Introduction: Regulation of Allergen Products and the German Regulation for Therapy Allergens

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Regulatory Background

- **Allergens subjected to European pharmaceutical legislation in 1989 (Directive 89/342/EEC)**

- **Definition of directive 2001/83/EC: "medicinal product which is intended to identify or induce a specific acquired alteration in the immunological response to an allergizing agent"**

Regulatory Background

Article 2 of Directive 2001/83/EC (Scope)

1. This Directive shall apply to medicinal products for human use intended to be placed on the market in Member States and either prepared industrially or manufactured by a method involving an industrial process.

Directive 2001/83/EC

Marketing authorization (Article 6)

1. No medicinal product may be placed on the market of a Member State unless a marketing authorization has been issued by the competent authorities of that Member State in accordance with this Directive or an authorization has been granted in accordance with Regulation (EEC) No 2309/93.

German Medicinal Products Act (Arzneimittelgesetz, last amendment July 2009)

- Scope of Directive 2001/83 fully implemented but:
- § 21:
  (2) A marketing authorization shall not be required for medicinal products which

  … 1g. are manufactured for individual persons on prescription as therapy allergens…

Named Patient Products - Background

Types of Named Patient Products

- Allergen extracts manufactured from allergenic source material originating from the environment of an individual patient.
- Allergen extracts prepared from commercial source material or intermediate products (bulks) on the basis of a prescription for an individual patient.
- Allergen extract mixtures prepared from industrially manufactured intermediate products (bulks) on the basis of a prescription for an individual patient.

May S, Haustein D, Bundesgesundheitsbl. 2001, 44:719-723

Rationale of Named Patient Products

- **Offer SIT as therapeutic option to those patients, whose allergies can not be treated with authorized products because**

  - the patients suffer from “rare” allergies;
  - the patients are poly-sensitized to a certain combination of allergens.

Regulatory requirements for NPPs

- Manufacturing license (§13 Sect. 1 AMG) (authorities of federal states in consultation with PEI).
- Production according to good manufacturing practice audited.

NPPs – differences to authorized products

- No independent evaluation of quality, efficacy, and safety required.
- No demand for manufacturer to notify adverse events.
- No independent risk-benefit analysis possible.

Bypassing marketing authorization?

- According to product lists of manufacturers 26 single allergen extracts from birch pollen are marketed in Germany.
- Marketing authorizations have been granted for six.
- Prevalence of birch pollen allergy is estimated at 10%.

Initiative of German Federal Ministry of Health

„Verordnung über die Ausdehnung der Vorschriften über die Zulassung der Arzneimittel auf Therapieallergene, die für einzelne Personen auf Grund einer Rezeptur hergestellt werden, sowie über Verfahrensregelungen der staatlichen Chargenprüfung“

(Therapieallergene-Verordnung)

Regulation for Therapy Allergens

Regulation for Therapy Allergens – Content

- NPPs produced from industrially manufactured bulks are subjected to marketing authorization.
- Industrially manufactured bulks used for preparation of NPPs are subjected to batch release by the Paul-Ehrlich-Institut.
- List of allergens concerned given in *Appendix*

List of Allergens – Content

Appendix

- Grass species of the Poaceae family except Poa mays
- Betula sp. (birch)
- Alnus sp. (alder)
- Corylus sp. (hazel)
- Dermatophagoides sp. (dust mites)
- Bee venom
- Wasp venom

Mixtures containing one or more allergens from the list are subjected to marketing authorization.

Transition Periods according to the New Regulation and Relevant Dates

- Notification of product to PEI within 6 months.
  Done on the 14th of May 2009
- Application for marketing authorization by
  December 1st, 2010

- Prolongation of transition period of up to 7 years possible, if justified.

Paediatric Investigation Plans (PIPs)

- Authorization of new medicines requires a PIP approved by PDCO (Regulation (EC) No 1901/2006).

- Without approved PIP no marketing authorization for adults will be granted.

PIPs related to German Regulation for Therapy Allergens

- 178 applications for marketing authorization have been announced
- Approved PIPs have to be submitted with the application (December 1st 2010)
- Concept of „Homologous Groups“ may reduce the number of necessary PIPs to approx. 80
- To reduce the expenditure of work during the evaluation phase an EMEA/PDCO Draft Standard PIP for Allergen Products for SIT was developed.

European Medicines Agency
Pre-Authorisation Evaluation of Medicines for Human Use

London, 20 November 2008
Doc. Ref. CHMP/EWP/18504/2006

COMMITTEE FOR MEDICINAL PRODUCTS FOR HUMAN USE (CHMP)

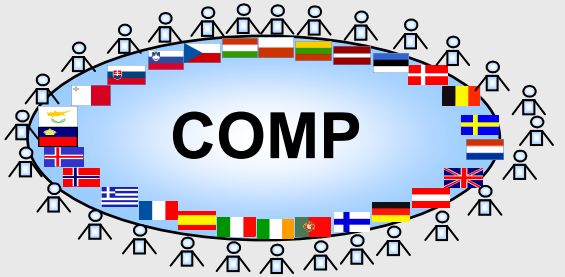
GUIDELINE ON THE CLINICAL DEVELOPMENT OF PRODUCTS FOR SPECIFIC IMMUNOTHERAPY FOR THE TREATMENT OF ALLERGIC DISEASES

DRAFT AGREED BY EFFICACY WORKING PARTY	April 2007
ADOPTION BY CHMP FOR RELEASE FOR CONSULTATION	24 May 2007
END OF CONSULTATION (DEADLINE FOR COMMENTS)	30 November 2007
AGREED BY EWP	15 October 2008
ADOPTION BY CHMP	20 November 2008
DATE FOR COMING INTO EFFECT	01 June 2009

The EMEA's committees

Committee for
Advanced Therapies

Committee for
Medicinal Products for Human Use



Committee for
Orphan Medicinal Products

Paediatric Committee

Committee on
Herbal Medicinal Products

Committee for
Medicinal Products for Veterinary Use