

IMMULITE 2000/XPi 3gAllergy Specific IgE

Apple Component Allergen, rMal d 4 (*Malus domestica*, A796L2)*

www.siemens.com/allergy

Background

Mal d 4, a member of the profilin family of allergens, is an approximately 14 kD protein associated with oral allergy syndrome (OAS) to apple.¹ It is a homologous protein to Bet v 2, which has been identified as a minor pollen sensitizer in approximately 10–30% of pollen-allergic individuals.² As with other profilins, Mal d 4 is highly thermolabile and rapidly enzyme degradable, accounting for its inability to elicit systemic reaction, and its loss of allergenicity in cooked foods.³ Primary sensitization to Mal d 4 develops through pollinosis and cross-reactivity to Bet v 2, and is not presumed to arise directly from apple ingestion without previous sensitization to birch or grass profilin.³⁻⁵



Biochemical Characteristics

Recombinant Mal d 4 (rMal d 4) protein was produced by heterologous expression in *E. coli*.

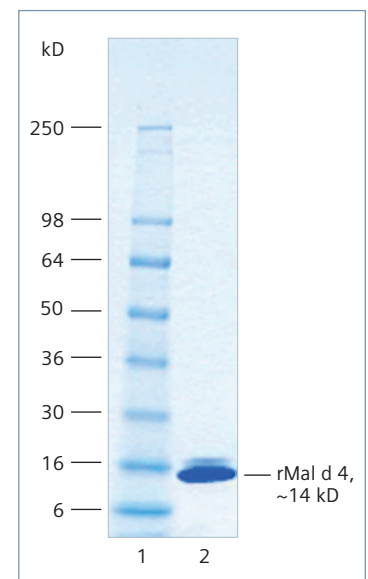
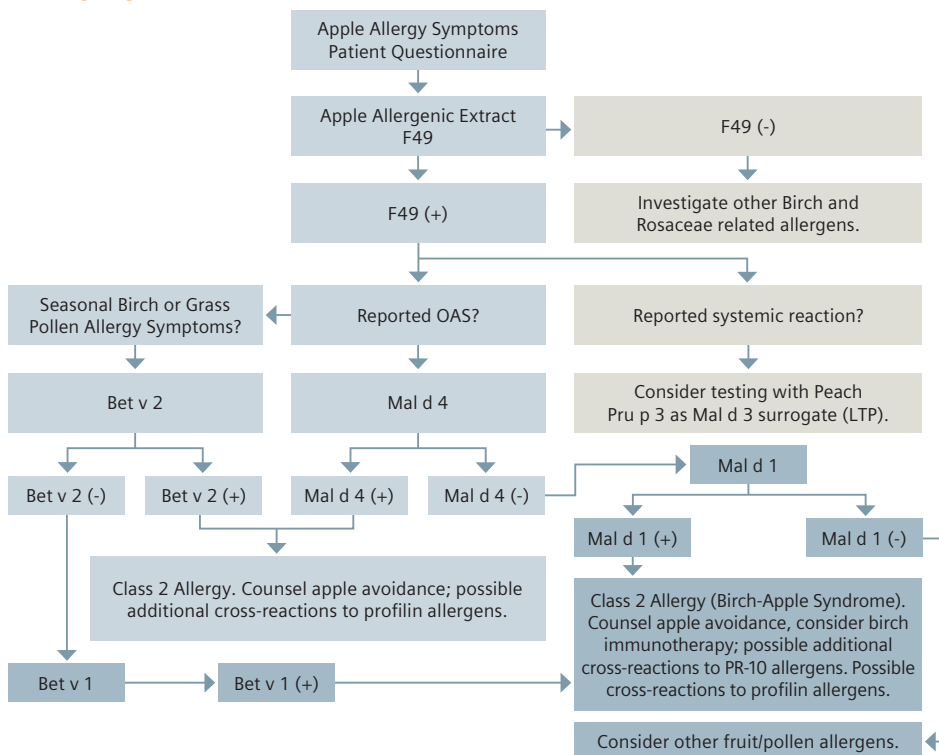


Figure 1. Coomassie Blue stained gel for rMal d 4 (lane 2).

Testing Algorithm²⁻⁶



Clinical Performance

Clinical performance was demonstrated by testing serum samples from atopic patients and apparently healthy individuals against the rMal d 4 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 4

IMMULITE 2000			
	Clinical	Normal	Total
Positive (≥ 0.10 kU/L)	29	0	29
Negative	27	100	127
Total	56	100	156

Sensitivity (95% Confidence Interval)	Specificity (95% Confidence Interval)	Overall Agreement
52% (39 to 65%)	100% (100 to 100%)	83%

Additional clinical performance of the rMal d 4 specific allergen was demonstrated in comparison to the whole apple extract allergen (F49); 159 clinical samples were tested with A796 and F49. The results are presented below.

Allergen: rMal d 4

IMMULITE 2000			
	F49 (Reference Method)		
A796 (Test Method)	27	5	Positive
	28	99	Negative
	Positive	Negative	

N=159

Overall percent agreement = 79% (126/159)
 Positive percent agreement = 49% (27/55)
 Negative percent agreement = 95% (99/104)

Analytical Performance

Precision: The average within-run and total precision using three samples and two lots of rMal d 4 allergen were 3.45% and 5.77%, 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 = 0.9776 – 0.0287	0.9442 to 1.011	0.998
2	Y = 0.9906 – 0.0134	0.9726 to 1.009	1.000

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

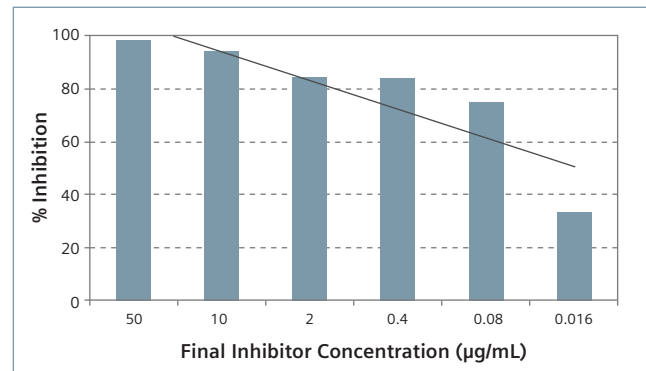
Global Siemens Healthcare Headquarters
 Siemens AG
 Healthcare Sector
 Henkestrasse 127
 91052 Erlangen, Germany
 Phone: +49 9131 84 - 0
www.siemens.com/healthcare

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

Order No. A91DX-CAI-120936-XC1-4A00
 08-2012 | All rights reserved
 © 2012 Siemens Healthcare Diagnostics Inc.

Identity Testing

Identity of rMal d 4 was verified through competitive inhibition testing using a single serum sample. 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:

- Oberhuber C, Ma Y, Marsh J, Rigby N, Smole U, Radauer C, et al. Purification and characterisation of relevant natural and recombinant apple allergens. *Mol Nutr Food Res*. 2008;52 Suppl 2:S208-19.
- Breiteneder H, Radauer C. A classification of plant food allergens. *J Allergy Clin Immunol*. 2004;113(5):821-30.
- 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.
- 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 Aug;118(2):481-8.
- Ma Y, Zuidmeer L, Bohle B, Bolhaar ST, Gadermaier G, Gonzalez-Mancebo E, et al. Characterization of recombinant Mal d 4 and its application for component-resolved diagnosis of apple allergy. *Clin Exp Allergy*. 2006;36(8):1087-96.
- 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;40(2):339-47.