EAACI statement on the diagnosis, management and prevention of severe allergic reactions to COVID-19 vaccines

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Abstract
The first approved COVID-19 vaccines include Pfizer/BioNTech BNT162B2, Moderna mRNA-1273 and AstraZeneca recombinant adenoviral ChAdOx1-S. Soon after approval, severe allergic reactions to the mRNA-based vaccines that resolved after treatment were reported. Regulatory agencies from the European Union, Unites States and the United Kingdom agree that vaccinations are contraindicated only when there is an allergy to one of the vaccine components or if there was a severe allergic reaction.
to the first dose. This position paper of the European Academy of Allergy and Clinical Immunology (EAACI) agrees with these recommendations and clarifies that there is no contraindication to administer these vaccines to allergic patients who do not have a history of an allergic reaction to any of the vaccine components. Importantly, as is the case for any medication, anaphylaxis may occur after vaccination in the absence of a history of allergic disease. Therefore, we provide a simplified algorithm of prevention, diagnosis and treatment of severe allergic reactions and a list of recommended medications and equipment for vaccine centres. We also describe potentially allergenic/immunogenic components of the approved vaccines and propose a workup to identify the responsible allergen. Close collaboration between academia, regulatory agencies and vaccine producers will facilitate approaches for patients at risks, such as incremental dosing of the second injection or desensitization. Finally, we identify unmet research needs and propose a concerted international roadmap towards precision diagnosis and management to minimize the risk of allergic reactions to COVID-19 vaccines and to facilitate their broader and safer use.

**KEYWORDS**
COVID, SARS-CoV, virus

1 | INTRODUCTION

The first COVID-19 vaccines are now available in many European countries, the United States (US) and worldwide. These vaccines are among the most remarkable science and medicine accomplishments in modern history and offer realistic hope for an end to the COVID-19 pandemic. To reach this goal, the vaccines must be administered throughout the world so that population-based immunity, also referred to as ‘herd immunity’, protects those who cannot be vaccinated or those who fail to mount a protective response to the virus after vaccination or natural infection.1,2

Soon after authorization was granted in the United Kingdom (UK) and the United States (US) in early-/mid-December 2020, there were single reports of hypersensitivity reactions in a very small number of patients, possibly due to a component in the Pfizer/BioNTech BNT162B2 or the Moderna mRNA-1273 vaccines, both of which are based on similar novel mRNA technologies.3 Since it was just approved in the UK on the 30th of December 2020,4 there is no information regarding the AstraZeneca recombinant ChAdOx1-S COVID-19 vaccine that uses a replication-deficient modified chimpanzee adenovirus vector encoding the SARS-CoV-2 Spike (S) glycoprotein. Fear of a hypersensitivity reaction, particularly among patients with pre-existing allergic disease, may lead to unwarranted vaccine hesitancy compromising achieving herd immunity, and thus, the pandemic will linger unnecessarily with devastating social, economic and health impact.

This EAACI position paper, initiated by the EAACI Research and Outreach Committee5 and issued on the 7th of January 2021, clarifies that unless the patient has a history of an allergic reaction to any of the vaccine components, there is no contraindication to administer the currently approved COVID-19 vaccines.6,7 Furthermore, the document provides guidance on recognizing and treating vaccination-induced allergic reactions when they occur, including recommendations on how to treat and monitor people who experienced a severe allergic reaction after the primary injection of the vaccine. Finally, it identifies unmet research needs and proposes a concerted international roadmap towards precision diagnosis and treatment of allergic reactions to facilitate safer and wider use of the COVID-19 vaccines (Box 1).

