	0.26	3.1	0.51	6.0
NOV	10.32	0.53	5.1	0.27	2.6	0.48	4.6	0.76	7.4
PP68	57.38	4.02	7.0	0.76	1.3	2.03	3.5	4.56	7.9

LYP: Lyphochek Positive Control Sample
NOV: NOVEOS Positive Control Sample
*One result was excluded from the final analysis dataset. The test result had an error flag for insufficient sample volume that was attributed to a bubble; the test was not repeated.

2. Linearity:

Linearity of each NOVEOS sIgE Assay was evaluated following CLSI guideline EP6-A by preparing three sets of dilution panel. Three positive serum samples (low, medium and high level) were each serially diluted in a two-fold scheme with a negative serum pool generating at least five consecutive dilutions. Each diluted sample was tested in replicates of five and each neat sample was tested in replicates of 15, all within one assay run using one reagent lot on one NOVEOS Immunoassay Analyzer. Results of the replicates for all three samples were analyzed for linearity. Regression statistics comparing the observed results (y) to expected results (x) of all samples in each and all three dilution panels are presented in the tables below.

NOVEOS sIgE Assay, E001					
Dilution Series	**Dilution Range (kU/L)**	**Regression Equation**	**Slope (95% CI)**	**Intercept (95% CI)**	**R^2**
1	0.03–4.90	y = 1.00x − 0.04	0.99 − 1.02	-0.08 − 0.00	1.000
2	0.03–49.36	y = 1.01x − 0.34	0.97 − 1.05	-1.17 − 0.49	0.999
3	0.03–101.62	y = 1.01x − 1.11	0.97 −1.04	-2.52 − 0.30	0.999
All	0.03–101.62	y = 1.00x − 0.37	0.98 − 1.01	-0.79 − 0.05	0.999

NOVEOS sIgE Assay, G006					
Dilution Series	**Dilution Range (kU/L)**	**Regression Equation**	**Slope (95% CI)**	**Intercept (95% CI)**	**R^2**
1	0.06−5.35	y = 1.01x + 0.00	0.97 − 1.06	-0.11 − 0.11	0.999
2	0.06−34.50	y = 0.99x − 0.03	0.96 − 1.02	-0.49 − 0.43	0.999
3	0.06−104.99	y = 1.00x + 2.75	0.93 − 1.07	-0.46 − 5.97	0.996
All	0.06–104.99	y = 1.02x + 0.58	0.99 − 1.05	-0.36 − 1.51	0.997

The data summarized in the tables above support linearity throughout the claimed measuring range from 0.17 kU/L to 100 kU/L for both the NOVEOS sIgE Assay, E001 and NOVEOS sIgE Assay, G006.

3. Analytical Specificity/Interference:

a) Inhibition study:

Immunological specificity of E001 (Cat Dander, *Felis domesticus*) and G006 (Timothy Grass, *Phleum pretense*) allergens was verified through competitive inhibition according to CLSI guideline I/LA20-A3. A positive sample with specific IgE concentration of ~7.6 kU/L for E001 and ~0.6 kU/L for G006 was used in the inhibition studies. The allergen solution (inhibitor) was diluted into the positive serum sample to achieve a starting concentration of 15 µg/mL for E001 and 50 µg/mL for G006. The sample solution was serially diluted five times in two-fold increments and each diluted sample was evaluated for dose-dependent inhibition in five replicates with one lot of reagent. The results of the dose-dependent inhibition study showed that >50% inhibition was achieved with E001 and G006 at a final inhibitor concentration of 15 µg/mL and 25 µg/mL, respectively.

For the NOVEOS sIgE Assay, E001, the related allergen E006 (guinea pig epithelia, *Cavia porcellus*), and the unrelated allergens, G013 (velvet grass, *Holcus lanatus*), W011 (Russian thistle, *Salsola kali*)) and M004 (*Mucor circinelloides f. lusitanicus*) were tested as potential inhibitors for at a final concentration of at least ten times the concentration of E001 at which >50% inhibition was achieved. All allergen inhibitors were spiked into the positive serum sample at a 1:1 dilution and evaluated with three lots of NOVEOS sIgE Assay, E001. The results of the single-dose inhibition studies using one related allergen (E006) and three unrelated allergens (G013, W011 and M004) did not show inhibition at a test concentration of 150 µg/mL for the related allergen and 150 µg/mL for the three unrelated allergens. The inhibition studies indicate that the NOVEOS sIgE Assay, E001 contains the immunologically relevant allergen.

