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Celiac Testing
tTG IgA, tTG IgG, dGliadin IgA, and dGliadin IgG
- New Assays -

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Ordering Information:

Test Name	tTG IgA	tTG IgG	dGliadin IgA	dGliadin IgG
PDM Number	1758066	1758068	1758062	1758064
LOINC Codes	46128-5	56537-4	63453-5	63459-2
CPT Codes	83516	83516	83516	83516
Sample	Serum	Serum	Serum	Serum
Stability (Temp)	Refrigerate	Refrigerate	Refrigerate	Refrigerate
Stability(Time)	48 hours	48 hours	48 hours	48 hours
Alternate Spec Type	Plasma (EDTA, Citrate)	Plasma (EDTA, Citrate)	Plasma (Heparin, EDTA, Citrate)	Plasma (Heparin, EDTA, Citrate)
Test Method:	Fluoroenzyme Immunoassay	Fluoroenzyme Immunoassay	Fluoroenzyme Immunoassay	Fluoroenzyme Immunoassay

Available Panels:

Test Name:	Celiac Screen	Celiac Monitoring (Gliadin Panel)
PDM Number:	1758070	1758060
Includes:	Total IgA tTG IgA Celiac Screen Interpretation	dGliadin IgA dGliadin IgG
Specimen:	Serum only Refrigerated for 48 hours	Serum or Plasma (Heparin, EDTA, Citrate) Refrigerated for 48 hours
CPT Codes	83516, 82784	83516 x 2

Additional panels may be built upon request.

Effective Date: Testing offered beginning on Monday, May 23, 2016.

Performed: Monday, Wednesday, and Friday dayshift

Reference Ranges:

Test	Previous Range (Quest)		New Range (CPAL)		
	Negative	Positive	Negative	Equivocal	Positive
tTG IgA	< 4 U/mL	≥ 4 U/mL	<7 U/mL	7 – 10 U/mL	>10 U/mL
tTG IgG	< 6 U/mL	≥ 6 U/mL	<7 U/mL	7 – 10 U/mL	>10 U/mL
dGliadin IgA	< 20 Units	≥ 20 Units	<7 U/mL	7 – 10 U/mL	>10 U/mL
dGliadin IgG	< 20 Units	≥ 20 Units	<7 U/mL	7 – 10 U/mL	>10 U/mL

In case of equivocal results, it is recommended that the patient be retested in 8 – 12 weeks

Background:

Celiac disease is a life-long condition in which ingestion of gluten, the water insoluble wheat-gliadin and the prolamins in rye and barley, leads to chronic inflammation and damage of the small intestinal mucosa. The term gluten refers to a whole set of proteins in the so-called endosperm, the nutritive tissue of the grain seed of wheat, rye, oats, and barley. The alcohol-soluble polypeptides of gluten, the gliadins, are solely responsible for the toxic effects to the intestinal mucosa.

The disease is multifaceted in nature with clinical presentations ranging from gastrointestinal manifestations to asymptomatic, silent, and extraintestinal forms. It is widely accepted that dermatitis herpetiformis, a bullous skin disease, is induced by gluten. Tissue transglutaminase has been identified as the major autoantigen in celiac disease. IgA antibodies against tTG are highly disease specific serological markers for celiac disease and dermatitis herpetiformis. tTG IgG antibodies are less specific for these diseases but are helpful markers in patients with IgA deficiency.

More recent research revealed that gliadin peptides deamidated by tissue transglutaminase represent more specific B-cell epitopes than native peptides. Further studies showed that increased specificity can also be observed for anti-gliadin assays based on deamidated peptides.

Principle of Test:

The EliA tTG IgA, tTG IgG, dGliadin IgA, and dGliadin IgG assays are performed on the Phadia 250 immunoassay system. The assays utilize human or human recombinant protein and enzyme-labeled antibodies against human IgA or IgG antibodies. Results are directly related to the signal produced.

Validation Data:

Precision:

For within run precision, two levels of control were run ten times each, within the same run. For between run precision, two levels of control were run five times each on two different days. The %CVs fall within the Manufacturer's claim of ≤12% for the positive control. The negative control was negative for all replicates.

