

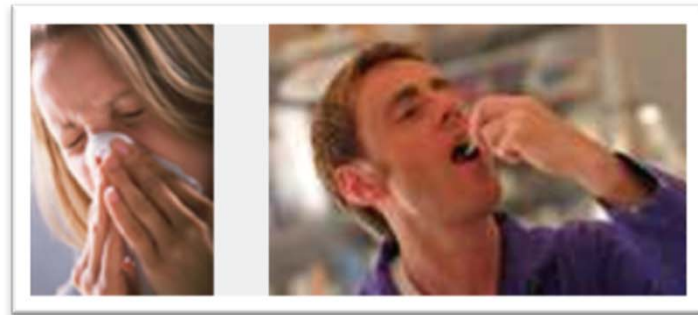


**IPA**

Institut für Prävention und Arbeitsmedizin  
der Deutschen Gesetzlichen Unfallversicherung  
Institut der Ruhr-Universität Bochum

# Occupational respiratory allergy and asthma - sensitizers and disease

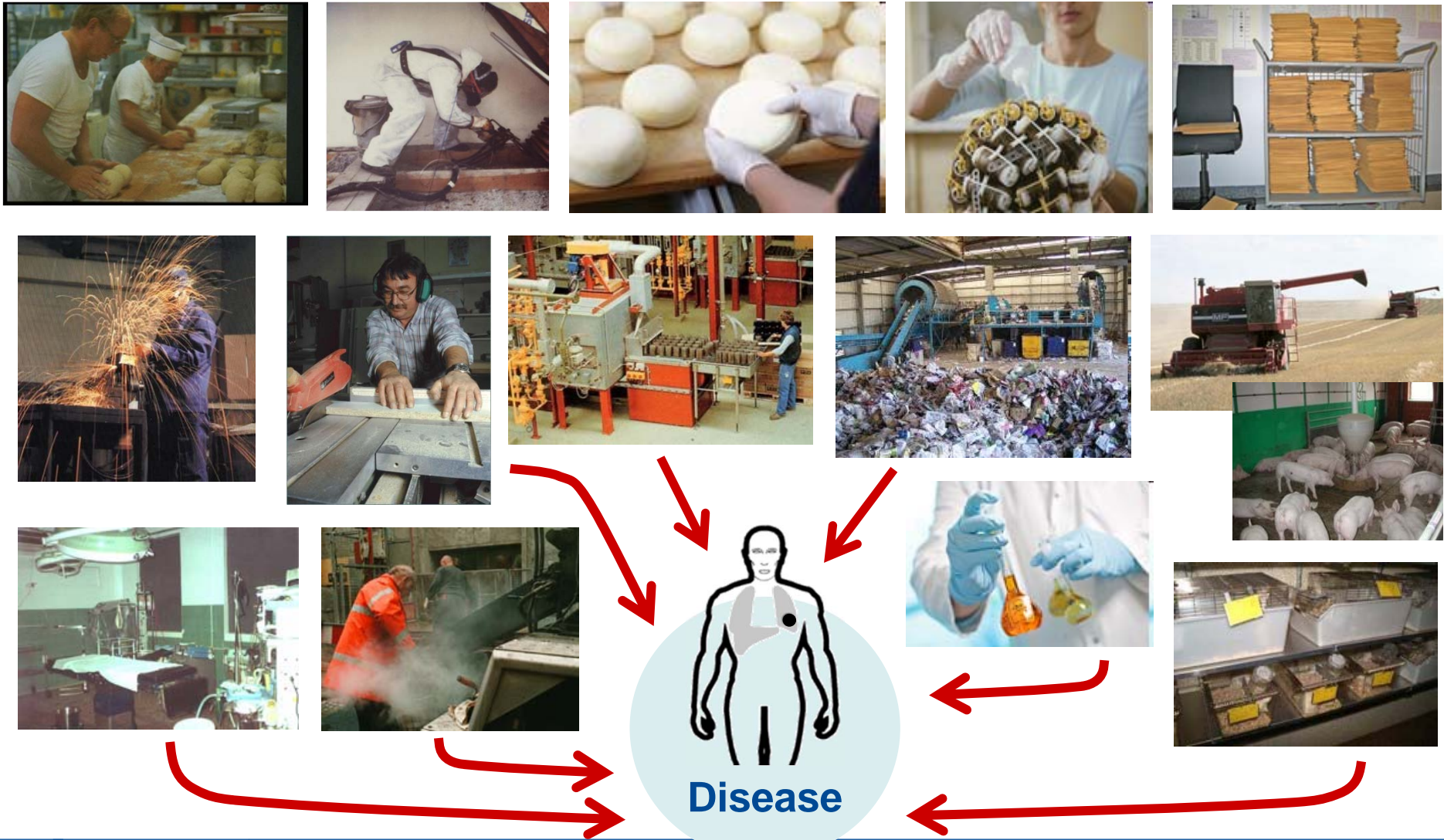
**Monika Raulf**

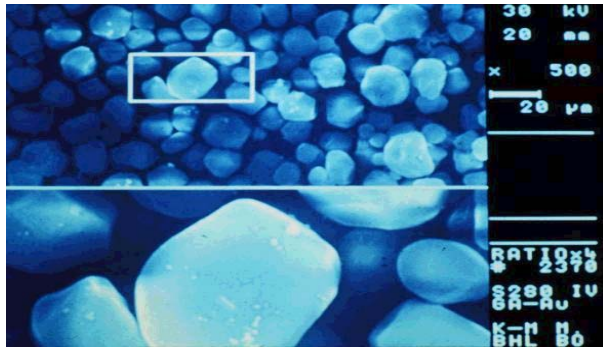


INRS / ISSA Symposium 2016;  
Paris, June 1.-3., 2016

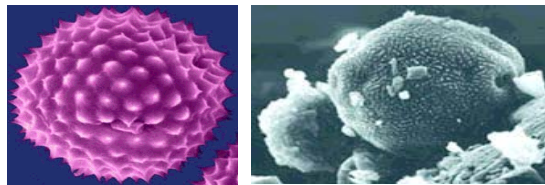
RUHR  
UNIVERSITÄT  
BOCHUM

