

# Medical algorithm: Diagnosis of plant food allergy

Plant food allergies are the most common food allergies from school age onwards. Their diagnosis starts with a detailed medical history (Figure 1). Information on interval between food intake and onset of reaction, type of symptoms experienced, reproducibility of reactions, association of cofactors, need of treatment, and presence of other allergic comorbidities, especially pollen or latex allergies, should be collected.<sup>1,2</sup> In adult patients with plant food allergies, it has been shown that immediate onset, reproducibility, oral allergy symptoms (OAS), and the presence of associated allergic rhinitis and asthma are the best predictors of probable food allergy.<sup>2</sup>

Information on how the food was eaten (raw or processed, peeled or not for fruits), whether food processing affects the reproducibility of reactions, and whether other plant foods elicit reactions should be collected. When a reaction is only triggered by a fresh (raw) food that is tolerated when processed, suggests the involvement of labile allergens. When patients react to other plant foods and have associated pollen or latex allergies, the involvement of cross-reactive allergens should be ruled out.<sup>3</sup>

The next step is the performance of skin prick tests (SPT) and/or serum-specific IgE (sIgE) determinations to whole extracts (Figure 1). When labile allergens are involved the sensitivity of the extracts may be reduced, and to overcome this problem prick-prick tests with the fresh plant foods are frequently needed. When cross-reactive allergens are involved specificity is reduced, and if the medical history does not provide clear-cut information on tolerance/reactivity to a given plant food, it will be necessary to perform oral food challenges (OFC) to establish an accurate diagnosis.<sup>1</sup>

Component-resolved diagnosis (CRD) is currently a cornerstone in the diagnosis of plant food allergies and a standard practice (Figure 1). CRD may compensate the reduced sensitivity of allergy tests when labile allergens are involved and elucidates the cross-reactivity among plant foods and with pollens/latex, allows to identify markers of genuine (species specific) sensitization, provides insight in sensitization pathways, and allows a risk assessment to help guide patient's management, since different allergens are associated with different severity of reactions.<sup>3</sup> Labile allergens such as Bet v 1 homologues and profilins are associated with mild reactions, mainly isolated OAS, whereas stable allergens such as the non-specific lipid transfer proteins (nsLTPs) or storage proteins

are associated with a higher frequency of systemic reactions and anaphylaxis.<sup>3</sup>

CRD can be performed by singleplex and multiplex techniques (Table 1). Clinicians should know the molecular epidemiology in their area for the correct indication of tests and interpretation of results.<sup>3</sup> Currently, recombinant allergens for SPT are not approved in the EU, but in some countries, natural date palm profilin and Pru p 3 are available for molecular diagnosis in SPTs.<sup>1,3</sup>

SPT, sIgE to extracts and CRD provide information on IgE sensitization and their results should be evaluated in the context of the medical history. With a highly suggestive medical history of allergy to a given food, and positive concordant SPT, sIgE, and/or CRD, the diagnosis can be established without the need of an OFC. However, when there are discrepancies OFC could be performed<sup>1</sup> (Figure 1). The common cross-reactivity in plant food allergies may account for positive tests to plant foods not implicated in reactions but that have not been eaten after a reaction to an index food. In this situation, only an OFC will establish the diagnosis and guide either safe inclusion in the diet or appropriate avoidance.<sup>1</sup>

In allergy to fruits and vegetables, the main allergens involved are the PR-10 proteins homologous to Bet v 1, profilins, and LTPs. PR-10 proteins are the major allergens in allergies to fruits, vegetables, peanut, and tree nuts linked to birch pollen. Profilins are involved in fruit allergies (typically *Cucurbitaceae*) in patients with grass pollen allergy from Southern Europe. PR-10 proteins and profilins are labile allergens and patients present (almost exclusively) OAS to fresh fruits/vegetables, but tolerate them when cooked/processed<sup>3</sup> (Figure 1). The PR-10 protein Bet v 1 and the profilins Bet v 2 or Phl p 12 can be used as markers of sensitization, although some food-specific allergen components are also available (Table 1).

