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EMA/CVMP/IWP/351882/2015
Committee for Medicinal Products for Veterinary Use (CVMP)

Concept paper on requirements for the production and control of allergen products for use in animals

Draft

Agreed by Immunologicals Working Party	June 2015
Adopted by CVMP for release for consultation	10 September 2015
Start of public consultation	18 September 2015
End of consultation (deadline for comments)	31 December 2015

The proposed guideline will replace 'Specific Requirements for the Production and Control of Allergen products (7BIm11a), adopted prior to September 1994; last revision September 1994.

Comments should be provided using this template. The completed comments form should be sent to vet-guidelines@ema.europa.eu

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1. Introduction

Recent developments require the revision of the existing CVMP/IWP Guideline on allergen products, 'Specific Requirements for the Production and Control of Allergen Products (7BIm11a, volume 7)' [1]. Since the revision of this guideline in 1994, the scientific knowledge on structures, cross-reactivity, and stability of allergens has increased drastically, and many allergens have been produced as recombinant proteins. This scientific progress has several implications for regulation and standardisation of allergen products. Special emphasis has to be granted to recombinant allergen products. Therefore, the revised guideline should redefine the statements on batch-to-batch consistency, characterisation and use of in house reference preparations (IHR), control test as well as on safety and efficacy testing. Moreover, it should be aimed at covering aspects specific for recombinant allergens that are not covered or specifically addressed by other guidelines on biotechnology-derived proteins.

2. Problem statement and Discussion

The `Note for Guidance on allergen products' (CPMP/BWP/243/96) [2] as well as the Monograph [3] on allergen products contain regulations on the technical quality of allergen products that are based on natural allergen extracts. It is recommended to express the potency in units of biological activity, despite the fact that a wide range of different unit systems is currently used on the market. Ph.Eur. provides a monograph for allergens and currently discussed the development of specific monographs for the various product groups such as allergen products, animal epithelia and outgrowths for allergen products, Hymenoptera venoms for allergen products, mites for allergen products, moulds for allergen products and pollens for allergen products. These monographs consider allergens for use in humans. Furthermore, the Note for Guidance on Allergen Products accepts that data obtained in trials with one member of a taxonomical family are extrapolated to other families, without providing further details of this concept. A detailed re-evaluation and elaboration of this concept is required.

3. Recommendation

The scope of the revised guideline will encompass production and quality issues concerning natural and biotechnology derived allergen products including derivatives with reduced IgE binding capacity and/or enhanced immunogenicity, as well as fusion constructs containing polypeptides derived from allergens as well as non allergenic functional polypeptides.

The following main topics were identified:

• Elaborate on requirements in allergen standardisation to change from potency units of allergen extracts to mass units of individual allergens.

• Redefine and elaborate in detail the concept of taxonomical allergen families. Define in detail phylogenetical relationships that are accepted for extrapolation of clinical data. Consider applying the principle of "allergen families" to biotechnology derived allergens.

• Define acceptance criteria for allergen mixtures from a single allergenic source and from different sources, respectively.

• Guidance is required on production related issues and expression systems for biotechnology derived allergens. Depending on the expression system used, the relevance of folding and post-translational modification needs to be elaborated in keeping with the fact that the drug substance is intended for application in subjects susceptible to developing hypersensitivity reactions.

• Guidance is required on appropriate potency assays for batch release of natural and recombinant allergen products with reduced IgE binding capacity. So far, total allergenic activity is exclusively based on IgE binding measurements despite the fact that T cell stimulation capacity is considered to be of major importance for the therapeutic effect.

• Elaborate on the relevance of folding and post-translational modification of allergens in regard to the establishment of batch control procedures.

• Formulation issues.

• Elaborate on stability testing of intermediate products (IMP) and end products.

The Guideline on allergen products (for human use): production and quality issues (CHMP/BWP/304831/2007) [4] will be considered.

4. Proposed timetable

Release of concept paper for 3 months consultation:	September 2015
Deadline for receipt of comments:	December 2015
Discussion in working parties:	Quarters 1 and 2 of 2016
Discussion of draft guideline at CVMP:	Quarter 3 of 2016
Anticipated release of draft guideline for public consultation:	Quarter 4 of 2016

5. Resource requirements for preparation

Input from members of IWP. In addition, the involvement of IWP observers from EDQM is foreseen.

6. Impact assessment (anticipated)

The guideline should provide improved guidance to Industry on the development of allergen products including products containing biotechnology derived proteins. It will result in a more consistent assessment of products by regulators. This will contribute to improved standardisation of existing allergen products and to the availability of novel allergen products with enhanced clinical efficacy and safety to the market, and thereby benefit animal health.

7. Interested parties

Regulatory authorities for medicinal products for veterinary use, the veterinary pharmaceuticals industry.

8. References to literature, guidelines, etc.

1. Specific Requirements for the Production and Control of Allergen Products (7BIm11a, volume 7)

2. Note for Guidance on "*Allergen products*" (CPMP/BWP/243/96)

3. European Pharmacopoeia Monograph on Allergen Products (2010:1063)

4. Guideline on allergen products (for human use): production and quality issues (EMEA/CHMP/BWP/304831/2007)

88