**RUB**





Sr z ghur #olw {#j cryhv

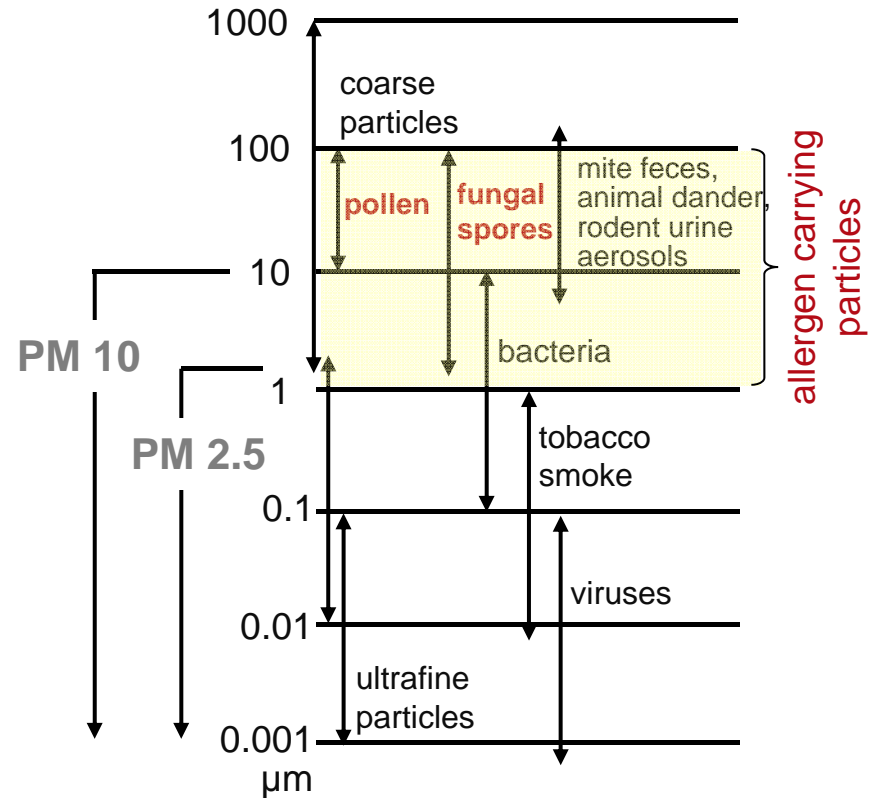


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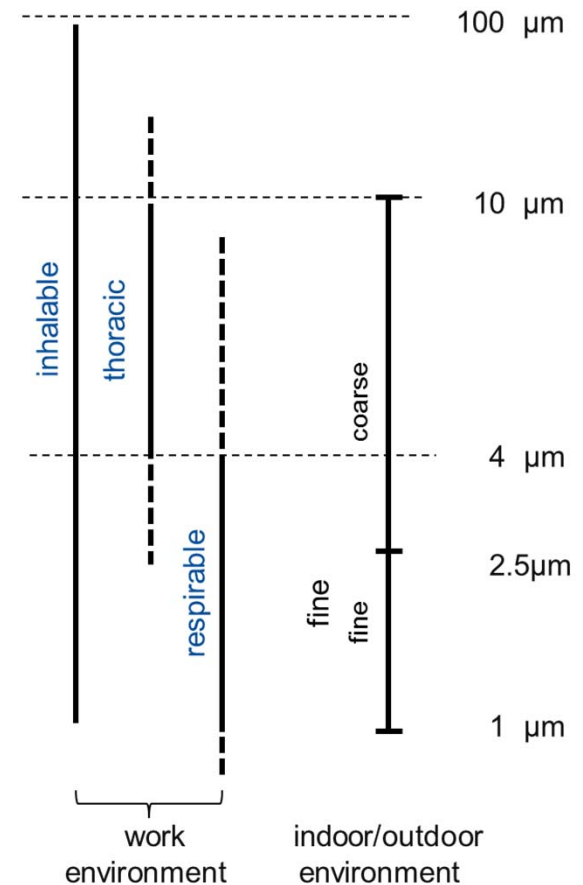
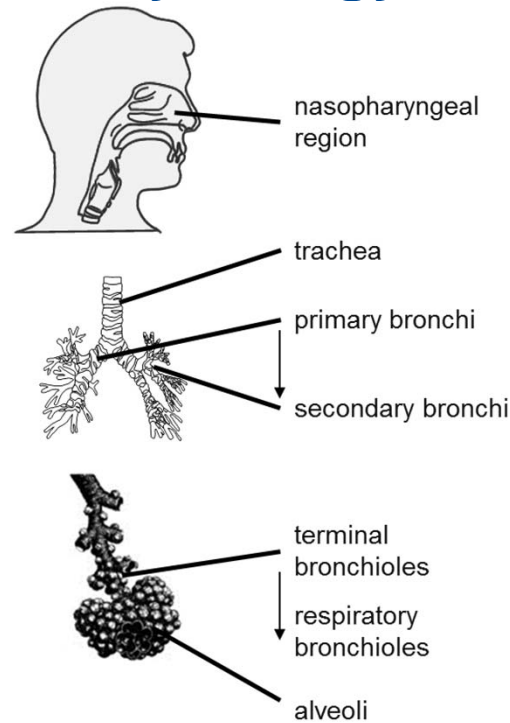
Z khdw #arxu

Most airborne allergens are components of, or carried by particles of 1 - 100 μm diameter.

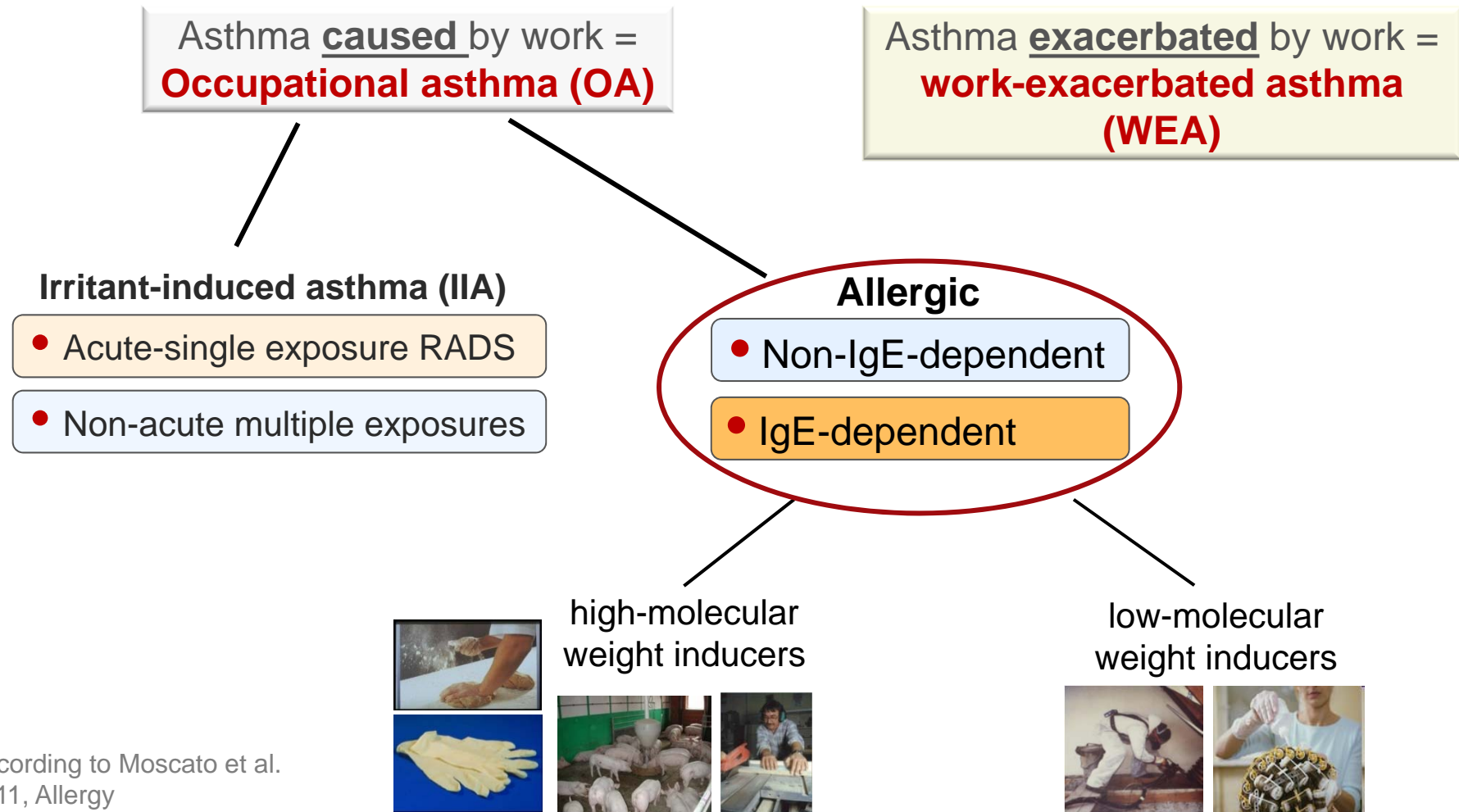




# The contact between the respiratory organ and the air containing the allergens is the key factor for the development of respiratory allergy