LTPs are stable allergens involved in reactions to raw and processed plant foods. The peach nsLTP, Pru p 3, is a dominant sensitizing allergen and peach is a common trigger, although multiple fruits, vegetables, peanut and other legumes, tree nuts, and cereals can be involved. nsLTPs are predominantly located in the outer layer of fruits (peels) and some patients may present only reactions when ingesting the fruit with the peel, something frequently seen with *Rosaceae* fruits. Symptoms vary from OAS to anaphylaxis, and cofactors may be needed for a reaction to appear or may increase

**Abbreviations:** BAT, basophil activation test; CRD, component-resolved diagnosis; nsLTP, non-specific lipid transfer protein; OAS, oral allergy symptoms; OFC, oral food challenge; sIgE, specific IgE; SPT, skin prick tests.

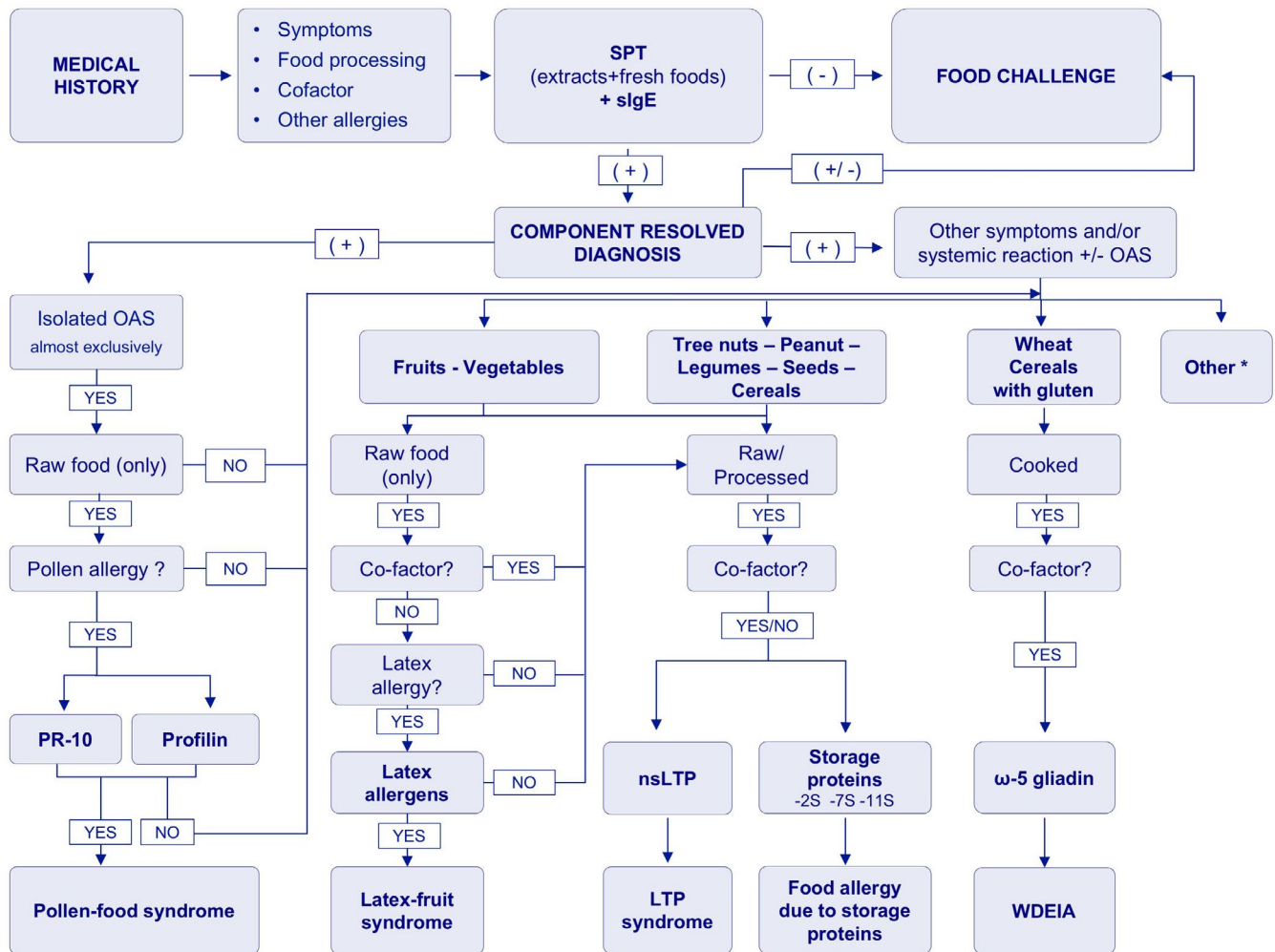


**FIGURE 1** Algorithm for plant food allergy diagnosis. BAT, basophil activation test; CRD, component-resolved diagnosis; nsLTP, non-specific lipid transfer proteins; OAS, oral allergy symptoms; sIgE, specific IgE; SPT, skin prick tests; WDEIA, wheat dependent exercise-induced anaphylaxis. Reported latex allergens involved in latex-fruit syndrome: Hev b 6 has significant cross-reactivity with chitinases in banana, avocado, and chestnut; Hev b 5 has homology to Act d 11 in kiwi; Hev b 7 has homology to patatin protein of the *Solanaceae* family; due to their high cross-reactivity with plant foods Hev b 8 (profilin) and Hev b 12 (nsLTP) may be relevant. \*Other: Gibberellin-regulated protein, peamaclein, is a peach allergen Pru p 7 involved in peach allergy in areas with high *Cupressus* tree pollen exposure; Act d 1 (actinidin) is involved in reactions (frequently systemic) to kiwi in patients monosensitized to this fruit; thaumatin-like proteins have been described as minor fruit allergens, especially in apple and kiwi, but their