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Occupational Airway Sensitizers: An Overview on The Respective Literature

V. van Kampen, PhD, R. Merget, MD, and X. Baur, MD*

Background *Worldwide, there is rigorous scientific activity concerning the further development of work safety regulations involving airway-sensitizing substances. Technical directives on hazardous substances are enforced in several countries and are being continuously updated. The European Union has established a code for several occupational substances, now labeled R 42 ("may cause sensitization by inhalation").*
Methods *We present an overview of the literature dealing with allergic occupational asthma. The literature was selected according to criteria of study design and diagnostic test methods. Approximately 300 publications were reviewed including both epidemiological studies and individual case reports.*
Results *Airway sensitizers are systematically arranged and separately listed according to chemicals and their origin from animals, plants, and microorganisms. The clinical data as well as threshold limit values (TLV) and R 42 labeling of 250 airway-sensitizing substances are presented.*
Conclusions *The most common sensitizing substances causing occupational asthma were dust of cereal flours, enzymes, natural rubber latex, laboratory animals as well as low molecular substances such as isocyanates and acid anhydrides.* Am. J. Ind. Med. 38:164–218, 2000. *© 2000 Wiley-Liss, Inc.*

KEY WORDS: airway sensitizers; occupational allergens; occupational asthma; epidemiological studies; case reports; clinical data

INTRODUCTION

Occupational asthma has become one of the most common occupational diseases in many industrialized countries [Chan-Yeung and Malo, 1994]. Many high-molecular-weight occupational agents and additionally some low-molecular-weight compounds induce asthma or rhinitis through an IgE-mediated mechanism. The directives for airway sensitizers are being continuously updated, and the European Union has labeled several substances with the R-phrase R 42 ("may cause sensitization by inhalation") [Ordinance on Hazardous Substances, 1996].

The medical literature was searched for all identified airway-sensitizing occupational agents. In general, the term "airway sensitizers" refers to substances which cause bronchial asthma in human beings. We have included rhinitis, conjunctivitis and/or other diseases induced by airborne substances in the workplace if immunological mechanisms (in contrast to irritative mechanisms) are ensured or are at least probable.

It should be mentioned that the information in Table I deviates from the German *MAK and BAT value list* (**M**aximale **A**rbeitsplatz**k**onzentration und **B**iologische **A**rbeitsstoff**t**oleranzwerte—Maximum Concentrations and Biological Tolerance Values at the Workplace)[1] elaborated

Research Institute for Occupational Medicine (BGFA), Institute at the Ruhr-University of Bochum, Bochum, Germany
*Correspondence to: Xaver Baur, MD, BGFA, Bürkle-de-la-Camp-Platz 1, 44789 Bochum, Germany. E-mail: kampen@bgfa.ruhr-uni-bochum.de

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[1] The MAK value is defined as the maximum concentration of a chemical substance in the workplace air which generally does not have known adverse effects on the health of the employee nor cause unreasonable annoyance even when the person is repeatedly exposed during long periods, given a 40-hour working week. The BAT value is defined as the maximum permissible quantity of a chemical substance or its metabolites or the maximum permissible deviation from the norm of biological parameters induced by the substances in exposed humans.

by the Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area of the ''Deutsche Forschungsgemeinschaft.'' In contrast to the MAK evaluations, Table I also considers agents whose airway-sensitizing potential was established in single cases, and thus is much more comprehensive. It was beyond the scope of this study to evaluate frequency of reported cases and frequency of exposure in workplaces. Further, the relative risk of individual substances, i.e., the frequency of adverse effects in relation to cumulated doses, was not estimated because concrete figures on the number of exposed subjects and exposure degree and duration are not available.

METHODS

Literature Selection and Evaluation

Abstracts were selected from the MEDLINE databank which contains about 9 million medical citations. The keywords ''occupational,'' ''asthma'' as well as ''allergy'' were used to search.

The criteria used for article selection were: (1) Cross-sectional or longitudinal studies completed using established epidemiological methods. (2) Sequential investigations on a large number of subjects, preferably including controls. (3) If epidemiological studies on the respective agent were not available case reports were chosen which included comprehensive diagnostic testing. If several studies were available for a given substance, we chose up to three publications which best corresponded to the above criteria and clearly verified the sensitizing potential of the substance. As specific bronchial challenge tests are considered the gold standard, studies with these data were preferred.

About 300 original publications, the Ordinance on Hazardous Substances (1996), and the *MAK and BAT value list* were the major sources of Table I. All R 42 labeled substances (EU category) were included. The label R 42 indicates that these substances ''may cause sensitization by inhalation.'' Frequently, R 42 is combined with R 43 (''may cause sensitization by skin contact''). These cases are indicated in the table. In addition, substances without the R 42 label are included which, according to international publications, have proven to be sensitizing.

Subjective influences due to literature selection cannot be excluded. Our aim was not to get a comprehensive list of all published studies or to summarize information from several studies but to denote airway sensitizers which, according to peer-reviewed publications (exceptions are labeled in Table I), have proven to be sensitizing.

