Dear Mr. Prats Monné,

RE: Allergen products in Europe for diagnosis and treatment

I am writing to you regarding a pressing matter which is of concern to all stakeholders in the allergy community. As you may be aware, there are some EU regulations for allergen extracts for diagnosis and treatment that are being enforced that could ultimately be detrimental to patient care across Europe. As EAACI President, I urge you in the strongest terms possible to help in preventing the diagnosis and treatment of allergic patients in Europe reverting back to a standard from the start of the previous century.

The European Academy of Allergy and Clinical Immunology (EAACI) is a non-profit organisation active in the field of allergic and immunologic diseases such as asthma, rhinitis, eczema, occupational allergy, food and drug allergy, and anaphylaxis. EAACI was founded in 1956 and has become the largest medical association in Europe in the field of allergy and clinical immunology. It includes over 9000 members from 121 countries, as well as 49 National Allergy Societies.

Background
Allergic diseases represent a major health burden because of their high prevalence (25% of the general population, with a very high incidence in childhood) and severity of some forms (severe asthma, anaphylactic reactions from food, drugs and insect venoms). Allergen products are widely used for both diagnosis of allergy – in-vivo (skin tests, provocation tests) or in-vitro (immunoassays, more expensive and less sensitive)- and for treatment of allergic diseases (specific allergen immunotherapy, oral or subcutaneous). Specific allergen immunotherapy is considered the only treatment with the potential to modify the natural course of allergic diseases and the progression from a disease to another (allergy march) or from mild to more severe forms.

Although Directive 2001/83/EC established that both in-vivo diagnostic and therapeutic allergen products are medicines, at present out of more than 3000 allergen products marketed in Europe, only 2 obtained a proper MA (mutual recognition), while most of other products are considered NPPs even if industrially manufactured.
In spite of the ad hoc Guidelines published by the European Medicines Agency (EMA) for Quality of Extracts and for Clinical Development of allergen products, there is still uncertainty on how preparing adequate dossiers for obtaining marketing authorisation of new allergen products, with special reference to study design, patient selection criteria, comparators and outcome measures to be adopted to support the four possible claims mentioned in the guidelines. In particular, studies in the pediatric population are found to be very difficult to perform, since EMA Guidelines request long term studies against placebo. Furthermore, with reference to diagnostic products, there is the risk that allergen manufacturers will never be ready to undergo the difficult, long and expensive studies to obtain marketing authorisation of products widely, effectively and safely used for allergy in-vivo diagnosis and research, but with insignificant economic return. This will possibly reflect, in the future, on the exclusive use of in-vitro tests that do not allow the same quality of care for the allergic patients and will cause higher costs for all NHSs. The situation is even more confusing about the efficacy, safety and pharmacovigilance obligations of allergen products marketed as NPPs that are at present handled with very heterogeneous approaches in different European countries.

To compound the difficulty of the situation, allergen manufacturers are usually small or middle sized pharma companies, that often do not have the experience and the resources needed to adhere to the present regulations. The paradox is that while the current stringent regulations, in the absence of any help from regulatory bodies and recognition from payers, discourage companies that have shown their availabilities to follow them for marketing authorisation and pharmacovigilance of their products, thousands of products often without evidence of quality, efficacy and safety continue to be on the market as NPPs even if industrially manufactured. In the case of test allergens for in-vivo diagnosis, for such companies to offer a range of test allergens would be financially prohibitive – the expense of initiation and maintenance of test allergens authorisations far exceed their related revenues and manufacturers may be forced to significantly limit their allergen portfolios. This has already happened in France, for example, with losses of about three quarters of skin prick allergens since 2004, and in Germany, where 443 authorized test allergens were lost in 2013. Thus, allergists can no longer offer full diagnostic evaluations to all patients with different kinds of allergies in Europe.

Impact on the allergy community – treating doctors and their allergic patients
In the scenario above, costs will increase significantly due to limited allergens available; rarely used test allergens may no longer be commercially available; larger member states may have a broader range of test allergens than in smaller member states due to commercial reasons. Physicians may be forced to use unstandardised allergens from available natural sources due to lack of availability of commercial suppliers which will revert the practice of allergology back to 100 years ago.

EAACI urgently calls on the European Commission to review EU-Directives 89/342/EEC and 2001/83/EC and to:

1. Distinguish between in-vivo diagnostic allergen products from therapeutic ones;

2. Develop facilitated pathways for marketing authorisation of allergen products, while giving clear indications on which allergen products can be considered NPPs and which should go to a (facilitated) marketing authorisation within a certain date.
Today’s reality is that European allergic patients have the opportunity to be diagnosed, treated and even cured thanks to the availability of commercial allergens. EAACI urges the European Commission to take action to ensure that this excellent quality of care does not become a thing of the past in Europe.

EAACI is ready to inform and support the EU Commission with any further information or testimonials that can help to illuminate this issue and solutions.

I look forward to hearing from you how we can move this issue forward.

Yours sincerely

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