1.1 | Prevention of the severe allergic reactions to vaccinations

Based on the experience with other vaccines, systemic allergic reactions to vaccine components are rare, within a range of 1–5 cases per million applications.8 For the Pfizer/BioNTech BNT162B2 COVID-19 vaccine, 11.1 cases of allergic reactions (including anaphylaxis) occurred per 1 million doses.9 Other novel vaccine formulations, such as the recently approved vector-based Ebola vaccine, may show a higher incidence of anaphylaxis.10,11 There are risk factors, which may aggravate allergic reactions that need to be identified while taking the patient’s medical history. As shown in Table 1, these include previous severe anaphylactic episodes, uncontrolled asthma, mastocytosis and other mast cell disorders.12,13

Additionally, medications like beta-blockers, commonly prescribed for cardiovascular diseases, can interfere with the treatment of anaphylaxis. Other known co-factors for precipitating or worsening an anaphylactic reaction include recent physical exercise, alcohol consumption, non-steroidal anti-inflammatory drugs (NSAIDs), or
menstruation. It is currently not known whether these co-factors are facilitating a severe allergic reaction after vaccine administration.

Importantly, anaphylaxis can happen to anyone, anywhere and anytime. There is no correlation with age, sex, asthma, atopic status or previous non-severe reactions. Therefore, it is essential that each vaccination facility, regardless of whether it is located outside or inside a medical centre, is prepared to recognize and treat severe allergic reactions (Table 2). Even when severe, anaphylaxis can resolve with little or no sequelae with immediate and proper management.

Allergy to drugs, foods, insect venoms or inhalant allergens (house dust mites, pollens, animal dander, moulds) is in general not a contraindication for any vaccines, including those for SARS-CoV-2. Vaccination is contraindicated only when a proven diagnosis of hypersensitivity to a vaccine component is diagnosed by a qualified physician and supported by the appropriate allergy test. The specific safety recommendations released by the EU, US and UK regulatory agencies for administering COVID-19 vaccines are overall consistent (Table 3). All agencies advise that the vaccines should be administered under close medical supervision with appropriate medical assistance available. The European Medicines Agency (EMA), US Food and Drug Administration (FDA), British Medicines Healthcare products Regulatory Agency (MHRA) as well as World Health Organization (WHO) advise that the vaccine should not be administered only i) when there is an allergy to one of the components of the vaccine and ii) when there was a severe allergic reaction to the first dose. Of note, at the beginning of the public vaccination campaign, MHRA issued more strict recommendations, but after reviewing the data from the ongoing mass vaccination programme and the publication of the report by the Joint Committee on Vaccination and Immunisation (JCVI), Public Health England and MHRA issued new recommendations, which are in line with those of FDA and EMA. Regarding the most recently approved AstraZeneca adenoviral COVID-19 vaccine, MHRA has already applied this revised view and has stated that a contraindication is only applicable in case of hypersensitivity to the active substance or any of the excipients present in the vaccine. The COVID-19 vaccines currently authorized in the EU, UK, and US, along with their dosing instructions, ingredients and common side effects are summarized in Table 4.

1.2 Diagnosis and treatment of a severe systemic allergic reaction

A systemic allergic reaction, often referred to as anaphylaxis, is currently defined as a serious reaction with rapid onset (minutes to hours) that is potentially life threatening. For the Pfizer/BioNTech BNT162B2 COVID-19 vaccine, 71% of allergic reactions occurred within 15 min of vaccination. Anaphylaxis usually manifests as a rapid, progressive reaction often involving (but not always) the skin or oral mucosa (such as lip or tongue swelling), the gastrointestinal system, the upper and lower respiratory tract, or cardiovascular system. The reaction can progress within minutes from the skin/oral mucosa to multiorgan involvement, abdominal cramps and vomiting, stridor, dyspnoea, wheezing, and circulatory collapse (due to massive volume loss into bodily tissues) (Figure 1).

