

IMMULITE 2000/XPi 3gAllergy Specific IgE

Apple Component Allergen, rMal d 1 (*Malus domestica*, A464L2)*

www.siemens.com/allergy

Background

Mal d 1 is a PR-10 protein associated with oral allergy syndrome (OAS) to apple.¹ It is a homologous protein to Bet v 1, which has been identified as a primary pollen sensitizer eliciting specific IgE antibodies.² Although Mal d 1 shares only 57% sequence homology with Bet v 1, 75% of the Mal d 1 tertiary structure binds anti-Bet v 1 antibodies.³ Approximately 50 to 93% of birch pollen-allergic patients develop concomitant OAS reactions to fruits, nuts, and vegetables. Mal d 1-allergic individuals do not experience systemic reactions as PR-10 proteins are susceptible to degradation by heat and gastric digestion.^{4,5}



Biochemical Characteristics

Recombinant Mal d 1 protein (rMal d 1) was produced by heterologous expression in insect cells with a recombinant baculovirus.

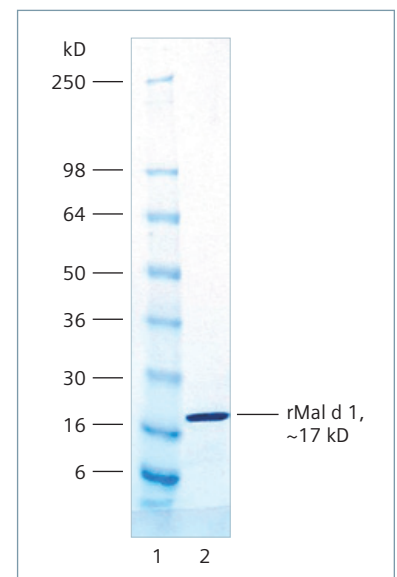
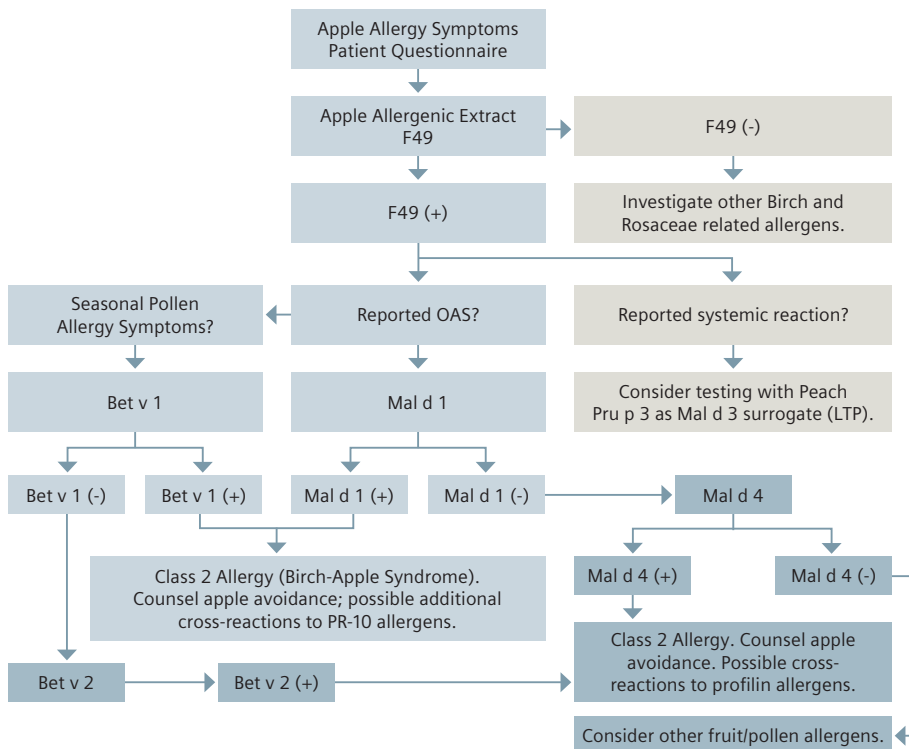


Figure 1. Coomassie Blue stained gel for rMal d 1 (lane 2).

Testing Algorithm^{1,2,4,6}



Clinical Performance

Clinical performance was demonstrated by testing serum samples from clinically diagnosed atopic patients and apparently healthy individuals against the rMal d 1 specific allergen. The results were obtained using the IMMULITE® 2000 3gAllergy™ Specific IgE assay. Overall agreement, sensitivity, and specificity are presented in the table on page 2.

*Not available for sale in the U.S.

Allergen: rMal d 1

IMMULITE 2000			
	Clinical	Normal	Total
Positive (≥ 0.10 kU/L)	37	0	37
Negative	8	100	108
Total	45	100	145

Sensitivity (95% Confidence Interval)	Specificity (95% Confidence Interval)	Overall Agreement
82% (71 to 93%)	100% (100 to 100%)	95%

Additional clinical performance of the rMal d 1 specific allergen was demonstrated in comparison to the whole apple extract allergen (F49). The same 145 clinical samples were tested with A464 and F49. The results are presented below.