clinical relevance is not established; Oleosins have been identified in nuts and seeds and may be associated with severe reactions, but under-represented in diagnostic extracts due to their lipophilic nature<sup>4</sup>

reaction severity (Figure 1). Pru p 3 is an allergen marker of the LTP syndrome, but several nsLTPs can be tested (Table 1).<sup>3,4</sup>

In allergy to peanut, tree nuts and seeds PR-10 proteins, profilins, nsLTP, and storage proteins (2S, 7S, 11S) may be involved with different clinical patterns. As discussed above nsLTPs may induce OAS and systemic reactions; PR-10 and profilins are involved in patients with a previous pollen allergy, usually, adolescents or adults and symptoms are predominantly mild OAS<sup>3,4</sup> (Figure 1). Sensitization to storage proteins may start in early childhood and these stable allergens are involved in systemic reactions including anaphylaxis to raw and processed foods. This has been shown for Cor a 9 and Cor a 14 (hazelnut), Jug r 1 and Jug r 4 (walnut), Ara h 2 and Ara h 6 (peanut), Ana o 3 (cashew nut) that are also markers of primary sensitization.<sup>4,5</sup> CRD increases the diagnostic accuracy of

peanut and tree nut allergies, which is higher than that of SPT and sIgE to whole extracts, may reduce the number of OFC,<sup>5,6</sup> and help identify those at risk of severe reactions in OFC.<sup>7</sup> Basophil activation test (BAT) is a highly specific research tool not yet included in the mainstream diagnostic tests. In peanut, tree nuts, and sesame allergies, it has been shown that when it is used in diagnostic algorithms as second step after SPT and CRD, the number of OFC and particularly the positive ones, is reduced.<sup>8,9</sup>

## ACKNOWLEDGMENTS

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TABLE 1 Allergen components present on the principal commercial diagnostic platforms available in Europe