The time elapsed from allergen exposure to cardiorespiratory failure can be within a few minutes. Therefore, upon first signs of anaphylaxis, it is necessary to immediately put the patient in recline position with legs up and administer intramuscular epinephrine (Figure 1). There is no contraindication to epinephrine in treatment of anaphylaxis – it is life-saving. In some cases, the evolution of anaphylaxis may be delayed, and cardiorespiratory failure can occur up to 8 hours after the start of the symptoms. Therefore, the initial milder symptoms should not be ignored.
Once epinephrine has been administered, secure intravenous access and start volume replacement with intravenous 0.9% NaCl, assess vital signs, clear the airways, give oxygen via facial mask at least 10 litres/minute (Figure 1). If there is rapid volume loss/hypotension, the patient may require up to 2–3 litres of intravenous 0.9% NaCl administered in 10–20 minutes. If there is no improvement within 5–10 minutes, repeat the intramuscular epinephrine injection and call additional emergency assistance. If there is severe dyspnoea and or wheezing, administer short-acting beta-agonists such as salbutamol puffs via large-volume spacer. Vaccination units within fully equipped medical centres may also consider nebulization with short-acting beta-agonists or if there are signs of severe upper airway obstruction (laryngeal/uvula/tongue oedema), nebulized epinephrine.16,28 However, due to the possibility of spreading

| Medication                  | Specification/Form | Administration          |
|----------------------------|--------------------|-------------------------|
| Epinephrine Vials          | solution of 1 mg/mL (1:1000) | Intramuscular 0.5 mg |
| Epinephrine autoinjector 0.3 mg* | Ready-to-be-used injection device | Intramuscular          |
| Short-acting beta-agonists (bronchodilator) eg salbutamol | Pressurized metered-dose inhaler (pMDI) | Inhalation through large-volume spacer |
| Oxygen                     | Gas                | Inhalation via mask     |
| Intravenous fluid (0.9% NaCl) | Bottles: solution of 500 mL | Intravenous           |
| Methylprednisolone 250 mg  | Vials               | Intravenous             |
| Methylprednisolone 32 mg   | Tablets             | Oral                    |
| Antihistamines**           | Tablets or vials    | Oral or IV              |

**Every COVID-19 vaccination centre should have at least 3 doses of epinephrine ready for immediate use at any given time.

**Oral antihistamines with early onset of action like cetirizine or levocetirizine are preferred; iv antihistamine – Diphenhydramine or Clemastinum.

***Nebulization with caution during COVID-19.

### Table 2: Recommended medications and equipment for initial treatment of severe allergic reactions

| Equipment                      | Specification/Form |
|--------------------------------|--------------------|
| Syringes                       | 1 mL, 2 mL, 10 mL, 20 mL |
| Needles for venipuncture       | 6-11 mm            |
| IV cannulas                    | 14G, 16G, 17G, 18G, 21G, 23G |
| Infusion systems               | For sterile iv infusions |
| Face masks for oxygen therapy  | Adult-size mask    |
| Laryngotracheal tubes          | 6-10 cm            |
| Large volume spacer            | For inhaled aerosol delivery |
| Resuscitation equipment/defibrillator |                    |
| Blood pressure gauge/cuff      |                    |
| Stethoscope                    |                    |
| Pulse oximeter                 |                    |
| Latex-free gloves              |                    |
| ECG/monitor                    |                    |
| Oxygen concentrator            |                    |

** Additional equipment **

Nebuliser
the SARS-CoV-2 virus during nebulization, sublingual epinephrine (tablets or spray) may be a better option.

Other medications for the treatment of allergic reactions include oral or intravenous glucocorticoids and oral or intravenous antihistamines, usually administered to treat reactions isolated to the skin or mucosa (eg localized oedema without severity location, pruritus or hives). Glucagon is used when patients on beta-blockers are unresponsive to epinephrine.

Patients without response to these initial steps should be immediately transferred to the nearest hospital's intensive care unit. At the ICU, within the first 2–3 hours after the beginning of the reaction, it is advised to draw blood for measuring mast cell tryptase (MCT), which can confirm anaphylaxis.30 A simplified algorithm for these initial treatment steps is shown in Figure 1.