For the NOVEOS sIgE Assay, G006, the related allergen G202 (cultivated corn, *Zia mays*), and the unrelated allergens, W043 (common sagebrush, *Artemisia tridentata*), F018 (brazil nut, *Bertholletia excelsa*) and M004 (*Mucor circinelloides f. lusitanicus*) were tested as potential inhibitors at a final concentration of at least ten times the concentration of G006 at which >50% inhibition was achieved. All allergen inhibitors were spiked into the positive serum sample at a 1:1 dilution and evaluated with three lots of NOVEOS sIgE Assay, G006. The results of the single-dose inhibition studies using one related allergen (G202) and three unrelated allergens (W043, F018 and M004) did not show inhibition at a test concentration of 250 µg/mL for the related allergen and 250 µg/mL for the three unrelated allergens. The inhibition studies indicate that the NOVEOS sIgE Assay, G006 contains the immunologically relevant allergen.

b) Interference:

(1) Endogenous Substance Interference:

The effect of the presence of elevated level of human albumin, hemoglobin, triglyceride, conjugated bilirubin, unconjugated bilirubin, and rheumatoid factor in serum samples was evaluated by testing three (one negative, one near the cut-off and one positive) serum sample pools spiked with varying levels of each interferent and analyzed in 12 replicates in one assay run with three lots of each NOVEOS sIgE Assay. The % recovery for each sample spiked with the potential interfering substance was calculated by comparing its result to that of the corresponding reference 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, unconjugated bilirubin up to 20 mg/dL, and rheumatoid factor up to 513 IU/mL.

(2) Exogenous Substance Interference:

The same protocol used in the endogenous substance interference study was used to evaluate potentially interfering exogenous substances. No interference was noted for samples containing biotin at a concentration of 3500 ng/mL, diphenhydramine at 19.6 µmol/L, methylprednisolone at 1000 ng/mL, omalizumab at 0.12 mg/mL and ranitidine at 19.1 µmol/L.

c) Cross-reactivity:

The potential cross-reactivity of non-IgE (IgA, IgD, IgG, and IgM) to the NOVEOS sIgE Assay, E001 and NOVEOS sIgE Assay, G006 was evaluated by testing two separate panel, one consisting of three human serum samples (one negative and two positives including one near 0.35 kU/L for E001) and another consisting of five human serum samples (one negative and four positives including one near 0.35 kU/L for G006). Each serum sample was spiked with the immunoglobulin stock solutions containing IgA, IgG, and IgM (IgGAM) at 76.86 mg/mL and IgD at 77.25 mg/mL. The control samples were prepared by adding a solvent to mimic the IgGAM and IgD spiked volumes. Test and control samples were analyzed in replicates of three in one assay run with one lot of the reagent. The % recovery was calculated by comparing measurements of the test and

control samples. No cross reactivity was noted up to 14.86 mg/mL for IgGAM and up to 0.173 mg/mL for IgD.

4. Assay Reportable Range:

The claimed measuring range is from 0.17 kU/L to 100 kU/L.

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

a) Traceability:

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

b) Kit Stability:

Shelf life stability: Both an ongoing real-time stability study and an accelerated stability study were performed in accordance with CLSI EP25-A using three lots of the NOVEOS E001 Capture Reagent and three lots of the NOVEOS G006 Capture Reagent. The accelerated stability data support the manufacturer's claim of 24-month unopened shelf-life stability for both the NOVEOS E001 Capture Reagent and NOVEOS G006 Capture Reagent. The real-time stability study is on-going and available data supports 16 months unopened shelf-life stability for both the NOVEOS E001 Capture Reagent and NOVEOS G006 Capture Reagent when stored at 2–8 °C per the manufacturer's instruction for use. 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, with the exception of the Fluo Beads reagent which has an extended shelf-life stability of up to 24 months based on the real-time stability data per K191510. The claimed shelf-life for individual assay components is listed in the table below:

