

January 2015

Dear Healthcare Provider,

The information contained in this packet may be very important to your practice. Below is a quick summary of the items that are included in this mailing. Please take a moment to read this and review the enclosed material for detailed information.

INDIANA'S "BITTER PILL" PAIN MANAGEMENT DRUG TESTING

- PCL Alverno offers a wide variety of pain management drug testing that will assist physicians practicing in Indiana to be compliant with the new "Bitter Pill" legislation. Testing will be offered on saliva and urine specimens. For more information, please see page 2.

NEW TESTS COMING IN JANUARY

- PCL Alverno will offer egg and milk component allergen testing by ImmunoCAP.[®] For details, please see pages 3-5 for milk component information and pages 6-8 for egg component information.

SIGN UP FOR PCL ALVERNO'S CLINICAL BLOG

- PCL Alverno has launched its new website! Visit our website at <http://www.pclalverno.com/media-center/media-center> and choose the Alverno Blog link.

HAVE YOUR DEMOGRAPHICS CHANGED?

- If your phone or fax numbers changed, or if there are changes in your office hours, building access hours, or days of operations, we need to know! Please take a minute to call our client services department at 800.937.5521 and tell our staff about the changes. This ensures that we continue to provide you with timely, high-quality testing and service.

HAVE QUESTIONS?

Your account executives are ready to answer your questions and help you in any way. If you do not know your account executive, call Donna at 800.937.5521, extension 3872.

- Dalia Alcantar – Northwest Indiana – 708.829.7734
- Kevin Bailey – Chicago – 708.704.2810
- Carolyn Cantele – Chicago, Northwest Illinois – 312.576.9599
- Michelle Miller – Indianapolis – 317.294.3525
- Paulette Paquette – Central Illinois – 708.609.9333



Dear Healthcare Provider,

PCL Alverno would like to give you information regarding the New Indiana Pain Management Law known as the Bitter Pill Mandate. It goes into effect in January 2015 and mandates that healthcare providers drug test all patients on prescription opioid pain medication. For additional information, Greg Zoeller, Indiana Attorney General, has created an online brochure that can be downloaded or printed at http://www.in.gov/bitterpill/files/First_Do_No_Harm_V_1_0.pdf.

PCL Alverno has just introduced new saliva and urine testing panels. They are all direct confirmation tests that comply with the Bitter Pill Mandate. Below is an outline of the three types of testing PCL Alverno offers you:

	Advantages	Disadvantages
Pain Management Saliva	<ul style="list-style-type: none"> Provides a Quantitative Value. Cannot be adulterated. 	<ul style="list-style-type: none"> Patients with excessive dry mouth may not provide enough sample. Patients with metabolic disorders may produce false negative results. Does not detect benzodiazepines well.
Pain Management Urine	<ul style="list-style-type: none"> Contains a large panel of combined opioids, benzodiazepines, and other illicit substances in one test. Provides a Qualitative Value. 	<ul style="list-style-type: none"> Can be easily adulterated. Not a good option for suspected drug seeking behavior.
Pain Management Urine with Interpretation	<ul style="list-style-type: none"> Contains a large panel of combined opioids, benzodiazepines, and other illicit substances in one test. Provides a Qualitative Value with additional information. This is a good option for new patients so that you may familiarize yourself with the report. 	<ul style="list-style-type: none"> Can be easily adulterated. Not a good option for suspected drug seeking behavior.

Please contact your local Account Executive for more information:

Dalia Alcantar	708.829.7734
Kevin Bailey	708.704.2810
Carolyn Cantele	312.576.9599
Michelle Miller	317.294.3525
Paulette Paquette	708.609.9333

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www.PCLAlverno.com



MILK COMPONENT ALLERGY PANEL
Available January 13, 2015

CLINICAL USE

PCL Alverno is pleased to announce that ImmunoCAP® milk component testing will be available starting January 13, 2015. The intended uses for component testing include the following: differentiating between the risk for persistent milk allergy and tolerance to milk allergens, evaluating the likelihood of a systemic reaction, and determining the necessary precautions that may be prescribed. If milk allergies are suspected or patient results for milk complete allergen extract (f2) are found to be positive, component testing may be warranted and can be ordered in combination with or as a reflex to milk allergy testing. Human IgE responses to cow's milk vary widely, therefore various sensitization patterns are likely to occur. The table below outlines the patterns of sensitization and discusses precautions that should be considered when assessing allergy management. It is important to note that allergy results are intended for specialist use and should correlate with clinical history, other laboratory findings, and in vivo reactivity to specific allergens.