## Work-related asthma (WRA) phenotypes

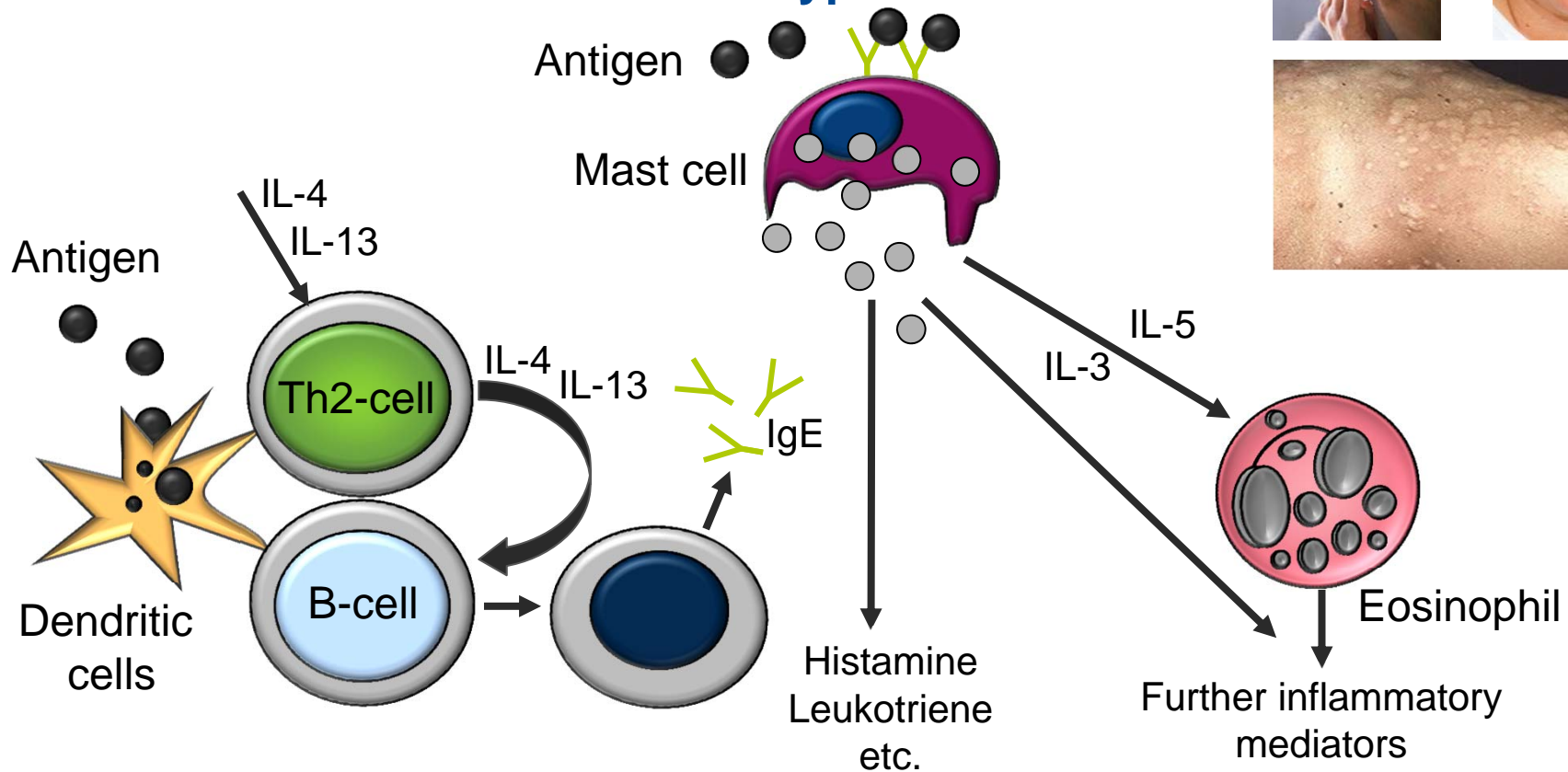


According to Moscato et al. 2011, Allergy

# Phases of the allergic reaction – IgE-mediated type I-reaction

## Sensitization

## Immediate type-reaction



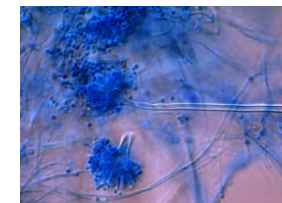
## Plant-derived agents

- Henna dye
- Natural rubber latex
- Plant enzymes (papain, bromelain)
- Psyllium
- Vegetable gums (arabic, guar, tragacanth)
- Wheat flour
- Wood dust (Obeche, locust etc.)



## Animal and insect-derived agents

- Bird proteins (feathers, serum)
- Crustaceans: snow crab, prawn
- Eggs (chicken)
- Insects
- Mammalian proteins in hair, dander, urine
- Pharmaceutical enzymes, e.g. pancrease
- Sea squirt (oyster parasite)



## Bacterial and fungal-derived agents

- *Bacillus subtilis*-derived enzymes
- *Penicillium caseii*
- Thermophilic molds



- **Persulfates** (in hair bleaching solutions)

- **Metals and metal salts**

Chromium

Cobalt

Nickel sulfate

Platinum



- **Organic chemicals**

Acid anhydrides (prototype: trimellitic anhydride)

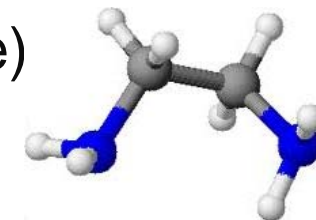
Acrylates, methacrylate (artificial nail glue)

Ethylendiamine

Paraphenyldiamine in hair dye

Polyisocyanates (prototype: toluene diisocyanate)

Pharmaceuticals (antibodies, cimetidine)





