

Gluten Immunogenic Peptide (GIP) Monitoring

David Winternheimer, PhD

Glutenostics, LLC

April 2018



Companies

Biomedal

- Founded 2002
- Seville, Spain based
- Innovator company
- IP proprietor



Glutenostics

- Founded 2016
- Virtual company
- N America commercial LLC
- Exclusive licensee



Team



David
Winterheimer
• CEO
• Los Angeles



Angel
Cebolla
• CSO
• Seville, Spain



Francisco
Leon
• Director
• DC

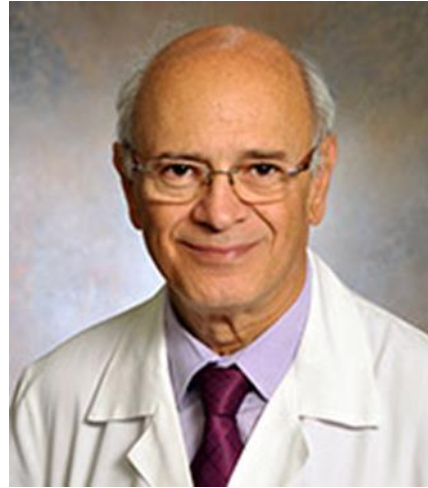


Tony
Garramone
• COO
• Boston



Vassili
Kotlov
• CMO
• San Diego

Advisors



Sheila
Crowe, MD

- UCSD
- AGA President

Stefano
Guandalini, MD

- Univ Chicago
- Celiac Pioneer

Ciaran
Kelley, MD

- Mass General
- Leading MD

Michelle
Pietzak, MD

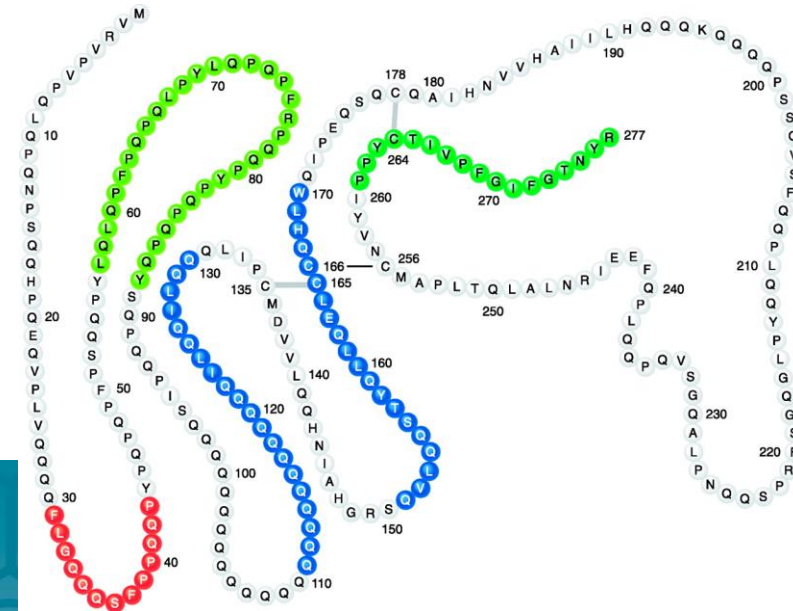
- USC/CHLA
- Leading MD

Pam
Cureton, RD

- Univ MD
- GFD Expert

Gluten Immunogenic Peptides (GIPs)

- 33-mer amino acid epitope of gluten resistant to digestion
- Present in healthy, celiac and gluten intolerant individuals
- Stimulates immune response in CD and NCGS
- Direct measure of gluten (not biological response like serology)
- Excreted in feces more than urine
- G12 antibody 99% specific for GIPs



Test Formats

ELISA (Lab-Based)

- Stool only
- Urine coming in late 2018
- LDT only
- iVYLISA branded



Lateral Flow (Rapid)

- Urine & Stool
- At-home
 - Gluten Detective (US/Canada)
 - Gluten Detect (EU)
- iVYCHECK
 - Clinical version
 - Semi-quantitative with reader



Urine vs Stool

Urine

- Time Window
 - 1-5 hours minimum
 - 6-12 hours optimal
 - 36 hours maximum
- Minimal Intake Detected
 - 500 mg
 - 2+ bites bread
- First morning urine ideal

Stool

- Time Window
 - 48 hours minimum
 - 48-60 hours optimal
 - 7 days maximum
- Minimal Intake Detected
 - 50 mg
 - Crumb bread
- Diarrhea may shorten window

Unmet Monitoring Need

- 1% refractory CD
- 10% of CD new to diet every year
- 10-30% of CD on GFD have elevated serology
- 30% (10-60%) asymptomatic CD
- 45% of new CD on GFD have intestinal damage after 1 year
- 60% of CD on GFD still have symptoms
- 20-40% of CD on GFD test GIP (+)
- 80%+ of CD interested in at-home testing (4-12x per year)
- 95%+ of CD caregivers interested in testing their children

GIP Research Publications

See corresponding editorial on page 537.