α-lactalbumin <i>Bos d 4 / f 76</i>	β-lactoglobulin <i>Bos d 5 / f 77</i>	Casein <i>Bos d 8 / f 78</i>	Management Considerations
+	+	-	
+	-	-	
-	+	-	
+/-	+/-	+	<ul style="list-style-type: none"> • Avoid all forms of cow's milk • Unlikely to become tolerant of cow's milk over time • Avoid cow's milk and baked milk products (yogurt, cookies, cakes), as well as products processed with milk (chocolate, sausage, potato chips)⁷⁸

As in all diagnostic testing, a diagnosis should be made by the physician based on both test results and patient history.

CLINICAL BACKGROUND

ImmunoCAP® testing will comprise of a panel that is designed to detect IgE antibodies to three major cow's milk proteins: alpha-lactalbumin (f76), beta-lactoglobulin (f77), and casein (f78). Casein accounts for 75-80% of all milk protein and is the main protein constituent in cheese. In addition to milk and cheese, casein is found in dairy products and foods that contain milk. It is also commonly added to foods in the form of extenders, tenderizers, and nutritional fortifiers.

Alpha-lactalbumin (ALA) and beta-lactoglobulin (BLG) are classified as whey proteins and account for 25% and 50%, respectively, of total protein in the lactosermum fraction of milk. Cow's milk contains less ALA than human milk; however, protein fractions enriched with ALA are added to infant formula to supplement the benefit of human ALA. Formula



also contains BLG as the dominant whey protein, yet it is not found in human milk. Aside from its ability to transport hydrophobic molecules like vitamin A to the intestine, clear function for BLG has not been elucidated.

The following table summarizes the characteristics and risks associated with exposure to alpha-lactalbumin, beta-lactoglobulin, and casein.

CHARACTERISTICS OF INDIVIDUAL PROTEINS

Cow's milk <i>f 2</i>	α -lactalbumin <i>Bos d 4 / f 76</i>	β -lactoglobulin <i>Bos d 5 / f 77</i>	Casein <i>Bos d 8 / f 78</i>
<ul style="list-style-type: none"> High levels of cow's milk IgE may predict the likelihood of sensitivity, but may not be solely predictive of reactions to baked milk or allergy duration³ 	<ul style="list-style-type: none"> Susceptible to heat denaturation⁴ HIGH RISK of reaction to fresh milk^{3,5} LOW RISK of reaction to baked milk^{3,5*} Patient likely to "outgrow" milk allergy⁶ 	<ul style="list-style-type: none"> Susceptible to heat denaturation⁴ HIGH RISK of reaction to fresh milk^{3,5} LOW RISK of reaction to baked milk^{3,5*} Patient likely to "outgrow" milk allergy⁶ 	<ul style="list-style-type: none"> Resistant to heat denaturation⁵ HIGH RISK of reaction to all forms of milk^{3,5,7} Patient unlikely to "outgrow" milk allergy with high levels of specific IgE to casein⁴
<p>*In clinical studies, extensively baked muffin, waffle, and cheese pizza were heated to the point of protein denaturation.</p>			

SPECIMEN REQUIREMENTS

Specimen: 1 mL serum (gel separator) or EDTA plasma (gel separator)
Stability: 2-8°C up to 7 days; otherwise freeze at -20°C

CAUSE FOR REJECTION

Insufficient quantity

METHOD

Fluorescent Enzyme Immunoassay (FEIA)

REFERENCE RANGE

<0.35 kU_A/L

TURNAROUND TIME

Monday, Wednesday, Friday (Day Shift Only)

CPT CODES*

86003 x3 (Component Panel Only)

*CPT codes provided are for informational purposes only. Questions regarding coding should be directed to the payor.