### TABLE 3 Regulatory recommendations for mRNA- and viral vector-based COVID-19 vaccines concerning anaphylaxis

| Regulatory body (region) | European Medicines Agency (EMA) EU | U.S. Food and Drug Administration (FDA) USA | Medicines and Healthcare products Regulatory Agency (MHRA) UK |
|--------------------------|------------------------------------|------------------------------------------|--------------------------------------------------------|
| Vaccine names (manufacturer) | 1. BNT162b2, Comirnaty (BioNTech/Pfizer) 2. mRNA−1273, commercial name not assigned (Moderna) | 1. BNT162b2, Comirnaty (BioNTech/Pfizer) 2. mRNA−1273, commercial name assigned (Moderna) | 1. BNT162b2, Comirnaty (BioNTech/Pfizer) 2. ChAdOx1-S recombinant, Covid−19 Vaccine AstraZeneca |
| Documents | 1. Fact sheet for healthcare providers administering vaccine (vaccination providers) emergency use authorization (EUA) of the Pfizer-Biontech COVID−19 vaccine to prevent coronavirus disease 2019 (COVID−19)19,20,37 2. Fact sheet for recipients and caregivers emergency use authorization (EUA) of the Moderna COVID−19 vaccine to prevent coronavirus disease 2019 (COVID−19) in individuals 18 years of age and older21,38 | 1. Information for Healthcare Professionals on Pfizer/BioNTech COVID−19 vaccine23,39 2. Information for Healthcare Professionals on COVID−19 Vaccine AstraZeneca4,36 |
| Website | https://www.ema.europa.eu/en/news/ema-recommends-first-covid-19-vaccine-authorisation-eu | https://www.fda.gov/emergency-preparation/redness-and-response/coronavirus-disease-2019-covid-19/pfizer-biontech-covid-19-vaccine | https://www.gov.uk/government/publications/regulatory-approval-of-pfizer-biontech-vaccine-for-covid-19/information-for-healthcare-professionals-on-pfizerbiontech-covid-19-vaccine |
| Date of access | 06.01.2020 | 30.12.2020 | 31.12.2020 |
| Safety recommendations | BNT162b2 and mRNA−1273: People who already know they have an allergy to one of the components of the vaccine should not receive the vaccine  BNT162b2 and mRNA−1273: People who have a severe allergic reaction when they are given the first dose of Comirnaty should not receive the second dose | BNT162b2 and mRNA−1273: People who already know they have an allergy to one of the components of the vaccine should not receive the vaccine  BNT162b2 and mRNA−1273: People who have a severe allergic reaction when they are given the first dose of the vaccines should not receive the second dose | BNT162b2: Hypersensitivity to the active substance or to any of the excipients (since 31.12.2020)  BNT162b2: A second dose of the COVID−19 mRNA Vaccine BNT162b2 should not be given to those who have experienced anaphylaxis to the first dose of COVID−19 mRNA vaccine BNT162b2  ChAdOx1-S recombinant: Hypersensitivity to the active substance or to any of the excipients |
by an allergy specialist that the vaccine did not induce the allergic reaction, they should not receive the second dose of the vaccine.