Monitoring of gluten-free diet compliance in celiac patients by assessment of gliadin 33-mer equivalent epitopes in feces¹⁻³

Isabel Comino, Ana Real, Santiago Vivas, Miguel Ángel Síglez, Alberto Caminero, Esther Nistal, Javier Casqueiro, Alfonso Rodríguez-Herrera, Ángel Cebolla, and Carolina Sousa

Am J Clin Nutr 2012;95:670–7. Printed in USA. © 2012 American Society for Nutrition

ORIGINAL ARTICLE

Detection of gluten immunogenic peptides in the urine of patients with coeliac disease reveals transgressions in the gluten-free diet and incomplete mucosal healing

María de Lourdes Moreno,¹ Ángel Cebolla,² Alba Muñoz-Suano,² Carolina Carrillo-Carrion,² Isabel Comino,¹ Ángeles Pizarro,³ Francisco León,⁴ Alfonso Rodríguez-Herrera,⁵ Carolina Sousa¹

Moreno ML, *et al.* *Gut* 2015;0:1–8. doi:10.1136/gutjnl-2015-310148

ORIGINAL CONTRIBUTIONS 1

Open

Fecal Gluten Peptides Reveal Limitations of Serological Tests and Food Questionnaires for Monitoring Gluten-Free Diet in Celiac Disease Patients

Isabel Comino, PhD¹, Fernando Fernández-Bañares, MD, PhD², María Esteve, MD, PhD², Luis Ortigosa, MD, PhD³, Gemma Castillejo, MD, PhD⁴, Blanca Fambuena, MS⁵, Carmen Ribes-Koninckx, MD, PhD⁶, Carlos Sierra, MD, PhD⁷, Alfonso Rodríguez-Herrera, MD, PhD⁸, José Carlos Salazar, MD⁹, Ángel Caunedo, MD¹⁰, J.M. Marugán-Miguelsanz, MD, PhD¹¹, José Antonio Garrote, MD, PhD¹², Santiago Vivas, MD, PhD¹³, Oreste lo Iacono, MD, PhD¹⁴, Alejandro Nuñez, BSc¹⁵, Luis Vaquero, MD, PhD¹⁶, Ana María Vegas, MD¹², Laura Crespo, MD¹², Luis Fernández-Salazar, MD, PhD¹¹, Eduardo Arranz, MD, PhD¹¹, Victoria Alejandra Jiménez-García, MD¹⁰, Marco Antonio Montes-Cano, MD, PhD¹⁵, Beatriz Espín, MD, PhD⁹, Ana Galera, MD⁹, Justo Valverde, MD⁹, Francisco José Girón, MD⁷, Miguel Bolonio, MSc⁶, Antonio Millán, MD, PhD⁵, Francesc Martínez Cerezo⁴, César Guajardo, MD³, José Ramón Alberto, MD³, Mercè Rosinach, MD, PhD², Verónica Segura, BSc¹, Francisco León, MD, PhD¹⁶, Jorge Marinich, PhD¹⁷, Alba Muñoz-Suano, PhD¹⁷, Manuel Romero-Gómez, MD, PhD⁵, Ángel Cebolla, PhD¹⁷ and Carolina Sousa, PhD¹

Am J Gastroenterol advance online publication, 20 September 2016;