Arrangement of Substances

Airway sensitizers are systematically arranged in four general categories: chemicals, and their origin in animals, plants or microorganisms. The authors endeavored to group the multitude of chemicals. According to corresponding botanical and zoological systems, substances from these origins were arranged. Those clearly originating from plants (e.g., abietic acid, 3-carene) or animals (casein, egg protein) were assigned accordingly. Enzymes were grouped independently of their original organisms while indicating their origin in brackets.

Other Data Presented

USA TLV-TWA. The USA TLV-TWA (threshold limit value-time weighted average) refers to the concentration (weight and volume proportion) of a hazardous substance in workplace atmospheres. If not otherwise indicated, TLV-TWA values are shift mean values of an 8-hour exposure/day and of an average 40-hour working period/week.

European label (EU label). This column shows whether the respective substance is classified as airway-sensitizing pertaining to category R 42 or R 42/43.

German TLV-TWA. The German TLVs-TWAs in this column are published in the Technical Directive on Hazardous Substances 900 (TRGS 900) ''Limit values in workplace atmospheres.'' In 1996 and 1997, 155 foreign (international) exposure limit values were incorporated into the TRGS 900. Nonstatutory categorizations that deviate from mentioned limit values are indicated in brackets; these MAK values are health-based and recommended. So far, they have not been included in the TRGS 900.

Sa or Sah (atemwegssensibilisierender Stoff or atemwegs- und hautsensibilisierender Stoff). ''Sa'' is used in the *MAK and BAT value list* to designate substances which can cause allergic symptoms of the airway and also of the conjunctiva (substances causing airway sensitization). Substances which have sensitizing effects on the airway and the skin are designated with ''Sah.''

Symptoms: This column shows work-related symptoms reported by the exposed workers (usually in a questionnaire). If indicated in published longitudinal or cross-sectional studies, prevalences, and incidences of individual symptoms were incorporated. If not differentiated in detail, the indicated total prevalence refers to the total of work-related symptoms.

Methods.

LFT. Lung function tests were performed.

Skin prick test (SPT). It was noted if skin prick tests with the respective substance were performed and how many subjects showed a reaction. If other types of skin test (patch, scratch or intradermal) were performed, it is indicated in the table.

Specific challenge. If specific challenge tests with the respective substance were performed, the number of subjects who showed a positive response is indicated. If not otherwise indicated, bronchial challenge was performed. A decline of FEV1 $\geq$ 20% was regarded as positive.

Antibodies. It was remarked if allergen-specific antibodies were measured in the serum and, if yes, which antibody classes were investigated. In case of positive findings, the percentage of patients with antibodies is indicated.

RESULTS AND DISCUSSION

The clinical data of about 250 occupational airway sensitizers were evaluated on the basis of approximately 300 scientific publications. Sensitizers were classified into four groups: chemicals and agents originating from animals, plants or microorganisms. Within these groups the substances (in alphabetical order) were arranged in subgroups such as isocyanates, anhydrides or amines in the group of chemicals and mites, insects or fish (Table I).

Not only pure substances but also product mixtures used in workplaces were considered. In case of cyanoacrylates for instance, clinical tests (bronchial challenge tests etc.) were generally performed with adhesives which contained components of other materials up to 5%. Due to the probability that the symptoms of subjects were induced by cyanoacrylates and not by additives, these agents were also included in the table with a corresponding note.

Instead of itemizing each individual substance, groups of substances with the same effect were listed (e.g., chloroplatinates, chromates). Wood for instance was even evaluated when only the genus (e.g., oak) and not the species (e.g., silver oak) had been reported. Thus, our procedure differs from that of the *MAK Commission* whose list almost uniformly evaluates individual substances. Even if identical mechanisms are assumed and/or the European labeling R 42 of a whole group exists, we did not include structural analogues in the table when substance-specific investigations in humans are lacking. Phenyl isocyanate for instance was not listed since human investigations have not been performed.

It can be assumed that many workers described in individual studies were exposed to a mixture of materials. The individual substances in Table I are the components with which the subjects were tested (skin test, specific bronchial challenge test and antibody determination).

Table I includes the clinical data on airway-sensitizers described in international investigations that fulfil our quality requirements. Since these original data are heterogeneous due to different study designs and applied test methods, a comparative assessment of individual substances, e.g., the potency of sensitization, was not performed.

However, the listed data show that some substances or substance groups are of major importance:

1. The list of airway-sensitizing agents includes 16 enzymes. Their strongly sensitizing potential was demonstrated in almost every study by skin prick test (prevalences of positive results were 5.2–41%) and detection of specific IgE antibodies (prevalences 16–52%) as well as additionally in about 50% of investigations by specific bronchial challenge tests. Enzymes at air concentrations of approximately 1 ng/m^3 were shown to be important occupational allergens.
2. Among plant allergens, cereal flour dust is particularly relevant due to its wide distribution. In Germany, currently 15–20 million tons of wheat flour are annually produced, and the number of exposed people in bakeries amount to about 100,000. Obstructive airway diseases due to airway sensitizations to wheat/rye flour in this trade were reported with an annual incidence rate of approximately 800 per 100,000 employees.
3. The worldwide consumption of natural rubber latex was about 6 million tons in 1997 and is calculated to increase to 11 million tons up to the year 2020. Regarding the risk of sensitization, the use of natural rubber latex gloves in health care work is of great importance. The yearly consumption in the USA amounts to about 10 billion pairs and in Germany to about 1 billion pairs. In 1997, 365 (35.6%) of a total of 1025 reports of occupational diseases due to suspected allergic obstructive airway diseases that were registered by the German ''Berufsgenossenschaft für Gesundheit und Wohlfahrtspflege'' (Statutory Accident Insurance Institute for Health Care) were attributed to natural rubber latex exposure. Accident insurance carriers in the public sector registered a comparable number (Report by the German Federal Ministry of Labor and Social Affairs, 1998).
4. The prevalence of airway diseases due to dust originating from laboratory animals approaches 15% of exposed employees. No definite data on the number of exposed employees in Germany are available. For example, it has been estimated that approximately 90,000 workers in the USA and more than 30,000 in the United Kingdom handle laboratory animals (Fisher et al., 1998).
5. Among chemicals, isocyanates are of special relevance. The worldwide production is in the range of 5 million tons, and the number of exposed subjects is estimated to be about 500,000. The detection of specific IgE antibodies as well as specific bronchial challenge tests in several studies revealed average prevalences of immediate-type allergy of approximately 1%. The prevalence of airway diseases induced by isocyanates is about 5%.
6. The absolute number of subjects with platinum salt allergy are low, but in some occupational settings, e.g., precious metal refineries and catalyst productions those developing chronic airway diseases number 50%.

Although the yearly production amounts to only a few tons and worldwide only few workers (2,000–3,000 are exposed) the hazard is significant.

It should be mentioned that a direct comparison of prevalences or incidences given in different epidemiological studies seems not to be feasible here because the frequency of disorders may be modified by various parameters; e.g., in crosssectional studies the ‘‘healthy worker effect’’ can bias observed results while in longitudinal studies the duration of the observation period or the exposure time can influence the incidence.

It should also be noted that the information in Table I differs from hitherto published lists of allergens (e.g., Chan-Yeung and Malo, 1994) in that additional materials and aspects were included, and a greater number and more recent publications were considered.

In conclusion, we would like to mention that in spite of our efforts to select suitable and comprehensive references, this list does not claim to be complete. By definition, the list may contain some biases of perspective. Therefore, we caution non-scientists in its use when applying its conclusions to complex work-related problems. We have taken great care to correctly represent the data; however, we realize that some important publications may be missing or that errors in evaluating the material may have occurred.

Characteristics for exact identification of substances
Abbreviation
Formula
MW: molecular weight
CAS-number: chemical abstract service number
Threshold limit values and marking
TLV-TWA (USA): Threshold Limit Value-Time Weighted Average in the USA
EU-Label: R 42: may cause sensitization by inhalation
R 43: may cause sensitization by skin contact
TLV-TWA (Germany): Threshold Limit Value-Time Weighted Average in Germany
Sa: airway sensitizer according to the German *MAK and BAT value list*
Sah: airway and skin sensitizer according to the German *MAK and BAT value list*
( ): proposed of threshold limit value
Type of study
Reference: first two authors and year of publication
#: peer review: not ascertained
L: longitudinal study
C: cross-sectional study
S: investigation of symptomatic people
CR: case reports ($n > 1$)
I: individual case reports ($n = 1$)
n: number of examined exposed workers
Diagnoses/Symptoms
R: rhinitis
Con: conjunctivitis
A: asthmatic symptoms
Cou: cough
S: skin
Tot: total of work-related symptoms
nd: not done
Test methods
LFT: lung function test
SPT: skin prick test
Spec. challenge: specific bronchial challenge test
Antibodies: Antibody determination
×: done, +: positive, −: negative, nd: not done
If the whole collective was not investigated by skin prick test, challenge, or antibody determination this is indicated in the column, e.g. the entry ‘‘9% of 53’’ means that fifty-three people were tested; 9% of them with positive results.

TABLE I. Sensitizing Substances Which have been Shown to Cause Occupational Asthma[a]