## Workplaces with allergen exposure

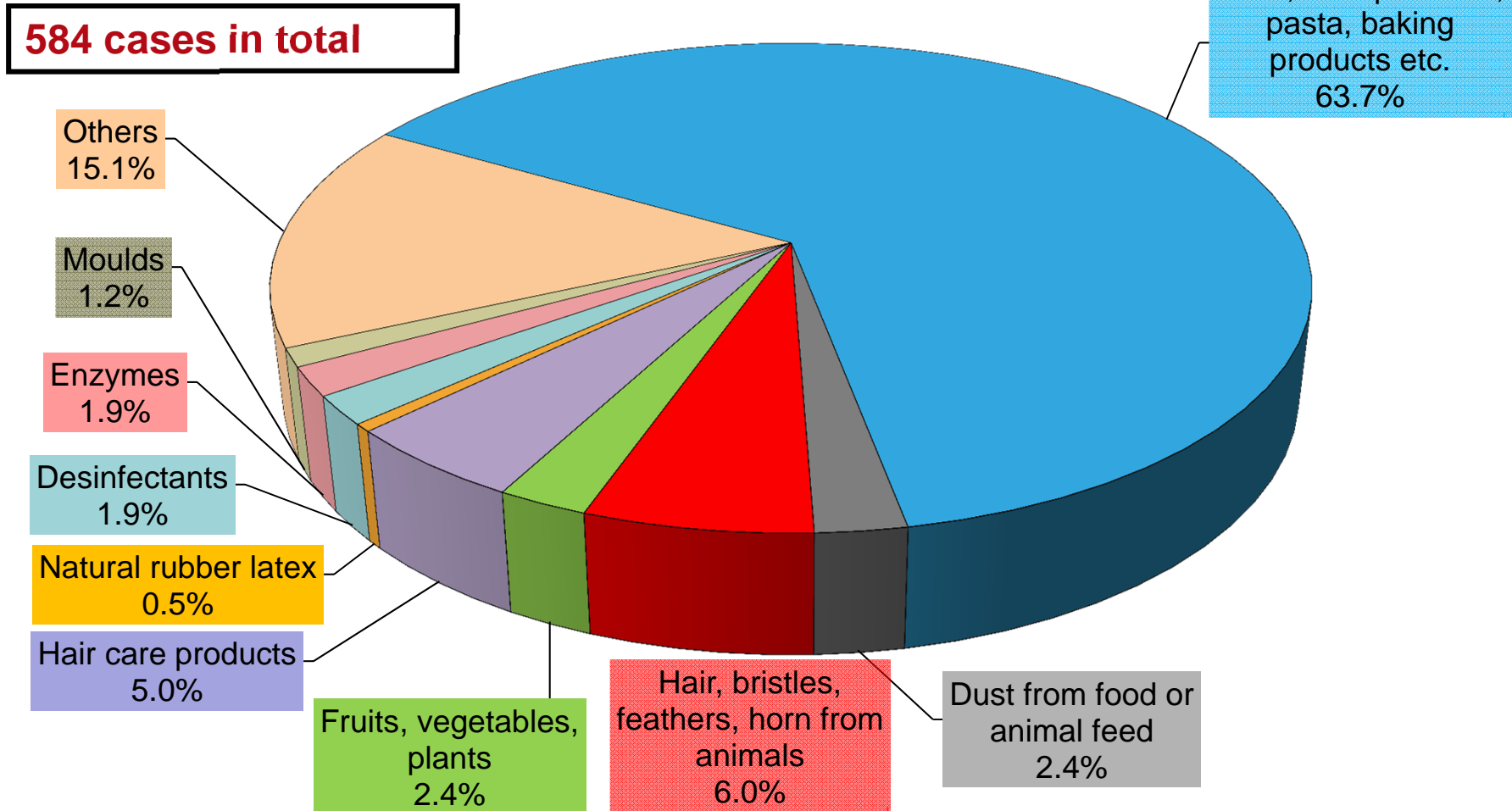
Trade/industry	Allergen sources
Agriculture	Cow hair, pollen, storage mites
Bakeries, mills	Wheat flour, rye flour, soya flour, $\alpha$ -amylase, xylanase, storage mites, insects
Fish processing	Fish allergens
Animal feed	Soya, phytase
Pharmaceutical industry	<i>Gummi arabicum</i> , enzymes
Laboratory animal care	Mouse allergens, rat allergens
Health care	Natural rubber latex
Detergent production	Enzymes: Proteases, cellulases, lipases, amylases
Wood processing	Wood dust
Composting plants	Molds, bacteria
Many others	House dust mites, molds, ubiquitous indoor allergens

# Occupational allergy

BK-No.	Skin- and respiratory diseases	Austria § 177; ASVG-list
1315	Isocyanate initiated diseases (chemical compounds used for the production of synthetics)	—
4201	Hypersensitivity pneumonitis (inflammatory changes of the pulmonary alveoli)	43
4301	obstructive respiratory diseases (incl. rhinopathy) caused by allergenic substances	30
5101	serious or repeated skin diseases	19
[5101/4301]	Allergy induced anaphylactic responses after latex sensitization	53



## Frequency of causative triggers for occupational asthma/rhinitis in Germany [BK 4301]



## Relevance of baker's asthma

- **One of the oldest recognized occupational diseases**  
 (First described by Bernardino Ramazzini (1633-1714) in “De Morbis artificum diatriba”)
- One of the most common forms of occupational asthma Examples:



in France: Incidence of baker's asthma among young bakers ranges from 0.3 to 2.4 cases per 1000 person-years [Remen et al. 2010]

in Norway: Incidence of occupational asthma among male bakers 2.4 and female 1 case per 1000 person-years [Leira et al. 2005]

in Germany: Incidence of occupational asthma among bakers ~2 cases per 1000 person-years [BGN, personal communication]