nutrients



Review

Biomarkers to Monitor Gluten-Free Diet Compliance in Celiac Patients

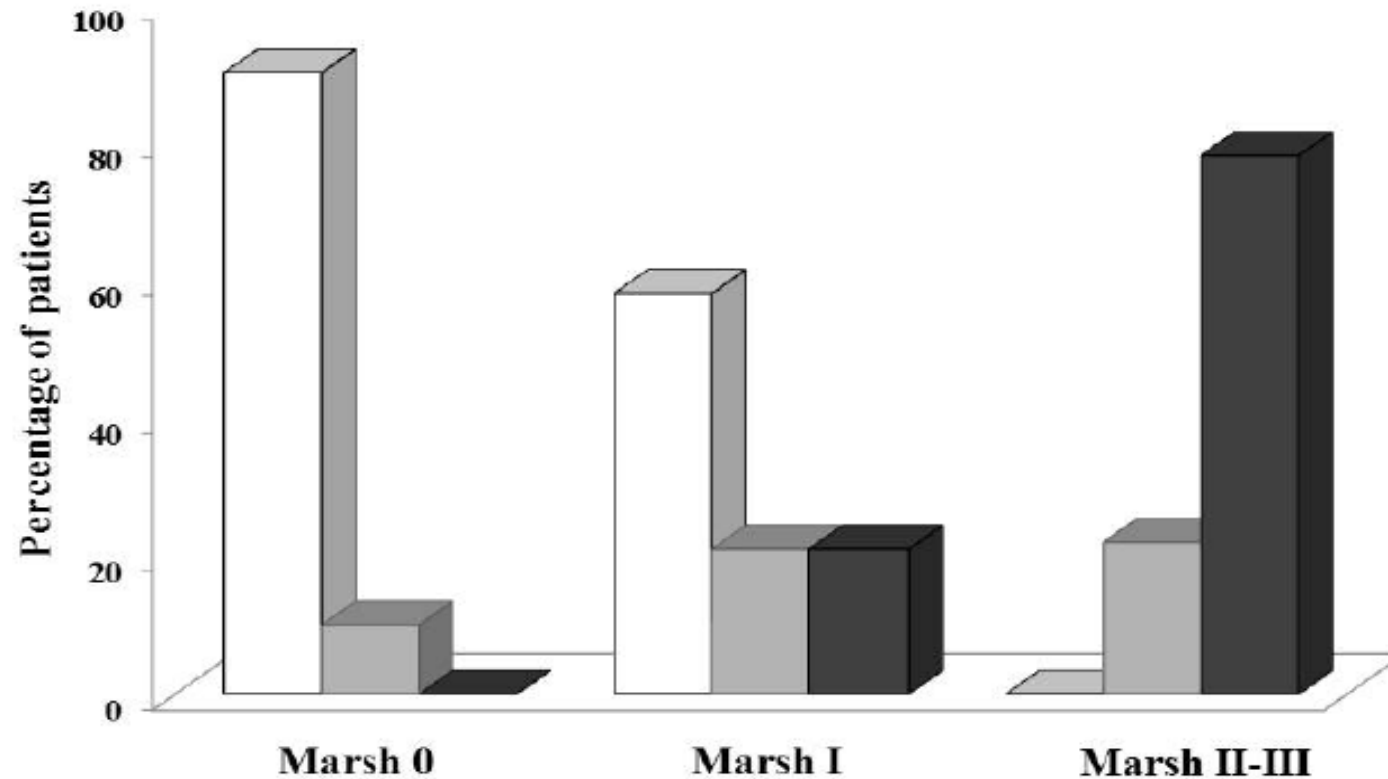
María de Lourdes Moreno¹, Alfonso Rodríguez-Herrera², Carolina Sousa¹ and Isabel Comino^{1,*}