2 | FUTURE DIRECTIONS AND RESEARCH ON ALLERGIC REACTIONS TO VACCINES

2.1 | Identification of the allergenic/immunogenic components

Currently, regulatory agencies, national research centres and academic institutions are investigating the pathogenesis of severe hypersensitivity reactions following the injection of mRNA-based COVID-19 vaccines to determine the culprit. The two first mRNA-based COVID-19 vaccines are packaged in multi-dose vials and must be diluted before use. While there are no added adjuvants or preservatives, the excipients that stabilize the active vaccine include several lipids, salts, sugars and buffers (Table 2). The main function of the lipids is to provide a nanoparticle carrier with a protective shield for the mRNA after injection and to facilitate its cellular uptake through the plasma membranes. The lipid nanoparticle (LNP) carrier consists of cationic lipids coating the polyanionic mRNA and zwitterionic lipids that mimic the phospholipids of the cell membrane. Cholesterol stabilizes the lipid bilayer of the LNP. Polyethylene glycol (PEG)-modified lipids improve the aqueous solubility of the LNPs. PEG, also known as macrogol, is a polyether compound widely used as an additive in cosmetics, pharmaceuticals, and foods. In the case of the mRNA-1273 and the BNT162b2 vaccine, a PEG with a molecular weight of 2000 g/mol is used (PEG 2000). While PEGs are considered generally safe for use in medical devices and drug formulations, IgE-mediated allergic reactions and anaphylaxis have been reported to PEGs of different molecular weights.

The first recombinant viral vector-based COVID-19 vaccine, which uses a modified replication-deficient chimpanzee adenovirus vector encoding the SARS-CoV-2 S glycoprotein, does not require freezing and can be stored at 2–8°C. To stabilize the product, the ChAdOx1-S vaccine includes as excipients polysorbate 80, the amino acid L-histidine, ethanol, salts, sugars and buffers (Table 2).

**TABLE 4** Comparison of the first available vaccines against SARS-CoV-2

| Name                      | mRNA−1273          | BNT162b2          | ChAdOx1-S recombinant |
|---------------------------|--------------------|-------------------|-----------------------|
| Manufacturer              | ModernaTX, Inc.    | BioNTech and Pfizer, Inc., | AstraZeneca          |
| Type of vaccine           | mRNA encoding the SARS-CoV−2 Spike (S) glycoprotein | Recombinant, replication-deficient chimpanzee adenovirus vector encoding the SARS-CoV-2 Spike (S) glycoprotein |
| Dose and interval         | 2 doses, (28 days apart) | 2 doses, (21 days apart) | 2 doses (4–12 weeks apart) |
| Efficacy                  | ~95% effective     | ~70% to 90% effective | ~70% to 90% effective |
| Age                       | 18 years and older | 16 years and older | 18 years and older |
| Ingredients               | mRNA (100 μg)      | lipids (SM-102, polyethylene glycol [PEG] 2000 dimyristoyl glycerol [DMG], cholesterol, and 1,2-distearyl-sn-glycero-3-phosphocholine [DSPC]) | recombinant ChAdOx1-S, produced in HEK 293 cells (0.5 mL, containing 5x10^10 viral particles) |
|                           | tromethamine and tromethamine hydrochloride | bis(2-hexyldecanoate), 2 lipids (4-hydroxybutyl azanediyl)bis(hexane-6,1-diyi) | L-histidine |
|                           | acetic acid        | [polyethylene glycol]-2000| L-histidine hydrochloride monohydrate |
|                           | sodium acetate     | 1,2-Distearyl-sn-glycero-3-phosphocholine, and cholesterol) | magnesium chloride hexahydrate |
|                           | sucrose            | potassium chloride and | polysorbate 80 |
|                           |                    | monobasic potassium phosphate | ethanol |
|                           |                    | sodium chloride and dibasic | sucrose |
|                           |                    | sodium phosphate dehydrate | sodium chloride |
|                           |                    | sucrose | disodium edetate dehydrate |
|                           |                    | | water for injections |
| Side effects              | Injection site pain, swelling, or redness | Tiredness | Injection site pain, swelling, or redness |
|                           | Tiredness          | Headache | Tiredness |
|                           | Headache           | Muscle pain | Headache/fatigue |
|                           | Muscle pain        | Chills | Muscle pain |
|                           | Chills             | Fever | Arthralgia |
|                           | Fever              | Nausea/vomiting | Chills |
|                           | Nausea/vomiting    | Swollen lymph nodes | Fever |
|                           |                    |                    | Nausea/vomiting |
| Storage and shipping      | Shipped at −20°C (−4°F). Stable for 30 days 2–8°C (36–46°F). Stable up to 6 months at −20°C and up to 12 hours at room temperature | Shipped for up to 10 days at −70°C (−94°F), Stored in ultra-low temperature freezers for up to six months. | Unopened multi-dose vials are shipped and stored at refrigerator temperature (2-8°C). Unopened vials have a shelf-life of 6 months. Do not freeze. Protect from light |
FIGURE 1  Diagnosis and management of severe allergic reaction after SARS-CoV-2 vaccination in the vaccination centre