**~ 10 % of all bakers develop asthma during their working life period**

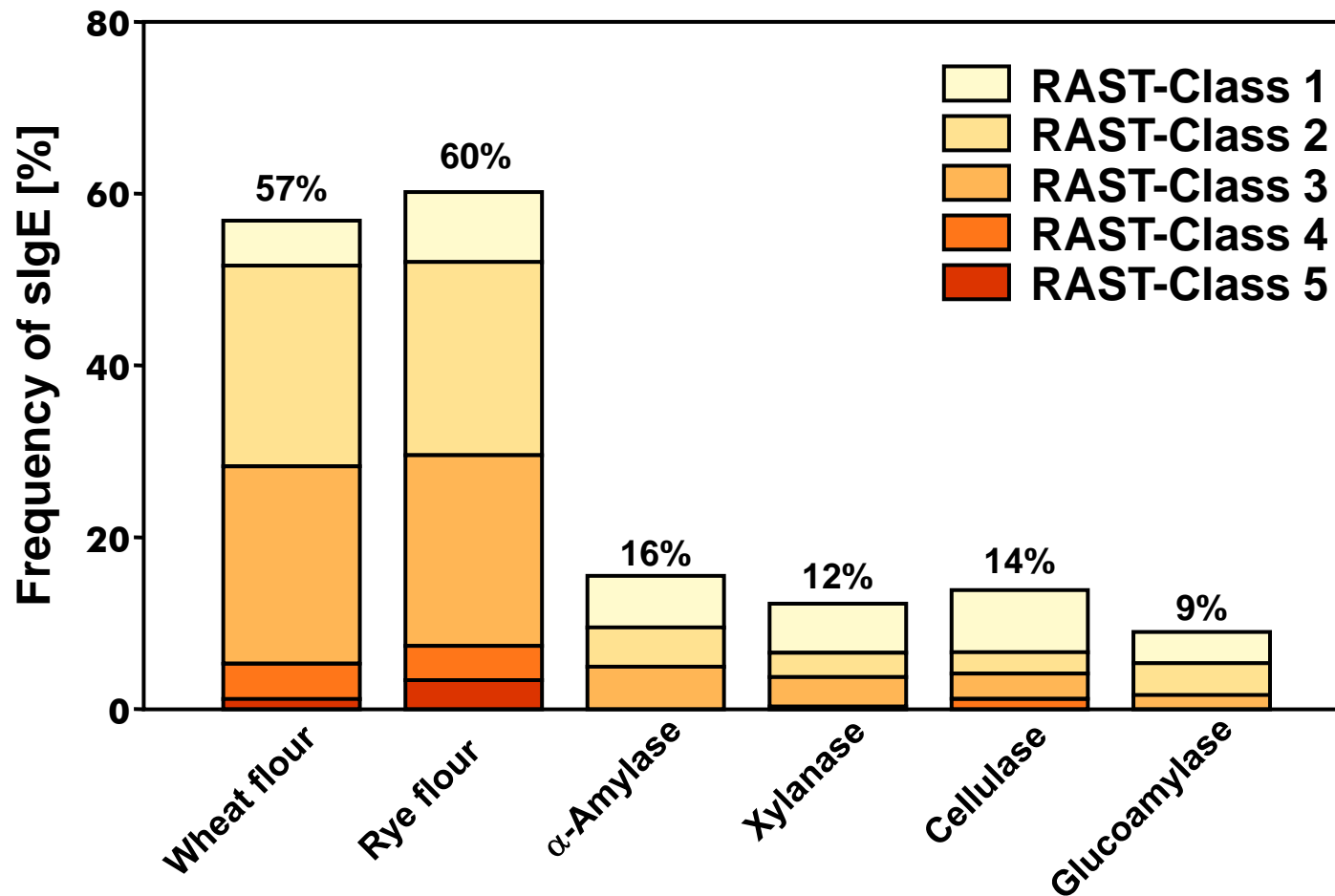


## Potential allergens in bakeries

- **Wheat flour**
- **Rye flour**
- Further cereal flours (e.g. barley)
- Enzymes ( $\alpha$ -amylase, cellulase etc.)
- Soy, Lupine flour
- Storage mites
- Flour pests (including flour worm, flour moth)
- Moulds
- Egg yolk and white, sesame seed, nuts, poppy etc.



## Specific IgE in 244 bakers with work-related complaints



# Enzymes used in bakeries

## $\alpha$ -Amylase

starch degradation  $\Rightarrow$  yeast fermentation,  $\text{CO}_2 \uparrow \Rightarrow$  volume  $\uparrow$ ,  
 dough processing, browning, crispness  $\uparrow$

## Glucoamylase

## Xylanase

## Cellulase



Often produced in *Aspergillus oryzae* and *A. niger*

## Exposure Prevention: Granulation of enzymes ( $\alpha$ -amylase since 90ies, Baking granulate Novo)



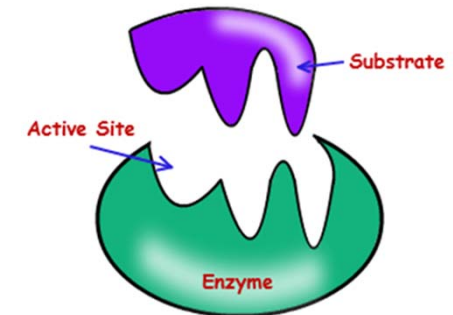
- ⇒ Reduces exposure by inhalation of enzyme dust
- ⇒ Aim: no sensitization to enzymes
- ⇒ Aim: no allergies to enzymes

Partikels instead of 5 - 50  $\mu\text{m}$   
200 - 400  $\mu\text{m}$



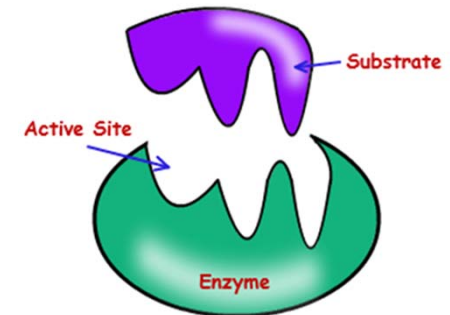
## Enzymes causing allergies - in food industry

Alpha-amylase Glucoamylase	<ul style="list-style-type: none"> <li>• <i>Aspergillus oryzae</i></li> <li>• <i>Aspergillus niger</i></li> </ul>
Cellulases Hemicellulases: Xylanases	<ul style="list-style-type: none"> <li>• <i>Aspergillus niger</i></li> <li>• <i>Trichoderma reesei</i></li> <li>• <i>Bacillus subtilis</i></li> </ul>
Papain, Bromelain	<ul style="list-style-type: none"> <li>• Papaya <i>Carica papaya</i></li> <li>• Pineapple <i>Ananas comosus</i></li> </ul>
Phytase	<ul style="list-style-type: none"> <li>• <i>Aspergillus niger</i></li> <li>• <i>Trichoderma reesei</i></li> </ul>
Pepsin, Chymosin, microbial Rennet, Pancreatin	<ul style="list-style-type: none"> <li>• Cow <i>Bos domesticus</i></li> <li>• Pig <i>Sus scrofa</i></li> <li>• <i>Cryphonectria, Rhizomucor</i></li> </ul>



## Enzymes causing allergies - in detergent industry

<b>Proteases:</b> Maxatase Alcalase Savinase	<ul style="list-style-type: none"> <li>• <i>Bacillus subtilis</i></li> </ul>
<b>Termamyl</b> ( $\alpha$ -amylase)	<ul style="list-style-type: none"> <li>• <i>Bacillus subtilis</i></li> </ul>
<b>Carezyme</b> (Cellulase)	<ul style="list-style-type: none"> <li>• <i>Bacillus subtilis</i></li> </ul>



# Exposure to animals

Private area

Occupational setting



## Allergy to laboratory animals

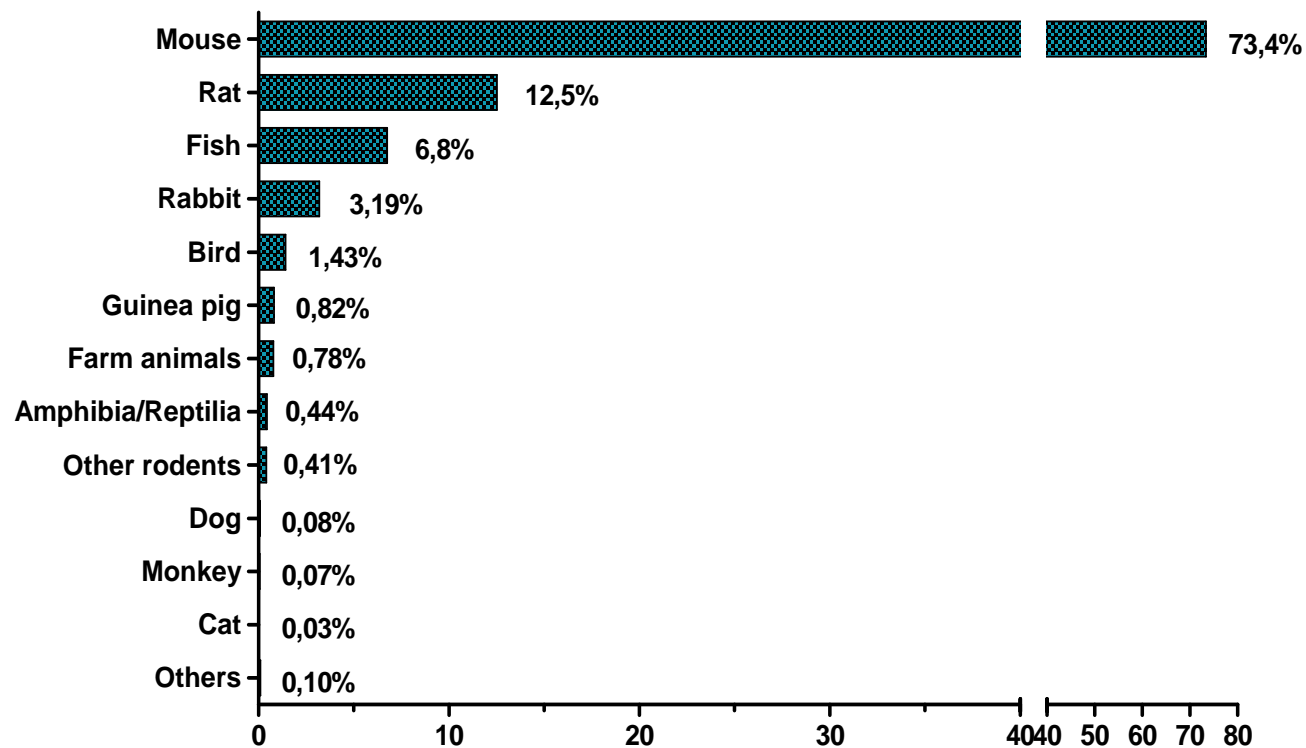
- Predominantly a typical occupational respiratory allergy
- First cases were described in the 50s
  - Chafee FH: **Bronchial asthma due to rat and mouse hair; report of two cases.** J Allergy 1952;
  - Sorrell AH and Gottesman J: **Mouse allergy: case report.** Ann Allergy 1957)
- Epidemiological cross-sectional studies were performed during the 1970s and 1980s (Bush RK and Stave GM: **Laboratory animal allergy: An update.** ILAR J 2003)
  - pharmaceutical industry
  - Universities and research institutes
  - commercial laboratory animal breeding
  - medical and veterinary universities