Nutrients 2017, 9, 46; doi:10.3390/nu9010046

Urine Study: Correlation with Biopsy

- 69 CD patients
- 50% <16 yo
- 50% CD not GF

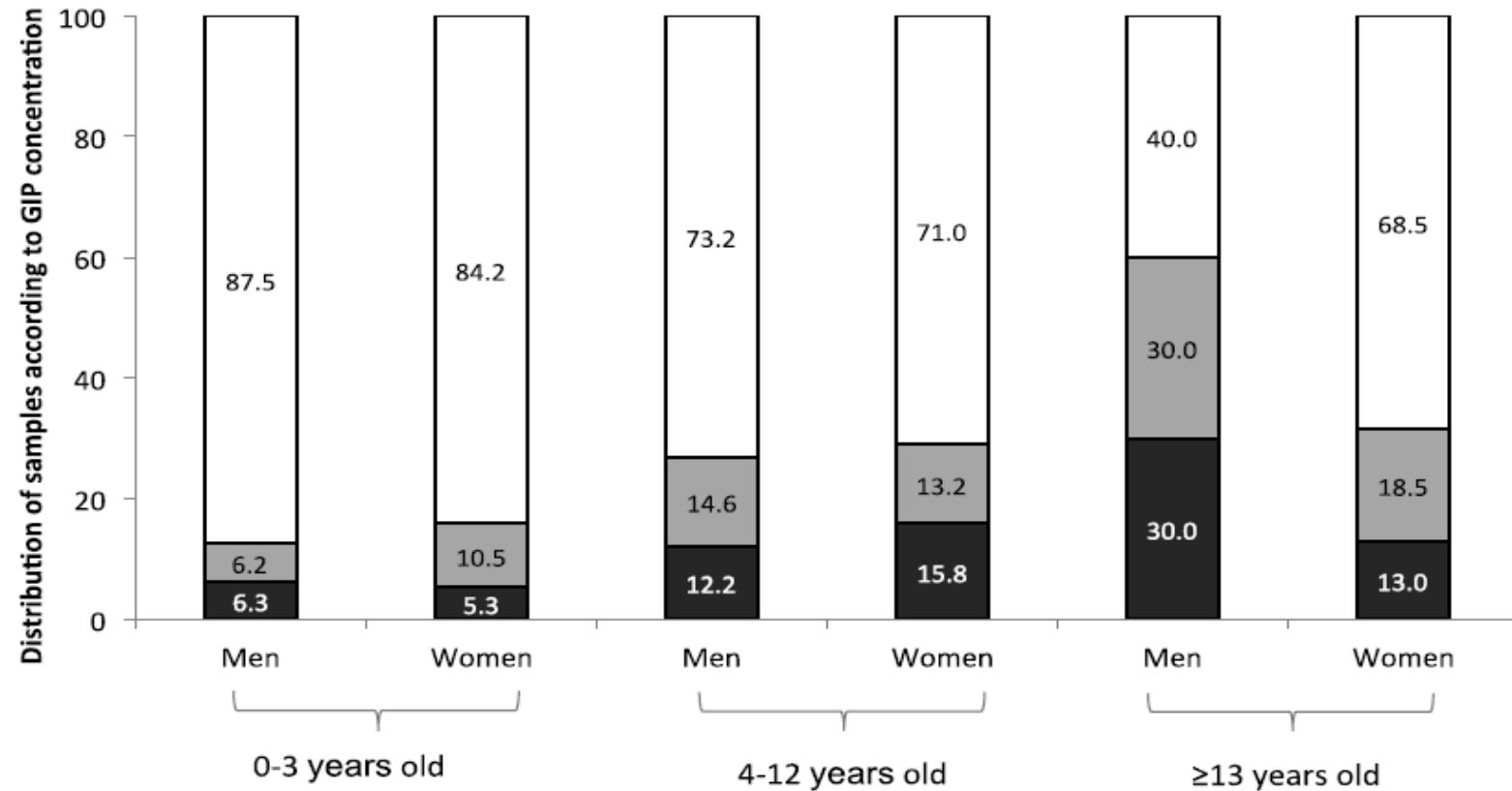
WHITE = GIP (-)
GREY = GIP (+)
BLACK = GIP (+) STRONG



Stool Study: Compliance Related to Age & Sex

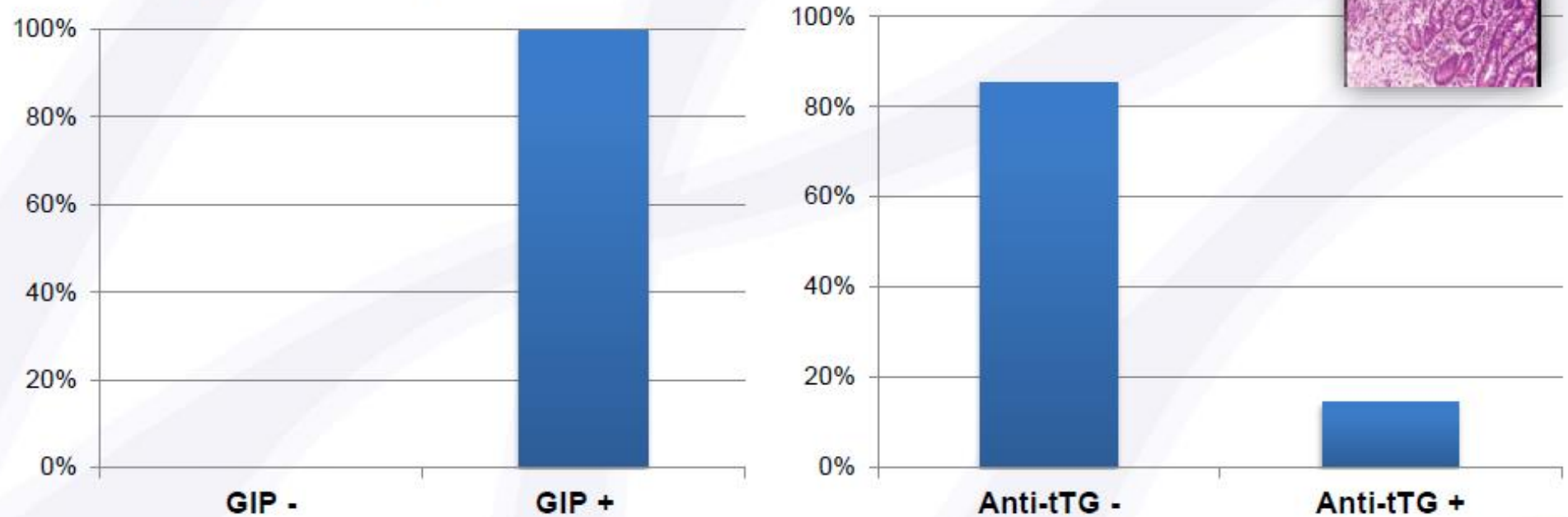
- 188 CD patients
- 30% CD not GF
- No GIP-serology correlation