| Allergen source                                      | Allergen component                            | Biochemical designation                  | Diagnostic platform#            |                            |                             |                             |                                |
|------------------------------------------------------|-----------------------------------------------|------------------------------------------|---------------------------------|----------------------------|-----------------------------|-----------------------------|--------------------------------|
|                                                      |                                               |                                          | ImmunoCap®<br>2021 <sup>†</sup> | ISAC®<br>2020 <sup>‡</sup> | ALEX2®<br>2020 <sup>‡</sup> | FABER®<br>2020 <sup>‡</sup> | Immulite®<br>2016 <sup>‡</sup> |
| FRUITS                                               | Apple ( <i>Malus domestica</i> ) <sup>b</sup> | Mal d 1                                  | X                               | X                          | X                           | X                           | X                              |
|                                                      |                                               | Mal d 2                                  |                                 |                            | X                           |                             |                                |
|                                                      |                                               | Mal d 3                                  | X                               | X                          | X                           |                             |                                |
|                                                      |                                               | Mal d 4                                  |                                 | X                          |                             |                             |                                |
| Cherry ( <i>Prunus avium</i> ) <sup>b</sup>          | Pru av 1                                      | PR-10                                    |                                 |                            |                             |                             | X                              |
|                                                      | Pru av 3                                      | nsLTP                                    |                                 |                            |                             |                             | X                              |
|                                                      | Pru av 4                                      | Profilin                                 |                                 |                            |                             |                             | X                              |
|                                                      | Act c 11                                      | PR-10                                    |                                 |                            |                             | X                           |                                |
| Gold kiwi ( <i>Actinidia chinensis</i> )             | Act c Chitinase IV                            | Chitinase IV                             |                                 |                            |                             | X                           |                                |
| Grape ( <i>Vitis vinifera</i> )                      | Vit v 1                                       | nsLTP                                    |                                 |                            | X                           |                             |                                |
| Kiwi fruit ( <i>Actinidia deliciosa</i> )            | Act d 1                                       | Cysteine protease                        |                                 | X                          | X                           | X                           |                                |
|                                                      | Act d 2                                       | Thaumatococin-like protein               |                                 | X                          | X                           | X                           |                                |
|                                                      | Act d 5                                       | Kiwifruitin                              |                                 |                            | X                           | X                           |                                |
|                                                      | Act d 8                                       | PR-10                                    | X                               | X                          |                             |                             |                                |
| Musk melon ( <i>Cucumis melo</i> ) <sup>c</sup>      | Act d 10                                      | nsLTP                                    |                                 |                            | X                           | X                           |                                |
|                                                      | Cuc m 2                                       | Profilin                                 |                                 |                            | X                           |                             |                                |
|                                                      | Car p 1                                       | Papain                                   |                                 |                            | X                           | X                           |                                |
|                                                      | Pru p 1                                       | PR-10                                    | X                               | X                          |                             |                             |                                |
| Papaya ( <i>Carica papaya</i> )                      | Pru p 3                                       | nsLTP                                    | X                               | X                          | X                           | X                           | X                              |
|                                                      | Pru p 4                                       | Profilin                                 | X                               | X                          |                             |                             |                                |
|                                                      | Pru p 7                                       | Gibberellin-regulated protein/Peamaclein | X                               |                            | X <sup>a</sup>              | X                           |                                |
|                                                      | Ana c 2                                       | Bromelain, CCD, MUXF3 <sup>d</sup>       | X                               | X                          | X                           | X                           | X                              |
| Pineapple ( <i>Ananas comosus</i> )                  | Pun g 1                                       | nsLTP                                    |                                 |                            |                             | X                           |                                |
| Pomegranate ( <i>Punica granatum</i> )               | Pun g 5                                       | Hevein-like protein                      |                                 |                            |                             | X                           |                                |
|                                                      | Pun g 7                                       | Gibberellin-regulated protein            |                                 |                            |                             | X                           |                                |
|                                                      | Pun g 14                                      | Chitinase                                |                                 |                            |                             | X                           |                                |
|                                                      | Fra a 1 + Fra a 3                             | PR-10 + nsLTP                            |                                 |                            | X                           |                             |                                |
| Strawberry ( <i>Fragaria ananassa</i> ) <sup>b</sup> | Sola l 6                                      | nsLTP                                    |                                 |                            | X                           | X                           |                                |
| Tomato ( <i>Solanum lycopersicum</i> )               |                                               |                                          |                                 |                            | X                           |                             |                                |

(Continues)

TABLE 1 (Continued)