												Symptoms						Methods				
Substances	**Abbre-viation**	**Formula**	**MW**	**CAS-Number**	**TLV-TWA (USA)**	**EU Label**	**TLV-TWA (Germany)**	**Sa Sah**	**Reference**	**Study**	**n**	**R**	**Con.**	**A**	**Cou.**	**S**	**Tot.**	**LFT**	**Skin test**	**Spec. challenge**	**Antibodies**	**Remarks**
Chemicals																						
Isocyanates																						
1,3-bis-(isocyanatomethyl)-cyclohexane, prepolymer		$C_6H_{10}(CH_2NCO)_2$	194.24	38661-72-2					Simpson, Garabrant et al. [1996]	S	23	–	–	+	+	–	nd	×	nd	nd	nd	Number of symptomatic subjects; n = 34 (68%)
Diphenylmethane diisocyanate	MDI	$C_{15}H_{10}N_2O_2$	250.26	Total MDI: 9016-87-9, 4,4′: 101-68-8, 2,4′: 5873-54-1, 2,2′: 2536-05-2	0.005 ppm; 0.051 mg/m^3	R 42	0.005 ppm; 0.05 mg/m^3	Sah	Zammit-Tabona, Sherkin et al. [1983]	S	11	–	–	+	–	–	nd	×	nd	× 64%	× IgE 18% IgG 36%	
Diphenylmethane diisocyanate, prepolymer	PMDI	2-6 × MDI		9016-87-9		R 42		Sah	Vandenplas, Malo et al. [1993b]	S	9	–	–	+	+	–	nd	×	nd	× 89%	× IgE 100% IgG 100%	Diagnosis in 8 subjects = hypersensitivity pneumonitis (BALF in 2 subjects)
Hexamethylene diisocyanate	HDI	$C_8H_{12}N_2O_2$	168.2	822-06-0	0.005 ppm; 0.034 mg/m^3	R 42/43	0.01 ppm; 0.07 mg/m^3 (0.035 mg/m^3)	Sa	Welinder, Nielsen et al. [1988]	C	30	43%	43%	33%	–	–	nd	nd	nd	nd	× IgE not elevated; IgG elevated	Comparison of median antibody values between exposed subjects and 22 controls
Hexamethylene diisocyanate, prepolymer									Vandenplas, Cartier et al. [1993a]	S	20	–	–	+	–	–	nd	×	nd	× 45%	× IgE 15% IgG 30%	Challenge: 4 out of 9 positive subjects reacted to polymers but not to monomers
Isophorone diisocyanate	IPDI	$C_{12}H_{18}N_2O_2$	222.29	4098-71-9	0.005 ppm; 0.045 mg/m^3	R 42/43	0.01 ppm; 0.09 mg/m^3	Sah	Clarke, Aldons [1981]	I	1	–	–	+	–	–	nd	×	nd	× +	nd	
Methylisocyanate	MIC			624-83-9	0.02 ppm; 0.047 mg/m^3	R 42	0.01 ppm; 0.024 mg/m^3		Avashia, Battigelli et al. [1996]	C	308	–	–	4,5%	–	–	nd	×	nd	nd	nd	Long-term exposure with low MIC concentrations: no LFT deterioration (may be concentration too low)
Naphthalene diisocyanate	NDI			3173-72-6		R 42	0.01 ppm; 0.09 mg/m^3	Sa	Fuortes, Kiken et al. [1995]	C	26	–	–	+	–	–	54%	×	nd	nd	nd	
"									Harries, Burge et al. [1979a]	CR	3	–	–	+	+	–	nd	nd	nd	× 100%	nd	Challenge: 1 dual reaction, 2 late bronchial ones
Toluene diisocyanate	TDI	$C_9H_6N_2O_2$	174.15	2,4: 584-84-9 2,6: 91-08-7	0.005 ppm; 0.036 mg/m^3	R 42	0.01 ppm; 0.07 mg/m^3	Sa	Baur, Fruhmann [1981]	C	195	–	–	+	–	–	28%	nd	nd	× 70.6% of 17	× IgE 4.6%	Cross-reactivity between different isocyanate-HSA conjugates
"									Moscato, Dellabianca et al. [1991]	S	113	–	–	+	+	–	nd	×	nd	× 40%	nd	Methacholine challenge test does not indicate isocyanate asthma
"									Mapp, Corona et al. [1988]	S*	35	–	–	+	+	–	nd	×	nd	× 77%	nd	*Follow-up examination after 11 months; 8 out of 30 (27%) not exposed subjects during this period were without symptoms
Toluene diisocyanate, prepolymer					0.5 mg/m^3				Vandenplas, Cartier et al. [1992]	CR	2	+	–	–	+	–	nd	nd	nd	× 100%	× IgE – IgG –	

TABLE I. (*Continued*)

Substances	Abbre-viation	Formula	MW	CAS-Number	TLV-TWA (USA)	EU Label	TLV-TWA (Germany)	Sa Sah	Reference
Toluene diisocyanate, hexamethylene diisocyanate, diphenylmethane diisocyanate									Baur [1986]
"									Baur [1995]
Anhydrides									
Hexahydrophthalic anhydride	HHPA	$C_8H_{10}O_3$	154.17	85-42-7				Sa	Drexler, Weber et al. [1994]
"									Moller, Gallagher et al. [1985]
Himic anhydride		$C_9H_8O_3$	164.16	2746-19-2					Rosenman, Bernstein et al. [1987]
Maleic anhydride	MA	$C_4H_2O_3$	98.06	108-31-6	0.25 ppm; 1 mg/m^3	R 42	0.1 ppm; 0.4 mg/m^3	Sah	Lee, Wang et al. [1991]
Methylhexahydrophthalic anhydride	MHHPA		169.19	19438-60-9					Tarvainen, Jolanki et al. [1995]
Methyltetrahydrophthalic anhydride	MTHPA	$C_9H_{12}O_4$	184	3-MTHPA: 88335 93-7; 4-MTHPA: 26590-20-5				Sa	Drexler, Weber et al. [1994]
"									Nielsen, Welinder et al. [1989]
"									Welinder, Nielsen et al. [1990]
Phthalic anhydride	PA	$C_8H_4O_3$	148.12	85-44-9	1 ppm; 6.1 mg/m^3		1 mg/m^3	Sa	Nielsen, Bensryd et al. [1991]
"									Wernfors, Neilsen et al. [1986]
Pyromellitic dianhydride	PMDA	$C_{10}H_2O_6$	218.13	89-32-7					Meadway [1980] #
Tetrachlorophthalic anhydride	TPCA	$C_8Cl_4O_3$	285.9	117-08-8					Liss, Bernstein et al. [1993]