WHITE = GIP (-)
GREY = GIP (+)
BLACK = GIP (+) STRONG



GIP vs tTG Correlation to Biopsy

% Adult celiac in GFD with histological damages in duodenal mucosa (Marsh II-III)



Related Publications

Downloaded from <http://gut.bmj.com/> on February 14, 2018 - Published by group.bmj.com

Gut Online First, published on February 13, 2018 as 10.1136/gutjnl-2017-314853

Coeliac disease



OPEN ACCESS

ORIGINAL ARTICLE

Outcome measures in coeliac disease trials: the Tampere recommendations

Jonas F Ludvigsson,^{1,2} Carolina Ciacci,³ Peter HR Green,⁴ Katri Kaukinen,^{5,6} Ilma R Korponay-Szabo,^{7,8} Kalle Kurppa,^{9,10} Joseph A Murray,¹¹ Knut Erik Aslaksen Lundin,^{12,13} Markku J Maki,^{14,15} Alina Popp,^{16,17} Norelle R Reilly,^{18,19} Alfonso Rodriguez-Herrera,²⁰ David S Sanders,²¹ Detlef Schuppan,^{22,23} Sarah Sleet,²⁴ Juha Taavela,²⁵ Kristin Voorhees,²⁶ Marjorie M Walker,²⁷ Daniel A Leffler²⁸

Ludvigsson JF, *et al. Gut* 2018;**0**:1–15. doi:10.1136/gutjnl-2017-314853

Average Celiac Patient Consumes 150-400 mg Gluten on GFD

Determination of gluten consumption in celiac disease patients on a gluten-free diet

Jack A Syage,¹ Ciarán P Kelly,² Matthew A Dickason,¹ Angel Cebolla Ramirez,³ Francisco Leon,³ Remedios Dominguez,³ and Jennifer A Sealey-Voyksner¹

¹ImmunogenX, Newport Beach, CA; ²Beth Israel Deaconess Medical Center, Harvard Medical School, Boston MA; and ³Biomedal, Seville, Spain

Am J Clin Nutr 2018;107:201–207.



First At-Home Study

- Collaborators:
 - Jocelyn Silvester (BCH)
 - Ciaran Kelley (Mass Gen)
- 200 biopsy diagnosed pediatrics
- Urine/Stool collected at:
 - Enrollment
 - 3x for 1st month
 - Monthly for 6 months
- Serology + RD Consultation conducted at:
 - Enrollment
 - Week 5
 - End of study (week 30)
- 2 cohorts:
 - At-home sampling (sent to lab for testing)
 - At-home testing (results reported by participants)
- **Goal: determine if at-home test results influence adherence**



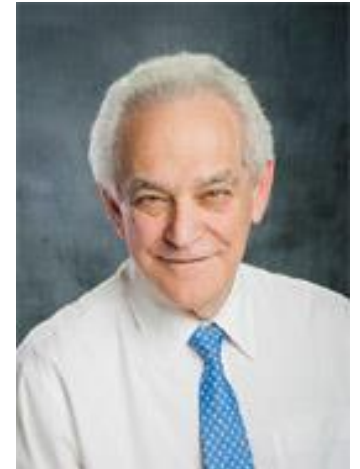
Biopsy Correlation Study

- Collaborators:
 - Maureen Leonard (MGH)
 - Alessio Fasano (MGH)
- Newly diagnosed pediatrics
- Biopsy at:
 - Diagnosis
 - 1-3 years
- **Goal: analyze correlation between GIP results and biopsies**