# Laboratory animals

2 997 153 animals for scientific purposes in 2013



Data from Federal Ministry of Food and Agriculture BMEL




## Allergy to laboratory animals



- Prevalence rate between 11 and 44% (depending on the study)
- Affected people: keeper, technical assistant, scientists, veterinarians
- Species: **mouse**, **rat**, guinea pig, rabbit, hamster, dog, cat, primates
- Symptoms:
  - allergic rhinitis and conjunctivitis (up to 80% )
  - skin reactions (ca. 40%)
  - asthma (up to 22 %)
  - anaphylaxis (very rare, e.g. by bites)
- Latency between begin of exposure and start of the difficulties is 3 years on average
- Risk depends strongly on the exposure intensity



## Airborne features

- Animal allergens exhibit a tendency, to bind on small particles  in the range of  $<1 \mu\text{m}$  to  $20 \mu\text{m}$
- Good „hovering properties“  the allergens stay in the air for a longer time and can easier be inhaled
- Binding on clothes and hair of exposed persons  easy transfer to initially not charged areas („unexpected contamination“)

## The determination of allergen exposure is necessary to

- a) Detect the association between **exposure** and **work-related allergic diseases**,
- b) Establish and also to monitor suitable measures for **reduction** or **avoidance** of **allergen exposure**.

## Dust exposure is not the same as allergen exposure

Filling of the purified cages with bedding

High dust exposure

No allergen exposure



Emptying of contaminated animal cages

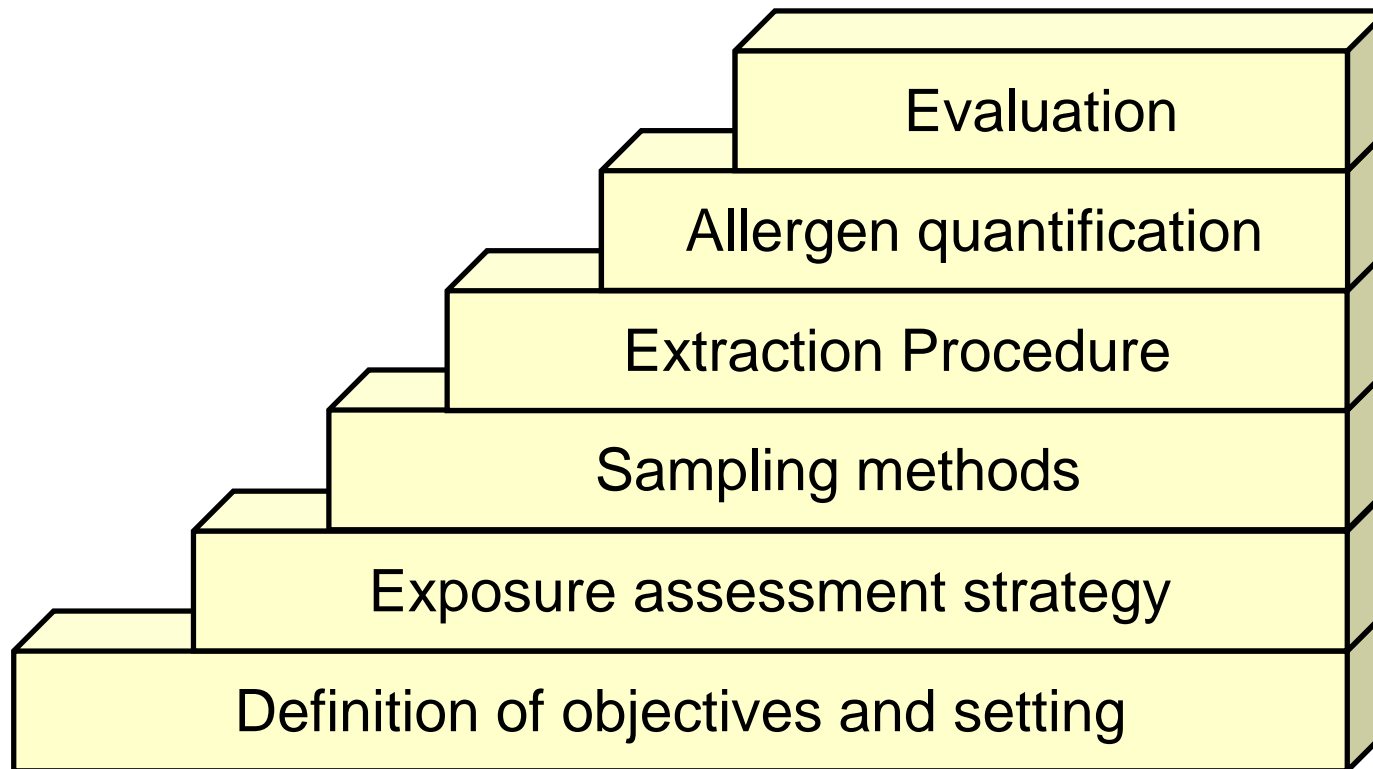
High dust exposure

High allergen exposure



It is a need to quantify the allergens

## Aeroallergen monitoring is a stepwise process



Raulf et al.: Monitoring of occupational and environmental aeroallergens-EAACI Position Paper. Allergy 2014; 69: 1280-1299