Reference	Study	n	Symptoms: R	Con.	A	Cou.	S	Tot.	Methods: LFT	Skin test		Spec. challenge		Antibodies			Remarks
Baur [1986]	C	621	+	+	+	–	+	40%	nd	×	9% of 53	×	100% of 2	×	IgE	5.8%	
Baur [1995]	S	14	–	–	+	+	–	nd	×	nd		×	100% of 5	×	IgE IgG	– 71%	Total group = 1780 subjects; Diagnosis = hypersensitvity pneumonitis (BALF in 6 subjects)
Anhydrides																	
Drexler, Weber et al. [1994]	C	110	+	+	+	–	–	nd	nd	×	54% of 13	×	75% of 8	×	IgE	14.7%	Mixed exposure: HHPA+MTHPA
Moller, Gallagher et al. [1985]	C*	27	+	+	+	–	–	81%	×	nd		nd		×	IgE IgG	44% 41%	*:Examination of voluntary subjects (majority presumably symptomatic)
Rosenman, Bernstein et al. [1987]	C	20	–	–	35%	–	–	nd	nd	nd		nd		×	IgE	43% of 7	Cross-reactivity between himic anhydride and HHPA
Lee, Wang et al. [1991]	I	1	+	–	+	+	–	nd	×	nd		×	100%	nd			Additional exposure to PA; but negative challenge with PA
Tarvainen, Jolanki et al. [1995]	I	1	+	–	–	–	–	nd	nd	×	+	nd		×	IgE	+	Cross-reactivity with MTHPA
Drexler, Weber et al. [1994]	C	110	+	+	+	–	–	nd	nd	×	+	×	75% of 8	×	IgE	13.8%	Mixed exposure: HHPA+MTHPA
Nielsen, Welinder et al. [1989]	I	1	+	–	+	+	–	nd	nd	×	+	nd		×	IgE IgG	+ –	When on vacation and in another workplace had fewer complaints
Welinder, Nielsen et al. [1990]	C	145	?	?	?	?	?	nd	nd	×	16%	nd		×	IgE IgG	18% 12%	Compared to controls, specific IgE in exposed subjects significantly elevated
Nielsen, Bensryd et al. [1991]	C	23	39%	48%	9%	17%	–	nd	×	×	–	nd		×	IgE IgG	Not elevated; signif. elevated	Antibodies compared to controls (n = 19). Symptoms in exposed subjects distinctly more frequent
Wernfors, Neilsen et al. [1986]	C	118	24%	–	28%	–	–	nd	×	×	27% of 11*	×	100% of 2	×	IgE	100% of 2	*Skin test: scratch Determination of allergen-specific IgE by Prausnitz-küstner test
Meadway [1980] #	C	7	+	–	+	–	+	57%	×	nd		×	29%*	nd			*Challenge: FEV1 decrease of 15% or 18% regarded as positive
Liss, Bernstein et al. [1993]	C	52	–	–	+	–	–	27% 36%	×	nd		nd		×	IgE IgG	31% of 49 39% of 49	

TABLE I. (*Continued*)