Newly Diagnosed Study

- Collaborators:
 - Benny Kerzner (Children's National)
- Pilot
 - 20 newly diagnosed
 - Follow for 1 month (or until clear)
- ***Goal: observe rate at which gluten is cleared from body and associated clinical presentation of celiac***



Importance of At-Home Monitoring

- Regular or regimented testing feasible
- On-demand probing of suspect situations
- Immediate feedback for newly diagnosed to learn diet
- Monitoring of cumulative gluten consumption
- Psychological relief for obsessive patients
- Reassurance and confirmation about dietary compliance

Gluten Detective (OTC)

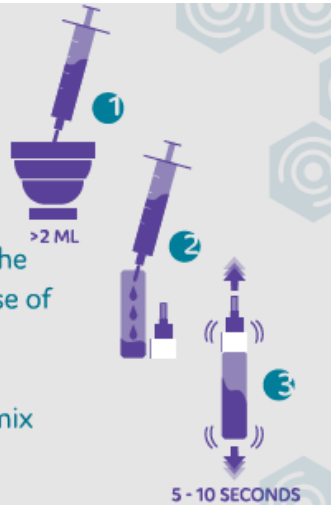
- Available exclusively at glutendetective.com in US & Canada
- \$22.50 per test (plus S&H)
- Not reimbursed
- Not FDA regulated
- Available as Gluten Detect in:
 - UK
 - Spain
 - Germany
 - Poland
 - Italy



Urine Instructions

collect your sample

- 1 Using the **collection cup**, collect 2 ml of urine. (for best results please use first urine of the day)
- 2 Using the **transfer syringe**, transfer 2 mls of the urine into the **conditioning solution** tube and close the cap tightly. Dispose of the syringe (do not reuse).
- 3 Shake tube for 5 - 10 seconds allowing the urine sample to mix with the conditioning solution.



process your test

- 4 Open the foil pouch containing the detection **test strip** and place on a flat surface. Unscrew the tip of the **conditioning solution** tube.
- 5 Invert the tube carefully and add 4 drops of the **solution** to the "S" zone of the **test strip**.
- 6 **DO NOT SHAKE.** Leave the **test strip** undisturbed for 15 minutes on the flat surface. **NOTE:** if there is a high concentration of gluten in the urine sample, the result may appear in less than 1 - 2 minutes.



Stool Instructions

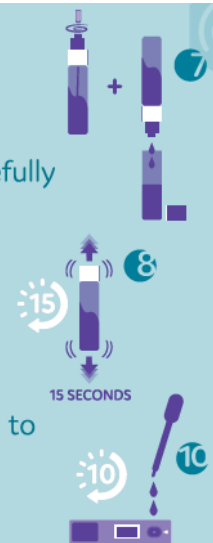
collect your sample

- 1** Pull apart the ends of the **stool collector**, exposing the adhesive. Secure the collector to the rim of the toilet using the two sticky sides.
- 2** Deposit the **stool sample** on the collection paper. **NOTE:** do not allow the stool sample to contact the toilet water until after the sample has been collected.
- 3** Open the **extraction solution** (red cap) and use the **collection stick** to fill the spoon with stool from three different sites of the sample until the sample touches the solution.
- 4** Gently stir the **collection stick** into the **extraction solution** (red cap). Close the cap tightly.
- 5** Shake the **extraction solution tube** (red cap) containing the sample intermittently over a 10 minute period (for example shake 1 minute, rest 1-2 minutes and etc.) until the sample appears fully liquid.



process your test

- 6** Let the sample stand for **2 minutes**.
- 7** Unscrew the clear cover of the **extraction solution tube** (red cap) and carefully add 10 drops into the **dilution solution** (blue cap). Close the cap tightly.
- 8** Mix the **dilution solution tube** (blue cap) softly for at least **15 seconds**.
- 9** Open the foil pouch containing the detection **test strip** and the **plastic dropper** - place on a flat surface.
- 10** With the **dropper** add 8 drops from the **dilution solution tube** (blue cap) to the "S" zone on the **test strip**.
Let stand for 10 minutes.



Gluten Detective Commercial Model

- Online D2C marketing channels
 - Celiac Disease Foundation & Beyond Celiac
 - Social Media
 - Other Venues
- Celiac Centers: Chicago, Boston, others
- Children's Hospitals
- GI Private Practices

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