Table 1: Precision

Test	Within Run Precision (N1778)				Within Run Precision (N1926)				Accept?
	Mean (Neg)	CV	Mean (Pos)	CV	Mean (Neg)	CV	Mean (Pos)	CV	
tTG IgA	0.19	16.6%	50.6	2.1%	0.10	0.0%	50.4	2.1%	Yes
tTG IgG	0.60	0.0%	37.5	1.4%	0.60	0.0%	36.4	1.4%	Yes
dGliadin IgA	0.34	24.8%	43.5	2.2%	0.21	15.1%	45.3	3.6%	Yes
dGliadin IgG	0.40	0.0%	123.9	1.8%	0.40	0.0%	131.1	2.8%	Yes

Table 2: Between Run Precision

Test	Between Run Precision (N1778)				Between Run Precision (N1926)				Accept?
	Mean (Neg)	CV	Mean (Pos)	CV	Mean (Neg)	CV	Mean (Pos)	CV	
tTG IgA	0.19	13.4%	50.1	2.9%	0.10	0.0%	50.9	2.3%	Yes
tTG IgG	0.60	0.0%	37.0	2.9%	0.60	0.0%	36.3	1.6%	Yes
dGliadin IgA	0.33	21.7%	43.1	2.9%	0.21	16.5%	45.2	2.9%	Yes
dGliadin IgG	0.40	0.0%	124.9	2.4%	0.40	0.0%	133.1	3.4%	Yes

Method Comparison:

Specimens were split and processed utilizing the Phadia 250 EliA Celikey (tTG) and dGliadin assays versus results from the Inova assay, Quest Diagnostics' method. (Figure 1).

Figure 1

Assay	Phadia 250				
	Positive Agreement vs Inova	Negative Agreement vs Inova	Overall Agreement	N	Acceptable?
tTG IgA	94.1%	100.0%	97.4%	38	Yes
tTG IgG	80.0%	100.0%	91.4%	35	Yes
dGliadin IgA	84.2%	95.0%	92.3%	39	Yes
dGliadin IgG	90.0%	100.0%	95.0%	40	Yes

The research article entitled 'Analytical and Clinical Comparison of Two Fully Automated Immunoassay Systems for the Diagnosis of Celiac Disease" evaluated the performance of Inova Diagnostics and ThermoFisher Scientific's Phadia EliA tTG and dGliadin assays. The article was published in the Journal of Immunology Research, Volume 2014 by Hindawi Publishing Corporation in March of 2014. The results demonstrated good qualitative agreement between the assays. The specificity of the Phadia 250 tTG IgA and tTG IgG assays were 99.3% and 100.0% respectively and the specificity of the Phadia 250 dGliadin IgA and IgG assays were 97.1% and 98.6% respectively.

Elsevier published a journal article titled "Testing for IgG class antibodies in celiac disease patients with selective IgA deficiency. A comparison of the diagnostic accuracy of 9 IgG anti-tissue transglutimase, 1 IgG anti-gliadin and 1 IgG anti-deaminated gliadin peptide antibody assays" published in March of 2007. The results demonstrated that the diagnostic sensitivity for Celiac Disease was 75% for Inova (Quest method) versus 95% for Phadia.

Reference Range:

Manufacturer's stated reference ranges were verified using the method comparison data.

Limitations:

1. A definitive clinical diagnosis should not be based on the results of a single diagnostic method, but should only be made by the physician after all clinical and laboratory findings have been evaluated.
2. Antibody prevalence in autoimmune patients varies widely depending on disease area. The proportion of sera from a normal population found positive for tTG antibodies covered by the EliA Celikey IgA and IgG test, is below 1%.
3. Antibody prevalence in autoimmune patients varies widely depending on disease area. The proportion of sera from a normal population found positive for gliadin antibodies covered by the EliA Gliadin^{DP} IgA test is below 1%. Expected values may vary depending on the population tested.
4. The following substances in concentrations corresponding to those indicated in un-diluted samples were analyzed for interference with EliA Gliadin^{DP} IgA: Bilirubin F/C (38.2/41.2 mg/dl), Chyle (31.8 FTU), Hemoglobin (9.88 mg/dl) and Rheumatoid factor IgM (11 IU/ml). No interference could be observed.

5. The following substances in concentrations corresponding to those indicated in un-diluted samples were analyzed for interference with EliA Gliadin^{DP} IgG: Bilirubin F/C (19.1/20.6 mg/dl), Chyle (15.9 FTU), Hemoglobin (4.9 mg/dl) and Rheumatoid factor IgM (5.5 IU/ml). No interference could be observed.

References:

1. EliA Celikey IgA package insert, February 2015.
2. EliA Celikey IgG package insert, February 2015.
3. EliA Gliadin^{DP} IgA package insert, February 2015.
4. EliA Gliadin^{DP} IgG package insert, February 2015.
5. 'Analytical and Clinical Comparison of Two Fully Automated Immunoassay Systems for the Diagnosis of Celiac Disease', Journal of Immunology Research, Volume 2014, March of 2014.
6. 'Testing for IgG class antibodies in celiac disease patients with selective IgA deficiency. A comparison of the diagnostic accuracy of 9 IgG anti-tissue transglutimase, 1 IgG anti-gliadin and 1 IgG anti-deaminated gliadin peptide antibody assays', Elsevier, March 2007.