Substances	Abbreviation	Formula	MW	CAS-Number	TLV-TWA (USA)	EU Label	TLV-TWA (Germany)	Sa Sah	Reference	Study	n	Symptoms						Methods				Remarks
												R	Con.	A	Cou.	S	Tot.	LFT	Skin test	Spec. challenge	Antibodies	
Tetrachlorophthalic anhydride									Barker, Harris et al. [1998a]	S*	6	–	–	+	–	–	nd	×	× 60% of 5	nd	× IgE 100%	*Examination: 12 years after activity termination. SPT at the beginning: 100% out of 6, IgE decreased in 100% during 12 year
Trimellitic anhydride	TMA	$C_9H_4O_5$	192.13	552-30-7		R 42	0.04 mg/m^3	Sa	Zeiss, Mitchell et al. [1992]	C	474	+	–	+	–	–	nd	nd	nd	nd	× IgE 6.8%	Sensitivity probability increases together with activity duration
Pyromellitic dianhydride, phthalic anhydride, maleic anhydride									Baur, Czuppon et al. [1995b]	C	92	+	+	+	–	+	61%	×	× +	nd	× IgE 16.3%	
Phthalic anhydride, trimellitic anhydride, maleic anhydride									Barker, van Tongeren et al. [1998b]	C	401	+	–	+	–	–	9%	×	× 3.2% of 378	nd	nd	Positive SPT correlates with symptoms
Amines																						
Amino ethyl ethanolamine		$C_4H_{12}N_2O$	104.15	111-41-1					Pepys, Pickering [1972]	S	3	–	–	+	+	–	nd	×	nd	× 100%	nd	
Aliphatic amines	EDA, DETA, TETA								Ng, Lee et al. [1995]	C	12	+	+	33%	58%	–	nd	×	nd	× 50% of 2*	nd	*Challenge.: EDA
2-Dimethyl ethanolamine		$C_4H_{11}NO$	89.14	108-01-0					Vallieres, Cockcroft et al. [1977]	I	1	+	–	+	–	–	nd	×	× +*	× 100%	nd	SPT in non-exposed controls positive —>irritative effect
3-Dimethylamino propylamine	3-DMAPA	$C_5H_{14}N_2$	102.18	109-55-7					Sargent, Brubaker et al. [1976]	C	25	–	24%	44%	–	–	nd	×	nd	nd	nd	
"									Brubaker, Muranko et al. [1979]	C	28	18%	–	–	–	–	nd	×	nd	nd	nd	Same enterprise as in Sargent, Brubaker et al. [1976] but after ventilation installation; ambient air load reduced to 1/7
2-Ethanolamine		C_2H_7NO	61.08	141-43-5	3 ppm; 7.5 mg/m^3		3 ppm; 8 mg/m^3 (5 mg/m^3)		Savonius, Keskinen et al. [1994]	I	1	+	–	+	+	–	nd	×	nd	× +	nd	Fever indicated hypersensitivity pneumonitis, could not be confirmed by LFT
Ethylenediamine		$C_2H_8N_2$	60.1	107-15-3	10 ppm; 25 mg/m^3	R 42/43	10 ppm 25 mg/m^3		Nakazawa, Matsui [1990]#	CR	2	–	–	+	+	–	nd	×	× +	× +	× IgE 100%; IgG –	Skin test: patch negative; intradermal positive
Hexamethylenetetramine	HTMA	$C_6H_{12}N_4$	140.19	100-97-0		R 42/43			Gamble, McMichael et al. [1976]	C	52	+	–	+	+	–	nd	×	nd	nd	nd	HMTA was available as HMTA resorcinol. LFT: comparison to 50 non-exposed controls —> values of exposed subjects significantly lower
4-Methylmorpholine	NNM	$C_5H_{11}NO$	101.15	109-02-4			20 mg/m^3		Belin, Wass et al. [1983]	C	48	–	+	27%	–	–	nd	×	nd	nd	nd	Also exposure to isocyanates but concentrations below MAK; NMM concentration 10,000 times higher
Piperazine		$C_4H_{10}N_2$	86.14	110-85-0	5 mg/m^3	R 42/43		Sah	Hagmar, Welinder [1986]	C	72	–	–	31%	–	–	nd	×	nd	nd	× IgE 7%	IgE specifity confirmed by RAST inhibition
Piperazine dihydrochloride		$C_4H_{10}N_2(2HCl)$	159.05	142-64-3					Welinder, Hagmar et al. [1986]	CR	2	–	–	+	–	–	nd	×	× 50%	nd	× IgE 100%	IgE antibodies to piperazin and N-methyl piperazin; RAST inhibition

TABLE I. (*Continued*)

												Symptoms						Methods								
Substances	**Abbre-viation**	**Formula**	**MW**	**CAS-Number**	**TLV-TWA (USA)**	**EU Label**	**TLV-TWA (Germany)**	**Sa Sah**	**Reference**	**Study**	**n**	**R**	**Con.**	**A**	**Cou.**	**S**	**Tot.**	**LFT**	**Skin test**		**Spec. challenge**		**Antibodies**			**Remarks**
Triethylene tetramine		$C_6H_{18}N_4$	146.24	112-24-3					Fawcett, Taylor et al. [1977]	I	1	+	+	+	–	–	nd	nd	×	–*	×	100%	nd			*Skin test: patch
"									Savonius, Keskinen et al. [1994]	CR	2	+	+	+	+	–	nd	×	nd		×	100%	nd			
Metals and their compounds																										
Chromium																										
Chromium (VI) salts		Cr	52	7440-47-3	0.01 – 0.5 mg/m^3		*0.05 – 0.1 mg/m^3																			*:Dependent on processing
Chromium sulphate		$Cr_2(SO_4)_3$	374	15244-38-9					Park, Yu et al. [1994]	CR	4	+	–	+	–	–	nd	×	×	+	×	100%	nd			SPT: 2 out of 4 positive; patch: 2 different subjects positive
Chromium sulphate and nickel sulphate		$Cr_2(SO_4)_3$ and $NiSO_4$							Novey, Habib et al. [1983]	I	1	–	–	+	+	–	nd	×	×	–	×	+	×	IgE	100%	Challenge: Cr: immediate bronchial reaction, Ni: dual bronchial reaction
Cobalt		Co	58.93	7440-48-4	0.02 mg/m^3	R 42/43	*0.1 – 0.5 mg/m^3	Sah	Gheysens, Auwerx et al. [1985]	CR	3	+	+	+	+	+	nd	×	nd		×	100%	nd			*: Dependent on processing. Challenge with cobalt powder: 2 late bronchial reactions, 1 immediate reaction
"									Shirakawa, Morimoto [1997]	C	281	–	–	14%*	–	–	nd	nd	nd		nd		×	IgE	2.5%	*: Asthma IgE to Co-HSA. Significantly elevated IgE level of exposed compared to non-exposed subjects
Cobalt sulphate		$CoSO_4$	137	60459-08-7					Pisati, Zedda [1994]	S	9	–	–	+	–	–	nd	×	×	44%	×	100%	nd			After 1 year: 8 workers quit job: 2 healthy, 5 improved, 1 stable
Cobalt and nickel sulphate									Shirakawa, Kusaka et al. [1990]	CR	8	–	–	+*	–	–	nd	×	×	Co 75% Ni 63%	×	Co 100% Ni 88%	×	IgE	Co 63% Ni 50%	*: Hard metal asthma; IgE in comparison to controls. According to authors, tungsten inert, does not induce asthma
Iridium																										
Iridium Chloride		$IrCl_3$	298.56	10025-83-9					Bergman, Svedberg et al. [1995]	I	1	+	+	+	–	–	nd	nd	×	+	nd		nd			SPT with hexachloroplatinate negative
Nickel		Ni	58.69	7440-02-0	(1 mg/m^3)		0.5 mg/m^3																			
Nickel sulphate		$NiSO_4$	154.86	7786-81-4		R 42/43		Sah	Estlander, Kanerva et al. [1993]	I	1	–	–	+	+	+	nd	nd	×	+	×	+	×	IgE	Elevated	Patch also positive
"									Malo, Cartier et al. [1982]	I	1	–	–	+	–	–	nd	×	×	+	×	+	×	IgE	Elevated	
Platinum		Pt	195.08	04.06.7440	1 mg/m^3		1 mg/m^3	Sah																		
Chloroplatinates					0.002 mg/m^3 (salt)		0.002 mg/m^3	Sah	Baker, Gann et al. [1990]	C	107	43%	–	26%	–	12%	nd	×	×	14%	nd		nd			Positive SPT with elevated total IgE and positive challenge associated with cold air
Hexachloroplatinate		H_2PtCl_6						Sah	Merget, Schultze-Werninghaus et al. [1988]	C	30	–	–	+	–	–	27%	nd	×	38% of 26	nd		×	IgE	Elevated	SPT of highly exposed subjects positive. Elevated specific IgE in symptomatic