2434 Interstate Plaza Drive, Hammond, IN 46324
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References

1. Eckman J, Saini S, Hamilton R. Diagnostic evaluation of food-related allergic diseases. *Allergy Asthma Clin Immunol.* 2009;5(1):2.
2. Thermo Fisher Press Release. Data on file. Kalamazoo, MI.
3. Shek LP, Bardina L, Castro R, Sampson HA, Beyer K. Humoral and cellular responses to cow milk proteins in patients with milk-induced IgE-mediated and non-IgE-mediated disorders. *Allergy.* 2005;60(7):912-919.
4. Wal JM. Bovine milk allergenicity. *Ann Allergy Asthma Immunol.* 2004;93(5 Suppl 3):S2-S11.
5. Nowak-Węgrzyn A, Bloom KA, Sicherer SH, et al. Tolerance to extensively heated milk in children with cow's milk allergy. *J Allergy Clin Immunol.* 2008;122(2):342-347.
6. Sicherer SH, Sampson HA. Cow's milk protein-specific IgE concentrations in two age groups of milk-allergic children and in children achieving clinical tolerance. *Clin Exp Allergy.* 1999;29(4):507-512.
7. Boyano-Martinez T, Garcia-Ara C, Pedrosa M, Diaz-Pena JM, Quirce S. Accidental allergic reactions in children allergic to cow's milk proteins. *J Allergy Clin Immunol.* 2009;123(4):883-888.
8. Yman. Allergic reactions to casein/doses. http://www.slv.se/upload/dokument/risker/allergi/Allergic_reactions_milk.pdf. Accessed May 8, 2013.

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EGG ALLERGY COMPONENT PANEL Available January 13, 2015

CLINICAL USE

PCL Alverno is pleased to offer ImmunoCAP® egg component testing, starting January 13, 2015. The intended uses for egg component testing include differentiating between risk for persistent egg allergy and tolerance to egg allergens, evaluating the likelihood of a systemic reaction, and determining the necessary precautions that may be prescribed. Component testing may be warranted if egg allergies are suspected or patient results to egg white complete allergen extract (f1) are found to be positive. Consequently, component testing can be ordered in combination with **or** as a reflex to egg white allergen testing. When assessing allergy management, the precautions suggested in the table below should be considered. It is important to note that allergy results are intended for specialist use and should correlate with clinical history, other laboratory findings, and in vivo reactivity to specific allergens.

Ovalbumin <i>Gal d 2 / f 232</i>	Ovomucoid <i>Gal d 1 / f 233</i>
+	-
+/-	+

Management Considerations

- Avoid uncooked eggs
- Likely to tolerate cooked egg
- Cooked egg oral food challenge with a specialist may be appropriate
- Consider repeating ImmunoCAP IgE Component test biennially during childhood to determine potential tolerance
- May be transferred via breast milk, so mothers of infants with egg allergy should take caution when breast-feeding^{4,12}
- Avoid all forms of egg
- Consider repeating ImmunoCAP IgE Component test biennially during childhood to determine potential tolerance
- Patients sensitized to ovalbumin with low levels of IgE to ovomucoid may react to egg that is not fully cooked^{3,5,11}

As in all diagnostic testing, a diagnosis should be made by the physician based on both test results and patient history.

CLINICAL BACKGROUND

Egg white is considered to be the most substantial source of egg allergens. Although the total number of egg proteins is unknown, over 40 have been suggested for egg white alone, and up to 24 different antigenic protein fractions have been isolated. Ovomucoid and ovalbumin have demonstrated the highest prevalence of these isolated fractions in study patients with confirmed egg allergies.