|                                            |                                    |                                             | Diagnostic platform#            |                            |                             |                             |                                |   |  |
|--------------------------------------------|------------------------------------|---------------------------------------------|---------------------------------|----------------------------|-----------------------------|-----------------------------|--------------------------------|---|--|
|                                            |                                    |                                             | ImmunoCap®<br>2021 <sup>Ⓜ</sup> | ISAC®<br>2020 <sup>Ⓜ</sup> | ALEX2®<br>2020 <sup>Ⓜ</sup> | FABER®<br>2020 <sup>Ⓜ</sup> | Immulite®<br>2016 <sup>Ⓜ</sup> |   |  |
| VEGETABLES                                 | Allergen source                    | Allergen component                          | Biochemical designation         |                            |                             |                             |                                |   |  |
|                                            | Carrot ( <i>Daucus carota</i> )    | Dau c 1                                     | PR-10                           |                            |                             | X                           |                                |   |  |
|                                            | Celery ( <i>Apium graveolens</i> ) | Api g 1.01                                  | PR-10                           |                            | X                           |                             | X                              |   |  |
|                                            |                                    | Api g 2                                     | nsLTP                           |                            |                             |                             | X                              |   |  |
|                                            |                                    | Api g 6                                     | ns LTP                          |                            |                             |                             | X                              |   |  |
| Horseradish ( <i>Armoracia rusticana</i> ) | Arm r HRP                          | Horseradish peroxidase; CCD-bearing protein |                                 |                            |                             | X                           | X                              |   |  |
| Potato ( <i>Solanum tuberosum</i> )        | Sola t 1                           | Patatin, CCD-bearing protein                |                                 |                            |                             | X                           |                                |   |  |
| LEGUMES                                    | Pea ( <i>Pisum sativum</i> )       | Pis s 3                                     | nsLTP                           |                            |                             |                             | X                              |   |  |
|                                            | Peanut ( <i>Arachis hypogaea</i> ) | Ara h 1                                     | 7S globulin                     |                            | X                           |                             | X                              |   |  |
|                                            |                                    | Ara h 2                                     | 2S albumin                      |                            | X                           |                             | X                              |   |  |
|                                            |                                    | Ara h 3                                     | 11S globulin                    |                            | X                           |                             | X                              |   |  |
|                                            |                                    | Ara h 6                                     | 2S albumin                      |                            | X                           |                             | X                              |   |  |
|                                            |                                    | Ara h 8                                     | PR-10                           |                            | X                           |                             | X                              |   |  |
|                                            |                                    | Ara h 9                                     | nsLTP                           |                            | X                           |                             | X                              |   |  |
|                                            |                                    | Ara h 15                                    | Oleosin                         |                            |                             |                             | X                              |   |  |
|                                            | Soy ( <i>Glycine max</i> )         | Ara h Agglutinin                            | Agglutinin, Lectin              |                            |                             |                             |                                | X |  |
|                                            |                                    | Gly m 1                                     | Hydrophobic seed protein        |                            |                             |                             |                                | X |  |
|                                            |                                    | Gly m 4                                     | PR-10                           |                            | X                           |                             | X                              |   |  |
|                                            |                                    | Gly m 5                                     | Beta-conglycinin                |                            | X                           |                             | X                              |   |  |
|                                            |                                    | Gly m 6                                     | Glycinin                        |                            | X                           |                             | X                              |   |  |
|                                            |                                    | Gly m 8                                     | 2S albumin                      |                            |                             |                             | X                              |   |  |
|                                            |                                    | Gly m Agglutinin                            | Agglutinin, Lectin              |                            |                             |                             |                                | X |  |
| Gly m TI                                   |                                    | Trypsin inhibitor                           |                                 |                            |                             |                             | X                              |   |  |

(Continues)

TABLE 1 (Continued)