TABLE I. (*Continued*)

Substances	Abbre-viation	Formula	MW	CAS-Number	TLV-TWA (USA)	EU Label	TLV-TWA (Germany)	Sa Sah	Reference	Study	n	R	Con.	A	Cou.	S	Tot.	LFT	Skin test		Spec. challenge		Antibodies			Remarks
																										subjects. Correlation with high total IgE—> non-specific binding
Ammonium hexachloroplatinate		$Cl_6H_8N_2Pt$	443.89	16919-58-7				Sah	Murdoch, Pepys et al. [1986]	C	306	–	–	–	–	–	nd	nd	×	12%	nd		×	IgE	Elevated (in 7.5%)	Elevated specific IgE in 61% of SPT positive subjects, but only in 6% of SPT negative subjects
Potassium																										
Potassium dichromate		$K_2Cr_2O_7$	294.19	7778-50-9					Keskinen, Kalliomaki et al. [1980]	CR	2	–	–	+	–	–	nd	nd	×	50%*	×	100%	nd			*Skin test: patch patients are welders
Potassium dichromate and nickel chloride		$K_2Cr_2O_7$ and $NiCl_2$							Bright, Burge et al. [1997]	CR	7	–	–	+	–	–	nd	×	×	Cr 29% Ni 57%	×	Cr: 100% of 7; Ni: 40% of 5	nd			Challenge: Cr: 5 immediate, 3 late bronchial reactions; Ni: 2 late bronchial reactions
Potassium hexachloroplatinate		K_2Cl_6Pt	486.01	16921-30-5				Sah	Bolm-Audorff, Bienfait et al. [1992]	C	65	+	+	+	–	–	23%	×	×	19% of 64	nd		×	IgE	Elevated	Elevated specific and total IgE in symptomatic subjects. No increase in histamine release
Tungsten		W	183.85	7440-33-7	1–5 mg/m^3		*1–5 mg/m^3																			*: According to solubility
Tungsten carbide		W_2C	379.71	11130-73-7	1–5 mg/m^3		*1–5 mg/m^3		Bruckner [1967]	I	1	–	–	+	+	–	nd	nd	nd		nd		nd			*: According to solubility; workplace observations: mask ∅ 0,6 μm; symptoms remain
Zinc (fume, steam)		Zn	65.39	7440-66-6					Malo, Cartier et al. [1993]	I	1	+	–	+	–	–	nd	×	×	+	×	+	×	IgE	Not elevated	
Zinc chloride and ammonium chloride									Weir, Robertson et al. [1989]	CR	2	–	–	+	+	–	nd	×	nd		×	+	nd			Challenge: pure substances: weak bronchial reactions
Medicaments																										
Aminophylline		$C_{16}H_{24}N_{10}O_4$	420.4	317-34-0					Rosenberg, Aaronson et al. [1984]	CR	2	–	–	+	+	–	nd	×	×	50%	×	100%	nd			Challenge: bronchial reaction after 8 h
Ampicillin		$C_{16}H_{19}N_3O_4S$	349.4	69-53-4					see Davies, Hendrick et al. [1974]																	
Amprolium hydrochloride				121-25-5					Greene, Freedman [1976]	I	1	+	–	+	–	–	nd	×	nd		×	+	nd			
Cephalosporin C zinc salt		$C_{16}H_{19}N_3O_8SZn$	478.79	59143-60-1					Stenton, Dennis et al. [1995]	I	1	+	–	+	–	–	nd	×	nd		×	+	nd			Tests with ceftazidim (cephalosporin of the third generation)
"									Coutts, Dally et al. [1981]	CR	2	–	–	+	+	–	nd	nd	×	100%	×	100%	nd			7-Aminocephalosporin acid (7ACA)+tylosilate dihydrate derivate (7CTD)
Chlorhexidine		$C_{22}H_{30}Cl_2N_{10}$	505.46	55-56-1					Waclawski, McAlpine et al. [1989]	CR	2	–	–	+	+	–	nd	×	nd		×	100%*	nd			*Challenge: FEV1 decline 13 or 22%
Cimetidine		$C_{10}H_{16}N_6S$	252.34	51481-61-9					Coutts, Lozewicz et al. [1984]	C	55	–	–	+	–	–	36%	nd	×	–	×	25% of 4	nd			Challenge: Additionally to 1 late bronchial reaction 2 nasal reactions