		Shelf-life Stability (2–8 ºC)
Specific IgE Capture Reagent E001*		24 months
Specific IgE Capture Reagent G006*		24 months
IgE Common Kit	Diluent A	48 months
	Conjugate IgE	18 months
	Substrate A and B	24 months
	Fluo Beads	24 months
IgE Calibrator Set		24 months
Calibrator Antibody IgE		24 months
Controls	IgE Positive Control Pack	24 months
	IgE Negative Control Pack	48 months
Others	Wash Buffer Concentrate	48 months
	Cuvette Wash Pack	24 months
	Probe Wash Pack	24 months
*Results based on accelerated stability data		

On-board stability: A real-time stability study using three lots of the NOVEOS E001 Capture Reagent and three lots of the NOVEOS G006 Capture Reagent supports the on-board stability claim 28 days. The on-board stability for all the other assay components has been previously established per K182479 and are summarized in the table below.

		On-board Stability (2–8ºC)
Specific IgE Capture Reagent E001		28 days
Specific IgE Capture Reagent G006		28 days
IgE Common Kit	Diluent A	14 days
	Conjugate IgE	14 days
	Substrate A and B	14 days
	Fluo Beads	14 days
IgE Calibrator Set		48 hours
Controls	IgE Positive Control Pack	48 hours
	IgE Negative Control Pack	48 hours
Others	1x Wash Buffer	28 days
	Cuvette Wash Pack	28 days
	Probe Wash Pack	Not applicable

6. Detection Limit:

The limit of blank (LoB), limit of detection (LoD), and limit of Quantitation (LoQ) of the NOVEOS sIgE Assay, E001 and the NOVEOS sIgE Assay, G006 on the NOVEOS Immunoassay Analyzer were determined according to CLSI guideline EP17-A2.

LoB was determined by testing five IgE-free human serum samples in two replicates per run, one run per day, for six days using three lots of each NOVEOS sIgE Assay. The runs were spread out on three different NOVEOS Immunoassay Analyzers. The LoB was estimated as the 95th percentile of 60 measurements for each of the lots tested.

LoD was determined using five serum samples with low IgE concentrations with the NOVEOS sIgE Assay, E001 and six serum samples with low IgE concentrations with the NOVEOS sIgE Assay, G006. Each sample was tested in replicates of 10 replicates per run, one run per day, for six days using three lots of each NOVEOS sIgE Assay. The runs were spread out on three different NOVEOS Immunoassay Analyzers. The LoD was determined for each lot based on 300 measurements for E001 or 360 measurements for G006 as the mean concentration of the lowest sample with 95% or more of its replicates recovering above the LoB.

LoQ was determined as functional sensitivity using a set of five samples with low IgE concentrations. Each sample was tested in duplicates per run, two runs per day for 20 days with three lots of each NOVEOS sIgE Assay on one instrument for a total of 80 data points per sample per reagent lot. The LoQ is defined as the mean value of the 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 lots tested and are summarized in the table below.

	LoB	LoD	LoQ
NOVEOS sIgE Assay, E001	0.02 kU/L	0.06 kU/L	0.14 kU/L
NOVEOS sIgE Assay, G006	0.03 kU/L	0.06 kU/L	0.14 kU/L

7. Assay Cut-Off:

   See clinical cut-off

8. Accuracy (Instrument):

   Not applicable

9. Carry-Over:

   Evaluation of instrument carryover was conducted using one lot of reagent of each NOVEOS sIgE Assay on three NOVEOS Immunoassay Analyzers. The carryover assessment is based on five cycle counts per instrument. Pooled high-level patient samples with sIgE concentrations ranging from 99.1 to 100.0 kU/L for E001 and from 81.2 to 89.8 for G006 were aliquoted into five tubes and the pooled low-patient samples with sIgE concentrations of 0.04 and 0.05 kU/L for E001 and of 0.05 and 0.06 kU/L for G006, were aliquoted into 25 tubes. Each cycle consists of one high sample test followed by five low sample tests against the E001 or G006 capture reagent. Low Sample 1 following High Sample is denoted as "possibly affected" which has the highest chance of potential carryover thus leading to signal change > 0.10 kU/L. Low Samples 3–5 is denoted as "very probably unaffected" and therefore should not have elevated kU/L signal. Carryover assessment is done by measuring the change (Δ) of [mean concentration of Low Sample 1] and [mean concentration of Low Samples 3–5]. The results are summarized in the tables below:

NOVEOS sIgE Assay, E001				
NOVEOS Immunoassay Analyzer	**Mean Conc. of High Sample (kU/L)**	**Mean Conc. of Low Sample 1 (kU/L)**	**Mean Conc. of Low Sample 3-5 (kU/L)**	**Δ Carryover (kU/L)**
1	99.15	0.04	0.03	0.01
2	99.23	0.04	0.03	0.01
3	100.04	0.05	0.06	-0.01

NOVEOS sIgE Assay, G006				
NOVEOS Immunoassay Analyzer	**Mean Conc. of High Sample (kU/L**	**Mean Conc. of Low Sample 1 (kU/L)**	**Mean Conc. of Low Sample 3-5 (kU/L)**	**Δ Carryover (kU/L)**
1	81.19	0.06	0.05	0.01
2	82.38	0.06	0.05	0.01
3	89.84	0.05	0.05	0.00

B Comparison Studies:

1. Method Comparison with Predicate Devices:

At least 200 serum samples spanning the measuring range were tested with each NOVEOS sIgE Assay (candidate) and the respective ImmunoCAP Specific IgE (predicate). Agreement between the candidate and predicate devices was evaluated using a clinical cut-off value of 0.35 kU/L. The results are summarized in the following tables:

		ImmunoCAP sIgE, Allergen e1, Cat dander		
		Positive	**Negative**	**Total**
NOVEOS sIgE Assay, E001	**Positive**	89	2	91
	Negative	8	143	151
	Total	97	145	242
	Positive Agreement: 91.8% (89/97) 95% CI: 84.6% − 95.8% Negative Agreement: 98.6% (143/145) 95% CI: 95.1% – 99.6% Total Agreement: 95.9% (232/242) 95% CI: 92.6% – 97.7%			

		ImmunoCAP sIgE, Allergen g6, Timothy		
		Positive	**Negative**	**Total**
NOVEOS sIgE Assay, G006	**Positive**	89	4	93
	Negative	14	131	145
	Total	103	135	238
	Positive Agreement: 86.4% (89/103) 95% CI: 78.5% − 91.7% Negative Agreement: 97.0% (131/135) 95% CI: 92.6% – 98.8% Total Agreement: 92.4% (220/238) 95% CI: 88.4% – 95.2%			

2. Matrix Comparison:

Not Applicable

C Clinical Studies:

1. Clinical Sensitivity/ Specificity:

To demonstrate the clinical performance of each NOVEOS sIgE Assay, test results of the clinical samples from atopic and healthy, non-atopic donors evaluated in the method comparison study were compared to a clinical diagnosis of allergy. The atopic donors with a clinical history of allergy-like symptoms were identified as positive by skin prick testing (SPT) and clinical history; and the non-atopic donors with no reported allergy. Results are expressed as positive when a sample with a sIgE value is greater than or equal to 0.35 kU/L or negative when a sample with a sIgE value is less than 0.35 kU/L The clinical sensitivity and specificity in this study cohort are summarized in the following tables:

		Clinical Diagnosis		
		Atopic	**Non-atopic**	**Total**
NOVEOS sIgE Assay, E001	**Positive**	53	0	53
	Negative	17	130	147
	Total	70	130	200
	Sensitivity: 75.7% (53/70) 95% CI: 64.5% − 84.2% Specificity: 100.0% (130/130) 95% CI: 97.1% – 100.0%			

		Clinical Diagnosis		
		Atopic	**Non-atopic**	**Total**
NOVEOS sIgE Assay, G006	**Positive**	48	1	49
	Negative	15	124	139
	Total	63	125	188
	Sensitivity: 76.2% (48/63) 95% CI: 64.4% – 85.0% Specificity: 99.2% (124/125) 95% CI: 95.6% – 99.9%			

2. Other Clinical Supportive Data:

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	0.35 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 negative (< 0.35 kU/L) for a specific allergen in a non-atopic person. Each laboratory should establish its own expected value.

The expected value/reference range of NOVEOS sIgE, E001 and NOVEOS sIgE, G006 in the normal population were evaluated by testing samples from 132 apparently healthy subjects in the clinical study for E001 and 127 apparently healthy subjects in the clinical study for G006. All samples were below <0.35 kU/L.

F Other Supportive Instrument Performance Characteristics Data:

Not Applicable

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.