|           |                                                 |                                 | Diagnostic platform#            |                            |                             |                             |                                |
|-----------|-------------------------------------------------|---------------------------------|---------------------------------|----------------------------|-----------------------------|-----------------------------|--------------------------------|
|           |                                                 |                                 | ImmunoCap®<br>2021 <sup>a</sup> | ISAC®<br>2020 <sup>a</sup> | ALEX2®<br>2020 <sup>a</sup> | FABER®<br>2020 <sup>a</sup> | Immulite®<br>2016 <sup>a</sup> |
| TREE NUTS | Brazil nut ( <i>Bertholletia excelsa</i> )      | Ber e 1                         | X                               | X                          | X                           |                             |                                |
|           |                                                 | Ana o 2                         |                                 | X                          | X                           |                             |                                |
|           |                                                 | Ana o 3                         | X                               | X                          | X                           | X                           |                                |
|           | Cashew nut ( <i>Anacardium occidentale</i> )    | Cor a 1                         | X                               | X                          | X                           | X                           |                                |
|           |                                                 | Cor a 8                         | X                               | X                          | X                           | X                           |                                |
|           |                                                 | Cor a 9                         | X                               | X                          | X                           | X                           |                                |
|           |                                                 | Cor a 11                        |                                 |                            | X                           |                             |                                |
|           |                                                 | Cor a 12                        |                                 |                            | X <sup>a</sup>              |                             |                                |
|           |                                                 | Cor a 14                        | X                               | X                          | X                           | X                           |                                |
|           | Macadamia nut ( <i>Macadamia integrifolia</i> ) | Mac i 2S albumin                |                                 |                            | X                           |                             |                                |
|           | Pistachio ( <i>Pistacia vera</i> )              | Pis v 1                         |                                 |                            | X                           |                             |                                |
|           |                                                 | Pis v 2                         |                                 |                            | X                           |                             |                                |
|           |                                                 | Pis v 3                         |                                 |                            | X                           |                             |                                |
|           |                                                 | Pis v 4                         |                                 |                            | X <sup>a</sup>              |                             |                                |
|           |                                                 | Jug r 1                         | X                               | X                          | X                           |                             |                                |
| SEEDS     | Walnut ( <i>Juglans regia</i> )                 | Jug r 2                         |                                 |                            | X                           | X                           |                                |
|           |                                                 | Jug r 3                         | X                               | X                          | X                           | X                           |                                |
|           |                                                 | Jug r 4                         |                                 |                            | X                           |                             |                                |
|           | Mustard ( <i>Sinapis spp.</i> )                 | Jug r 6                         |                                 |                            | X                           |                             |                                |
|           |                                                 | Sin a 1                         |                                 |                            | X                           |                             |                                |
|           |                                                 | Ses i 1                         |                                 | X                          | X                           |                             |                                |
|           | Sesame ( <i>Sesamum indicum</i> )               | Pap s 2S albumin                |                                 |                            | X                           |                             |                                |
|           |                                                 | Fag e 2                         |                                 | X                          | X                           |                             |                                |
|           | Poppy seed ( <i>Papaver somniferum</i> )        | Zea m 14                        |                                 |                            |                             | X                           |                                |
|           |                                                 | Tri a 14                        | X                               | X                          |                             |                             |                                |
|           |                                                 | Tri a 18                        |                                 |                            |                             | X                           |                                |
|           |                                                 | Tri a 19                        | X                               | X                          | X                           |                             |                                |
|           |                                                 | Tri a 28                        |                                 |                            |                             | X                           |                                |
|           |                                                 | Tri a 7k-LTP                    |                                 |                            |                             | X                           |                                |
|           |                                                 | Tri a gliadin                   | X                               |                            |                             | X                           |                                |
|           |                                                 | Tri a aA_T1                     |                                 | X                          |                             |                             |                                |
| CEREALS   | Corn ( <i>Zea mays</i> )                        | nsLTP                           |                                 |                            |                             |                             |                                |
|           |                                                 | nsLTP                           |                                 |                            |                             |                             |                                |
|           |                                                 | Hevein-like, agglutinin, lectin |                                 |                            |                             |                             |                                |
|           | Wheat ( <i>Triticum aestivum</i> )              | Omega-5 Gliadin                 |                                 |                            | X                           |                             |                                |
|           |                                                 | Alpha-amylase inhibitor         |                                 |                            |                             |                             |                                |
|           |                                                 | nsLTP                           |                                 |                            |                             |                             |                                |
|           |                                                 | Tri a gliadin                   |                                 |                            |                             |                             |                                |
|           |                                                 | Alpha-amylase-Trypsin inhibitor |                                 |                            |                             |                             |                                |
|           |                                                 | Tri a gliadin                   | X                               |                            |                             |                             |                                |
|           |                                                 | Tri a aA_T1                     |                                 | X                          |                             |                             |                                |
|           |                                                 | Alpha-amylase-Trypsin inhibitor |                                 |                            |                             |                             |                                |
|           |                                                 | Tri a gliadin                   |                                 |                            |                             |                             |                                |
|           |                                                 | Alpha-amylase-Trypsin inhibitor |                                 |                            |                             |                             |                                |
|           |                                                 | Tri a gliadin                   |                                 |                            |                             |                             |                                |
|           |                                                 | Alpha-amylase-Trypsin inhibitor |                                 |                            |                             |                             |                                |
|           |                                                 | Tri a gliadin                   |                                 |                            |                             |                             |                                |
|           |                                                 | Alpha-amylase-Trypsin inhibitor |                                 |                            |                             |                             |                                |

(Continues)