Allergen: rMal d 1

IMMULITE 2000			
	F49 (Reference Method)		
A464 (Test Method)	36	1	Positive
	11	97	Negative
	Positive	Negative	

N=145

Overall percent agreement = 92% (133/145)
 Positive percent agreement = 77% (36/47)
 Negative percent agreement = 99% (97/98)

Analytical Performance

Precision: The average within-run and total precision using three samples and two lots of rMal d 1 allergen were 4.31% and 6.71%, respectively.

Linearity: Two samples were diluted in serial dilutions to 5 levels using two allergen lots. The undiluted (neat) and diluted samples were tested with the specific allergen to demonstrate linearity at concentrations within the assay limits. Regression statistics for each allergen comparing the observed results to expected results are presented below.

Lot	Regression Equation	Slope 95% CI	R ²
1	$Y = 1.005 + 0.1628$	0.9834 to 1.026	0.999
2	$Y = 1.032 - 0.0160$	0.9901 to 1.074	0.998

Siemens Healthcare Diagnostics, a global leader in clinical diagnostics, provides healthcare professionals in hospital, reference, and physician office laboratories and point-of-care settings with the vital information required to accurately diagnose, treat, and monitor patients. Our innovative portfolio of performance-driven solutions and personalized customer care combine to streamline workflow, enhance operational efficiency, and support improved patient outcomes.

3gAllergy, IMMULITE, and all associated marks are trademarks of Siemens Healthcare Diagnostics Inc. All other trademarks and brands are the property of their respective owners. Product availability may vary from country to country and is subject to varying regulatory requirements. Please contact your local representative for availability.

Global Siemens Headquarters
 Siemens AG
 Wittelsbacherplatz 2
 80333 Muenchen
 Germany

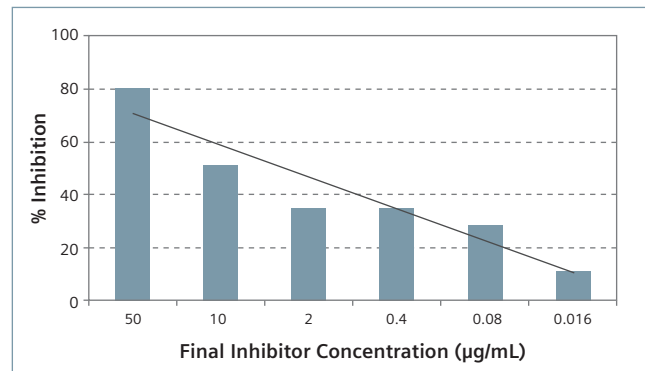
Global Siemens Healthcare Headquarters
 Siemens AG
 Healthcare Sector
 Henkestrasse 127
 91052 Erlangen, Germany
 Phone: +49 9131 84 - 0
www.siemens.com/healthcare

Global Division
 Siemens Healthcare Diagnostics Inc.
 511 Benedict Avenue
 Tarrytown, NY 10591-5005
 USA
www.siemens.com/diagnostics

Order No. A91DX-CAI-120919-XC1-4A00
 08-2012 | All rights reserved
 © 2012 Siemens Healthcare Diagnostics Inc.

Identity Testing

Identity of rMal d 1 was verified through competitive inhibition testing using a single serum sample or pool of sera. A negative sample was used to measure the background response. The percentage inhibitions are represented in the graph below showing correlation to increasing inhibitor concentrations.



References:

- Fernández-Rivas M, Bolhaar S, González-Mancebo E, Asero R, van Leeuwen A, Bohle B, et al. Apple allergy across Europe: how allergen sensitization profiles determine the clinical expression of allergies to plant foods. *J Allergy Clin Immunol.* 2006;118(2):481-8.
- Ebo DG, Bridts CH, Verweij MM, De Knop KJ, Hagendorens MM, De Clerck LS, et al. Sensitization profiles in birch pollen-allergic patients with and without oral allergy syndrome to apple: lessons from multiplexed component-resolved allergy diagnosis. *Clin Exp Allergy.* 2010 Feb;40(2):339-47.
- Jenkins JA, Griffiths-Jones S, Shewry PR, Breiteneder H, Mills EN. Structural relatedness of plant food allergens with specific reference to cross-reactive allergens: an in silico analysis. *J Allergy Clin Immunol.* 2005 Jan;115(1):163-70.6.
- Mauro M, Russello M, Incorvaia C, Gazzola G, Frati F, Moingeon P, et al. Birch-apple syndrome treated with birch pollen immunotherapy. *Int Arch Allergy Immunol.* 2011;156(4):416-22.
- Wuthrich B, Schindler C, Leuenberger P, Ackermann-Liebrich U. Prevalence of atopy and pollinosis in the adult population of Switzerland (SAPALDIA study). Swiss Study on Air Pollution and Lung Diseases in Adults. *Int Arch Allergy Immunol.* 1995 Feb;106(2):149-56.
- Andersen MB, Hall S, Dragsted LO. Identification of European allergy patterns to the allergen families PR-10, LTP, and profilin from Rosaceae fruits. *Clin Rev Allergy Immunol.* 2011;41(1):4-19.