## Air sampling (some common sampler)



**Gravikon VC 25**



**Rotorod/  
Impactor; >10 µm**



**GSP/filter sampling**



## Reservoir dust sampling



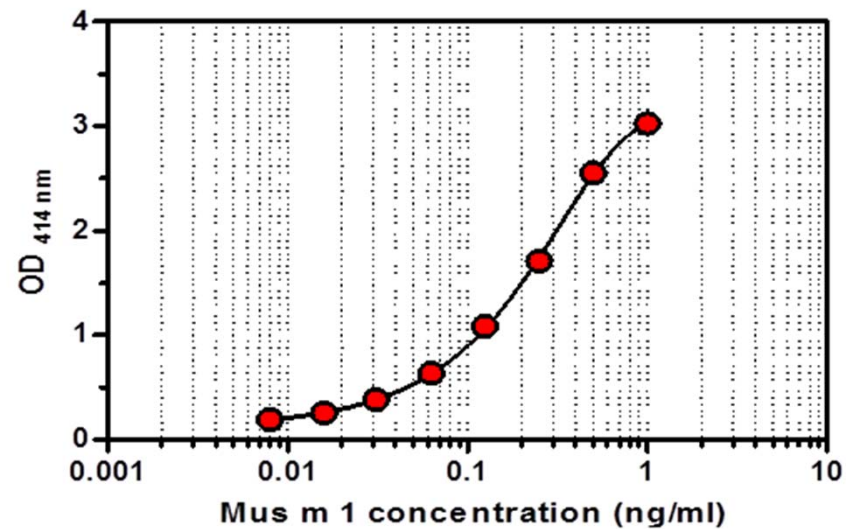
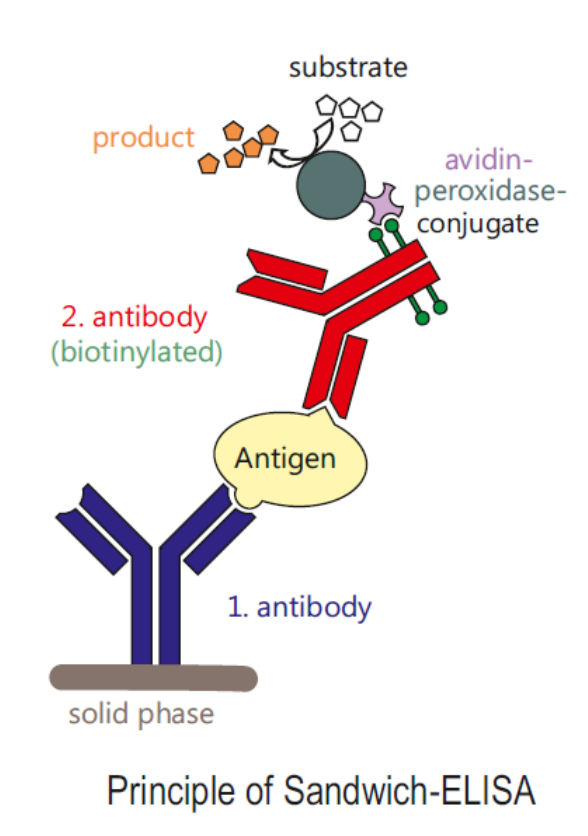
**Vacuum cleaning of a surface**

## Settled dust sampling

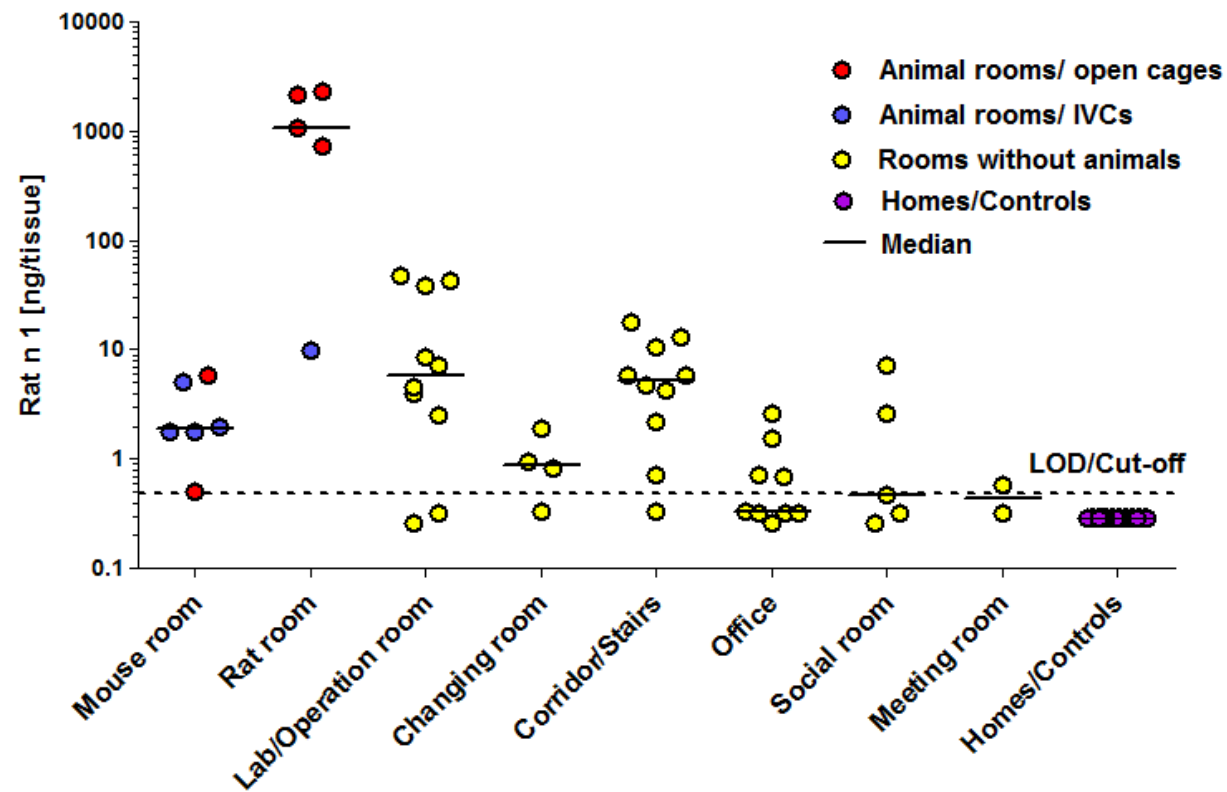


**Electrostatic dust collector (EDC)**

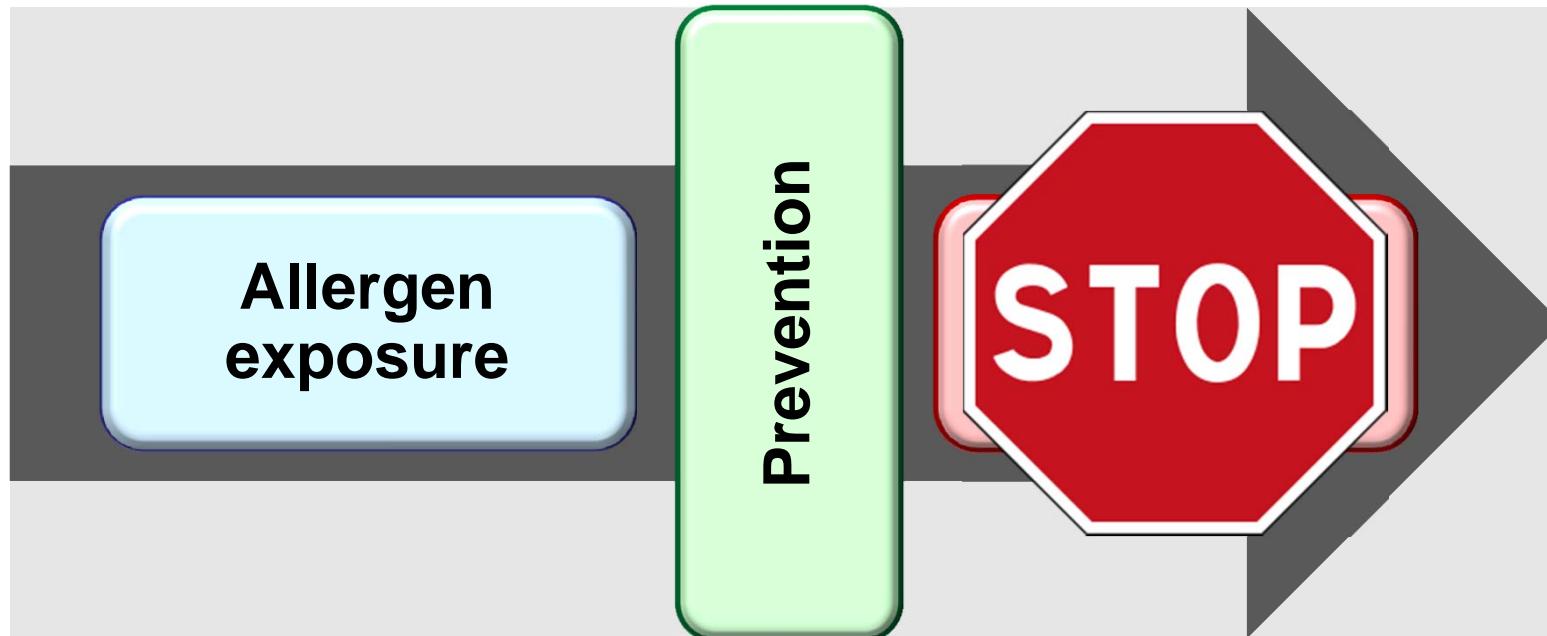
# Allergen analysis: Sandwich enzyme immunoassay (EIA)