TABLE 1 (Continued)

| Allergen source                        | Allergen component                       | Biochemical designation       | Diagnostic platform#            |                            |                             |                             |                                |
|----------------------------------------|------------------------------------------|-------------------------------|---------------------------------|----------------------------|-----------------------------|-----------------------------|--------------------------------|
|                                        |                                          |                               | ImmunoCap®<br>2021 <sup>a</sup> | ISAC®<br>2020 <sup>a</sup> | ALEX2®<br>2020 <sup>a</sup> | FABER®<br>2020 <sup>a</sup> | Immulate®<br>2016 <sup>a</sup> |
| LATEX<br>( <i>Hevea brasiliensis</i> ) | Hev b 1                                  | Elongation factor             | X                               | X                          | X                           | X                           |                                |
|                                        | Hev b 3                                  | Small rubber particle protein | X                               | X                          | X                           | X                           |                                |
|                                        | Hev b 5                                  | Acid latex protein            | X                               | X                          | X                           | X                           |                                |
|                                        | Hev b 6.01                               | Pro-Hevein                    |                                 | X                          |                             |                             |                                |
|                                        | Hev b 6.02                               | Hevein                        | X                               |                            | X                           | X                           |                                |
|                                        | Hev b 7                                  | Patatin -like protein         |                                 | X                          |                             |                             |                                |
|                                        | Hev b 8                                  | Profilin                      | X                               |                            | X                           | X                           |                                |
|                                        | Hev b 10                                 | SOD; Fe/Mn-SOD                |                                 |                            | X                           |                             |                                |
|                                        | Hev b 11                                 | Class 1 Chitinase             | X                               | X                          | X                           | X                           |                                |
|                                        | Phl p 12                                 | Profilin                      | X                               | X                          | X                           |                             |                                |
|                                        | Aln g 1                                  | PR-10                         |                                 |                            | X                           |                             |                                |
| POLLEN<br>(PR-10 and Profilin)         | Fag s 1                                  | PR-10                         |                                 |                            | X                           |                             |                                |
|                                        | Pho d 2                                  | Profilin                      |                                 |                            | X                           |                             |                                |
|                                        | Cor a 1.01                               | PR-10                         |                                 | X                          | X                           | X                           |                                |
|                                        | Bet v 1                                  | PR-10                         | X                               | X                          | X                           | X                           |                                |
|                                        | Bet v 2                                  | Profilin                      | X                               | X                          | X                           | X                           |                                |
|                                        | Ole e 2                                  | Profilin                      |                                 |                            |                             | X                           |                                |
|                                        | Grass pollen ( <i>Phleum pratense</i> )  |                               |                                 |                            |                             |                             |                                |
|                                        | Alder ( <i>Alnus glutinosa</i> )         |                               |                                 |                            |                             |                             |                                |
|                                        | Beech ( <i>Fagus sylvatica</i> )         |                               |                                 |                            |                             |                             |                                |
|                                        | Date palm ( <i>Phoenix dactylifera</i> ) |                               |                                 |                            |                             |                             |                                |
|                                        | Hazel ( <i>Corylus avellana</i> )        |                               |                                 |                            |                             |                             |                                |
|                                        | Birch ( <i>Betula verrucosa</i> )        |                               |                                 |                            |                             |                             |                                |
|                                        | Olive tree ( <i>Olea europaea</i> )      |                               |                                 |                            |                             |                             |                                |

Note: # Accessed July 12<sup>th</sup>, 2021. Year of the latest product catalog available online for each platform.

ImmunoCap/ISAC by ThermoFisher Scientific. [https://www.macroarraydx.com/products/alex](https://www.thermofisher.com/phadia/es/product-catalog.html?region=ES&solution=All&testType=Component.ALEX2, by MacroArray Diagnostics GmbH. <a href=). [https://a.storyblok.com/f/106109/x/c27bbe92c4/alex2\\_allergenlist.pdf](https://a.storyblok.com/f/106109/x/c27bbe92c4/alex2_allergenlist.pdf)

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<sup>a</sup>For research use only in the ALEX2 platform.

<sup>b</sup>Rosaceae fruits: <https://www.britannica.com/topic/list-of-plants-in-the-family-Rosaceae-2001612>

<sup>c</sup>Cucurbitaceae fruits: <https://www.britannica.com/plant/Cucurbitaceae>

<sup>d</sup>CCD, Cross-reactive carbohydrate determinants (CCDs) in plants and insect venoms can be responsible for positive in vitro tests without clinical relevance. A CCD test might be useful in these cases.

## CONFLICTS OF INTEREST

Dr. Vera-Berrios has nothing to disclose. Dr. Freundt-Serpa has nothing to disclose. Dr. Fernandez-Rivas reports grants from ISCIII (Spanish Government), personal fees from Aimmune Therapeutics, DBV, Novartis, SPRIM, grants from Aimmune, Diater, personal fees from Aimmune Therapeutics, ALK, Allergy Therapeutics, Diater, GSK, HAL Allergy, Medscape, outside the submitted work.

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