VACCINATION
observe at least 15 minutes
(monitor vital signs and observe at least 30 minutes in patients at high risk)

if patient develops the following symptoms

Generalized hives, generalized pruritus, generalized flushing, face angioedema

AND

Shortness of breath, wheeze, stridor

OR

Syncope, incontinence, blood pressure drop

OR

Swollen tongue-uvula, Cramping abdominal pain, vomiting, diarrhea

UGRICNTLY

Put the patient in the reclining position with legs up

Administer EPINEPHRINE (ADRENALINE)
0.3 mg in auto-injector
OR
0.5 mg per dose (of 1:1000 (1 mg/ml) of aqueous solution)
intramuscularly in the mid-outter thigh quadriceps muscle

AND

Secure intravenous access
and start infusion with 0.9% NaCl (10-20 ml/min)
Clear the airways
Administer Oxygen via facial mask (at least 10 liters/min)
Monitor vital signs

if symptoms are fully resolved

Discharge after 24 hrs
Refer to the allergy center for the urgent workup

if symptoms continue

Transfer to ICU

Blood pressure drop
2000-3000 ml of 0.9% NaCl intravenously in 10-20 min

No improvement in 5-10 min:
REPEAT EPINEPHRINE (ADRENALINE) intramuscularly

Bronchospasm
Salbutamol 4-10 puffs via large volume spacer

Antihistamines oral/parenteral
Glucocorticoids oral/parenteral observation 4 hr

Discharge 4-8 hrs after full resolution of the symptoms
Refer to the allergy center for the workup

if isolated and not progressing

CALL emergency assistance depending on your location (911, 112, ICU team)

if symptoms continue

Advise against second planned SARS-CoV-2 vaccination until clarified by the allergy center
2.2 | Diagnostic and preventive allergy workup

Studies on the pathogenesis of the severe allergic reactions following mRNA-based COVID-19 vaccine components need to be prioritized. The allergic components can be identified with in vitro approaches (e.g., basophil activation test and mast cell line assays) or in vivo skin testing before administration of the vaccine. Through potential collaboration with the vaccine producers and accessibility to vaccines or their components for allergy centres, novel procedures for in vivo and in vitro IgE testing and protocols for incremental dosing of the second (booster) COVID-19 vaccination in a subset of patients who may be at greater risk for anaphylaxis may become available. To further enhance safety in patients who experienced a severe allergic reaction after the primary vaccination, desensitization protocols with individual vaccine components can be envisaged. Molecular diagnostics may also be useful to develop a personalized approach to determine which vaccine platform is the most suitable one for an at-risk patient (Box 2).

2.3 | Research needs

In addition to the urgent clinical needs in diagnosing and treating patients who have suffered severe allergic reactions after vaccination, multiple other research challenges and questions remain open (Box 3). To address these unmet needs, EAACI provides a concerted roadmap towards precision diagnosis and treatment of severe allergic reactions after COVID-19 vaccination that includes besides clinical and scientific aspects, big-data management, and legal, ethical and regulatory
aspects (Figure 2). Data sets of state-of-the-art multilayer omics approach (eg proteomics, single-cell RNAseq transcriptomics, CyTOF mass cytometry of immune cells) from existing well characterized population cohorts can be combined with the ongoing vaccination campaign efforts in various countries. Such a multi-layered approach promises to solve the unmet needs for the following reasons: 1) to analyse protective immune profiles to COVID-19 vaccination; 2) to compare the individual COVID-19 vaccination outcome with existing immune profiling data (eg SARS-CoV-2 serology, cellular immune responses to SARS-CoV-2); and 3) to combine clinical and research data with computational and big-data approaches which guarantee rapid progress.