# EDC-sampler, Rat allergens



## Aim:



## Prevention strategies

Allergy **66** (2011) 1164–1173

### **EAACI Position Paper: Prevention of work-related respiratory allergies among pre-apprentices or apprentices and young workers**

G. Moscato<sup>1</sup>, G. Pala<sup>1</sup>, M. A. Boillat<sup>2</sup>, I. Folletti<sup>3</sup>, R. Gerth van Wijk<sup>4</sup>, D. Olgiati-Des Gouttes<sup>5</sup>, L. Perfetti<sup>1</sup>, S. Quirce<sup>6,7</sup>, A. Siracusa<sup>3</sup>, J. Walusiak-Skorupa<sup>8</sup> & S. M. Tarlo<sup>9,10</sup>

Eur Respir J 2012; 39: 529-545

### **Guidelines for the management of work-related asthma.**

Baur X, Sigsgaard T, Aasen TB, Burge PS, Heederik D, Henneberger P, Maestrelli P, Rooyackers J, Schlünssen V, Vandenplas O, Wilken D; on behalf of the ERS Task Force on the Management of Work-related Asthma.

publiziert bei:



<b>AWMF-Register Nr.</b>	<b>002/025</b>	<b>Klasse:</b>	<b>S1</b>
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Leitlinie der Dt. Ges. f. Arbeitsmedizin und Umweltmedizin (DGAUM)

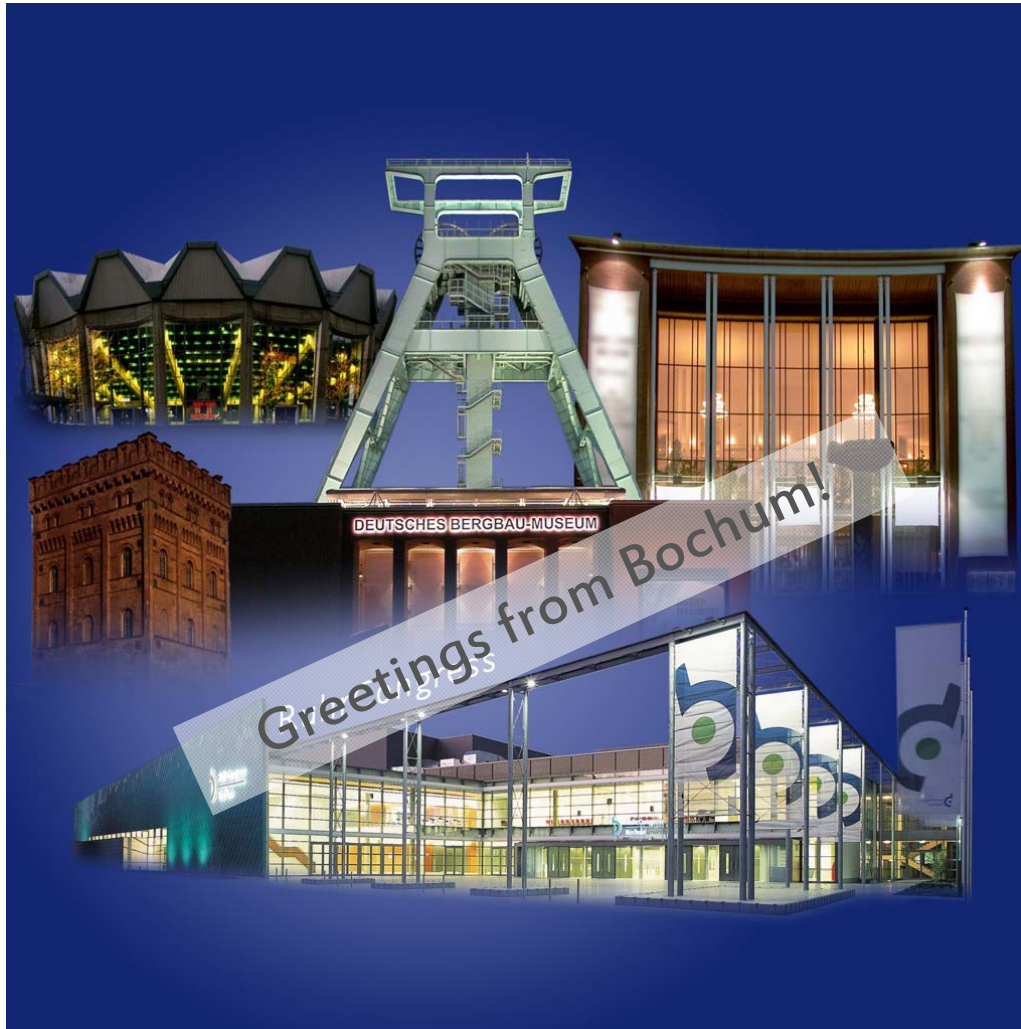
### **Prävention arbeitsbedingter obstruktiver Atemwegserkrankungen**



## Recommendation for prevention and management

- Screening in high risk areas.
- For job starter the incidence of work-related symptoms is highest in the first 2-3 years after begin of exposure (baseline-measurements recommended).
- Especially for HMW-allergens atopy is a risk factor.
- Persistent exposure at symptomatic is also a risk factor.
- Reduction of exposure cannot be routinely recommended as an alternative to cessation of exposure in the management of occupational asthma. (meta-analysis, Vandenplas et al., Eur Respir J 2011).
- Sector specific special programs, recommendations and guidelines should be used or realized.

- ✓ Occupational allergy (OA) is the result of an interaction between multiple genetic, environmental and behavioral influences.
- ✓ More than 400 agents are identified as sensitizers of occupational asthma, but only very few are characterized.
- ✓ Baker's asthma is one of the most frequently occurring forms of occupational asthma caused by workplace-related inhalation of cereal flour mainly wheat.
- ✓ Diagnosing OA is a complex undertaking; its primary goal is to demonstrate a causal relation between exposure to a specific agent encountered at work, allergic responses and symptoms. .
- ✓ Environmental control of exposure is crucial for prevention, an every effort should be made to keep the workplace without an exposure hazard.
- ✓ Immunological methods are helpful to quantify allergens



Bochum, Germany

Thank you for  
your  
attention!!