Date of submission: 28 June 2019

Submission of comments on 'A Guideline for allergen products development in moderate to low-sized study populations' (EMA/CHMP/251023/2018)

Comments from:

Name of organisation or individual
EFA – European Federation of Allergy and Airways Diseases Patients' Associations Submitted by EFA Policy Officer Panagiotis Chaslaridis (Panagiotis.chaslaridis@efanet.org) in coordination with EFA Food Allergy Working Group and EFA Allergy and Asthma Working Group. www.efanet.org

Please note that these comments and the identity of the sender will be published unless a specific justified objection is received.

When completed, this form should be sent to the European Medicines Agency electronically, in Word format (not PDF).

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1. General comments

Stakeholder number *(To be completed by the Agency)*	General comment (if any)	Outcome (if applicable) *(To be completed by the Agency)*
	EFA welcomes the initiative for a new EMA scientific guideline on the development of allergen products to treat allergies considered of low prevalence. It is encouraging for the European community of allergy patients to have the EMA proposing a framework on unmet medicals need in disease areas of limited or no targeted and effective treatment options, which are easily overlooked or considered as covered by existing guidelines and treatments. We hope that such guidance will clarify uncertainty around existing rules for the development of treatments for these specific populations, including on safety and ethical concerns for patients, companies, researchers or clinicians, while also helping balance the gaps in treatment options. As representatives of European allergy patients, it is promising to see that EMA continues to consider our remaining treatment needs as a priority and enables through this consultation to list all the allergy types and sub-types that need to be addressed, providing clear guidance on the methods of diagnosis and treatment that are in place for their particular condition, and therefore pointing out to the existing treatment gaps. Given that the guideline aims to accommodate, among others, the needs of even more specific allergic diseases (low prevalent), it has the potential to ensure that, in the future, no allergy patient will be left behind without treatment options. Furthermore, the guideline could indirectly affect the persisting inequalities in access and expertise in clinical practice to preventative treatments. Finally, we are glad to note that this EMA initiative may also constitute a step towards a more personalised medicine approach, an intermediate stage to address the complex	

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	and still unknown onset and development of allergy.	

2. Specific comments on text

Please add more rows if needed.

Line number(s) of the relevant text *(e.g. Lines 20-23)*	Stakeholder number *(To be completed by the Agency)*	Comment and rationale; proposed changes *(If changes to the wording are suggested, they should be highlighted using 'track changes')*	Outcome *(To be completed by the Agency)*
43		Comment: In the listing of the symptoms of Type I allergies (Discussion on the problem statement), it would be important to highlight the **systemic** character of anaphylactic reaction. Proposed change (if any): Rephrase to *'…even if the clinical condition may manifest differently as rhinitis/rhinoconjunctivitis, bronchial asthma, urticaria, pruritus, eczema, gastrointestinal symptoms, general inflammation, or severe **systemic** anaphylactic reactions.'*	
49-52		Comment: EFA recommends EMA to explicitly cite **the types of allergy that will fall under the proposed guideline** (possibly in an Annex), as a way to ensure regulatory clarity and informed decision-making by healthcare professionals and patients. Moreover, in line with the unmet needs-driven approach, we	

		think it is crucial for EMA to be more specific on the guidance it aims to provide to resolve problems within each particular allergy type, be it on the diagnosis or the treatment side. Proposed change (if any):	
49-52		Comment: Here it would also be interesting to mention that **some current diagnostic tests are unreliable.** Proposed change (if any): Add: *'Meanwhile, clinical practice has shown that some current diagnostic tests **may even fail** to detect certain types of allergies that are not IgE-mediated, or that may have emerged recently.'*	
53-60		Comment: In the discussion about allergic rhinitis/rhinoconjunctivitis, EFA suggests adding an element on the **quality of life of patients**, both in the case where the disease is left untreated, and also when the appropriate treatment addressing the disease pathogenesis is provided. Proposed change (if any): Rephrase to *'When it is left untreated (including immunotherapy with products lacking efficacy), or is only treated by symptomatic medication it is prone to evolve into asthma which can progress to a chronic and life-threatening disease **and lead to unnecessary impact on daily, educational and working life, considerable decreasing quality of life,…** and may prevent progression to more serious conditions **and ensure long medication free periods.'***	
79-90		Comment: To further support EMA's concern over the reliability of clinical trial outcomes in the event of co-existing allergies, EFA	

		recommends that the text include a reference to the **lack of measurability and understanding of impact** to the patient. Proposed change (if any): Rephrase to *'the number of respective patients with only one allergy may be limited in some situations as patients commonly suffer from multiple allergies which may be symptomatic simultaneously (e.g. in overlapping pollen seasons)* ***leading to an impact on the individual that is rarely measured and therefore not understood and tackled.'***	
79-97		Comment: Given the limits imposed by the difficulty to find patients with just one allergy, EFA considers important the **development of clinical trial samples that are closer to the real allergy patient population**, that is, people living with a spectrum of atopic disease and (allergic) asthma, beyond just one low prevalence allergy. Taking into account the high number of underdiagnosis in allergy, this approach could enable new solutions for patients, provided that in such trials they participate under the highest safety and control standards in case of adverse symptoms and reactions. However, we note that the evaluation of patients with several allergies at the same time can potentially yield misleading results, as it is difficult to determine which allergen patients are reacting to. This can lead to wrong conclusions when it comes to the development of the allergen product, and thus to inefficient and even harmful treatment. At the same time, EFA believes that low prevalence diseases could be better studied through less clinical techniques, such as the **collection and analysis of Real World Data** or even via the development and analysis of specific patient-reported	

		outcomes that could then lead to a more standard clinical trial approach. Proposed change (if any): In accordance with **EMA's priority to improve patient data generation**, add a reflection along the following lines: *'EMA acknowledges the added value of developing in the future clinical trials samples that are better adapted to the real allergy population, i.e. people living with a spectrum of atopic disease and (allergic) asthma, beyond just one low prevalence allergy. Accordingly, less clinical techniques, such as the collection and analysis of Real World Evidence data or even via the development and analysis of specific Patient-Reported Outcomes that could then lead to a more standard clinical trial approach should be considered'.*	
127-130		Comment: EFA suggests developing **a Q&A addressed to patients/public** with the outcome of this guidance, to be relayed by EFA and its national members, as well as healthcare professionals, to inform individual patients. Proposed change (if any):	
137		Comment: As representatives of people in Europe living with allergic diseases, EFA would wish to have its name included in **the Interested Parties section**. Proposed change (if any): Replace the general reference to 'patient organisations' with **'EFA - European Federation of Allergy and Airways Diseases Patients' Associations and national allergy patient groups'**.	

All		Comment: EFA believes that the general lines of effective diagnosis and treatment of allergy in clinical care should only be set by medical doctors with **specialised training in allergology**. Unfortunately, this is frequently not the case in many EU Member States, given that allergology is not yet recognised as a medical speciality everywhere in Europe or is downgraded as medical speciality. From the collective experience of our network the problem is precisely this one: delayed, downgraded or partial diagnosis leading to self-care without proper guidance or treatment. However, EFA acknowledges that, in light of their multi-systemic impact, allergies may affect various human systems such as the skin, the respiratory system, the digestive system, and organs such as the eyes and more. Thus EFA considers that primary care physicians and other medical specialisations should also include training on allergy, ultimately basing this choice in the high prevalence of these chronic non-communicable diseases. Proposed change (if any):	