Ovomucoid, or Gal d 1, is the dominant allergen of hen's egg, with the highest concentration found in egg white. This protein comprises approximately 10% of total egg white protein and is known to be highly allergenic and heat stable. Sensitization and



stimulation of allergy symptoms can occur through ingestion, inhalation, or skin contact. This, in turn, increases the probability of clinical reaction to egg in all forms.

Ovalbumin, also known as Gal d 2, is another major allergen of egg white. Comprising approximately 55% of the total proteins, it is the most abundant egg white protein. This heat susceptible protein is associated with a significant risk of reaction to uncooked egg, a lower risk of reaction to cooked egg, and allergic reaction to certain vaccines.

The following table briefly summarizes the characteristics and risks associated with exposure to ovomucoid and ovalbumin.

CHARACTERISTICS OF INDIVIDUAL PROTEINS

Egg White <i>f 1</i>	Ovalbumin <i>Gal d 2 / f 232</i>	Ovomucoid <i>Gal d 1 / f 233</i>
<ul style="list-style-type: none"> High levels of egg white IgE may predict the likelihood of sensitivity, but may not be solely predictive of reactions to cooked egg or allergy duration³ 	<ul style="list-style-type: none"> Susceptible to heat denaturation⁴ HIGH RISK of reaction to uncooked egg^{3,5} LOW RISK of reaction to cooked egg^{3,5*} Patient likely to "outgrow" egg allergy⁶ 	<ul style="list-style-type: none"> Resistant to heat denaturation⁴ HIGH RISK of reaction to all forms of egg³ Patient unlikely to "outgrow" egg allergy with high levels of specific IgE to ovomucoid^{7,8,9,10}
<p>*In clinical studies, extensively baked muffin and waffle were heated to the point of protein denaturation.</p>		

SPECIMEN REQUIREMENTS

Specimen: 1-mL serum (gel separator) or EDTA plasma (gel separator)
Stability: 2-8°C up to 7 days; otherwise freeze at -20°C

CAUSE FOR REJECTION

Insufficient quantity

METHOD

Fluorescent Enzyme Immunoassay (FEIA)

REFERENCE RANGE

<0.35 kU_A/L

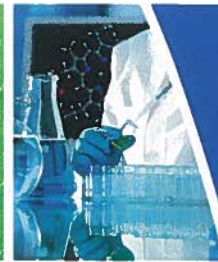
TURNAROUND TIME

Monday, Wednesday, Friday (Day Shift only)

CPT CODES*

86003 x2 (Component Panel only)

*CPT codes provided are for informational purposes only. Questions regarding coding should be directed to the payor.



References

1. Eckman J, Saini S, Hamilton R. Diagnostic evaluation of food-related allergic diseases. *Allergy Asthma Clin Immunol.* 2009;5(1):2.
2. Thermo Fisher Press Release. Data on file. Kalamazoo, MI.
3. Ando H, Movérare R, Kondo Y, et al. Utility of ovomucoid-specific IgE concentrations in predicting symptomatic egg allergy. *J Allergy Clin Immunol.* 2008;122(3):583-588.
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7. Urisu A, Yamada K, Tokuda R, et al. Clinical significance of IgE-binding activity to enzymatic digests of ovomucoid in the diagnosis and the prediction of the outgrowing of egg white hypersensitivity. *Int Arch Allergy Immunol.* 1999;120(3):192-198.
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10. Järvinen KM, Beyer K, Vila L, Bardina L, Mishoe M, Sampson HA. Specificity of IgE antibodies to sequential epitopes of hen's egg ovomucoid as a marker for persistence of egg allergy. *Allergy.* 2007;62(7):758-765.
11. Lemon-Mulé H, Sampson HA, Sicherer SH, Shreffler WG, Noone S, Nowak-Węgrzyn A. Immunologic changes in children with egg allergy ingesting extensively heated egg. *J Allergy Clin Immunol.* 2008;122(5):977-983.
12. Clark AT, Skypala I, Leech LC, et al. British Society for Allergy and Clinical Immunology guidelines for the management of egg allergy. *Clin Exp Allergy.* 2010;40(8):1116-1129.

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