As the novel COVID-19 vaccines are administered to millions of people over the next months and in the upcoming years, more data will become available to assess the incidence of hypersensitivity reactions and determine specific risk factors. As pharmacovigilance data are accumulated and analysed over the upcoming months, EAACI will revise and update these recommendations on the EAACI website. The current EAACI recommendations specifically target only those vaccines that have received conditional marketing authorization by EMA in the EU, and emergency use authorization by the FDA in the US and by MHRA in the UK.

**BOX 3  Research challenges and questions**
- Who is at risk of developing a severe allergic reaction to any of the new COVID-19 vaccines?
- What is causing sensitization to an ingredient of a COVID-19 vaccine?
- What is the potential immune mechanism other than IgE-mediated hypersensitivity?
- What is the impact of previous infection with SARS-CoV-2, other coronaviruses or previous vaccination on the individual risk?

**FIGURE 2**  Key pillars to improve the precision diagnosis and management of severe allergic reactions after COVID-19 vaccination
CONFLICT OF INTEREST

Dr. Sokolowska declares scientific grants from the Swiss National Science Foundation and GSK. Dr. Eiwegger reports to act as local PI for company sponsored trials by DBV and sub-investigator for Regeneron and holds grants from Innovation fund Denmark and CIHR. He is co-investigator or scientific lead in three investigator initiated oral immunotherapy trials supported by the Food Allergy and Anaphylaxis Program SickKids and serves as associate editor for Allergy. He/His laboratory received unconditional/kind contributions from Macro Array Diagnostics and ALK. He holds advisory board roles for ALK. Dr. Torres reports grants or personal fees from European Commission, SEAIAC, ISCIII, Diater laboratory, Leti laboratory and Aimmune Therapeutics. Dr. Barber reports grants and/or personal fees from ALK and Aimmune. Dr. Nadeau reports grants from NIAID, NHLBI, NIEHS, FARE, and other from WAO, Cour Pharma, Before Brands, Alladapt, Latitude, IgGenix, ITN and NIH clinical research centres. In addition, Dr. Nadeau has the following pending patents: Inhibition of Allergic Reaction to Peanut Allergen using an IL-33 Inhibitor, Special Oral Formula for Decreasing Food Allergy Risk and Treatment for Food Allergy, Basophil Activation Based Diagnostic Allergy Test, Granulocyte-based Methods for Detecting and Monitoring Immune System Disorders, Methods and Assays for Detecting and Quantifying Pure Subpopulations of White Blood Cells in Immune System Disorders, Mixed Allergen Compositions and Methods for Using the Same, and Microfluidic Device and Diagnostic Methods for Allergy Testing Based on Detection of Basophil Activation. Dr. Palomares reports research grants from ImmunoTek S.L., Novartis and Mineco. Dr. Palomares has received fees for giving scientific lectures or participation in Advisory Boards from: Allergy Therapeutics, Amgen, AstraZeneca, Diater, GSK, Immunotek S.L., Novartis, Sanofi-Genzyme and Stallergenes. Dr. Vieths reports personal fees from Swiss Society for Allergy and Immunology, Schattauer Allergologie Handbuch, Elsevier Nahrungsmittelallergien und Intoleranzen, Karger Food Allergy: Molecular Basis and Clinical Practice, non-financial support from German Research Foundation, European Directorate for the Quality of Medicines and Health Care, EAACI, GDC, AKM Allergiekongress, International Union of Immunological Societies, and SEAIAC. Dr. Agache serves as associate editor of Allergy and CTA. Dr. Shamji, Dr. Jutel, Dr. Ollert, Dr. Rabin, Dr. Del Giacco and Dr. Riggioni declare no COI related to this paper.

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