TABLE I. *(Continued)*

Substances	Abbreviation	Formula	MW	CAS-Number	TLV-TWA (USA)	EU Label	TLV-TWA (Germany)	Sa Sah	Reference
Ciprofloxacin									Broding, Chen et al. [1996]
Hydralazine		$C_8H_4N_4$	160.18	304-20-1					Perrin, Malo et al. [1990]
Ipecacuanha									Luczynska, Marshall et al. [1984]
Isonicotinic acid hydrazine	INH	$C_6H_7N_3O$	137.15	54-85-3					Asai, Shimoda et al. [1987]
”									Shimoda [1990]
Methyldopa		$C_{10}H_{13}NO_4$	211.12	555-30-6					Harries, Taylor et al. [1979b]
Opiate compounds									Biagini, Bernstein et al. [1992]
Penicillamine		$C_5H_{11}NO_2S$	149.21	52-67-5 (D-form)					Lagier, Cartier et al. [1989]
Penicillin and penicillin derivatives				1404-05-9					Davies, Hendrick et al. [1974]
”									Stejskal, Forsbeck et al. [1987]
”									Shmunes, Taylor et al. [1976]
Piperacillin		$C_{23}H_{26}N_5NaO_7S$	539.5	59703-84-3					Moscato, Galdi et al. [1995]
Phenylglycine acid chloride									Kammermeyer, Mathews [1973]
Psyllium				8063-16-9					Vaswani, Hamilton et al. [1996]
”									Marks, Salome et al. [1991]
Salbutamol (including prestages)		$C_{13}H_{21}NO_3$	239.31	18559-94-9					Agius, Davison et al. [1994]
Senna									Helin, Makinen-Kiljunen [1996]
”									Marks, Salome et al. [1991]
Spiramycin				8025-81-8					Moscato, Naldi et al. [1984]

Substances	Study	n	Symptoms: R	Con.	A	Cou.	S	Tot.	Methods: LFT	Skin test		Spec. challenge		Antibodies			Remarks
Ciprofloxacin	CR	2	–	–	+	–	–	nd	×	×	50%	×	100%	×	IgE	–	
Hydralazine	I	1	–	–	+	+	–	nd	nd	×	–	×	+	×	IgE IgG	– –	
Ipecacuanha	C	42	+	+	+	–	–	48%	nd	×	33%	nd		×	IgE	44% of 32	12 out of 18 SPT-pos. subjects and 2 out of 14 SPT-neg. subjects had spec. IgE
Isonicotinic acid hydrazine	I	1	+	–	+	–	–	nd	nd	×	+	×	+	×	IgE*	+	*IgE detection: Prausnitz-Küstner
”	C	8	–	–	+	–	–	25%	nd	×	25%	×	100% of 2	×	IgE	63%	Cross-reactivity between INH and metabolite isonicotin acid (INA)
Methyldopa	I	1	–	–	+	–	–	nd	nd	×	–	×	+	×	IgG	–	Challenge: late bronchial reaction (Max. FEV1 decline after 11 h)
Opiate compounds	C	39	–	–	+	–	+	54%	×	× *		nd		nd			*SPT: M-6-HS-HSA, dihydrocodein,hydrocodon, codein significant elevated compared to controls
Penicillamine	I	1	–	–	+	–	–	nd	×	×	–	×	+	nd			Reaction probably not IgE-mediated
Penicillin and penicillin derivatives	CR	4	+	–	+	–	+	nd	×	×	–	×	75%	nd			Challenge: late bronchial reactions
”	CR	8	+	–	+	–	+	nd	nd	×	63%	nd		nd			Lymphocyte transfer test: all subjects positive; penicillin sidechain important to reaction
”	C	169	–	+	+	–	+	40%	nd	×	11% of 9	nd		×	IgG IgM	43% and/or	
Piperacillin	I	1	+	–	+	–	+	nd	×	×	+	×	+	nd			IgE to other antibiotics negative
Phenylglycine acid chloride	C	24	–	–	+	–	–	29%	×	×	38%	×	100% of 2	×	IgE*	100% of 3	*IgE detection: Prausnitz-Küstner reaction
Psyllium	I	1	–	–	+	–	–	nd	nd	×	+	nd		×	IgE	+	ELISA inhibition positive
”	C	125	–	+	6%*	–	+	52%	×	×	8% of 118	nd		nd			*:Asthma
Salbutamol (including prestages)	CR	2	+	–	+	+	–	nd	×	×	–	×	100% of 1	nd			
Senna	I	1	+	+	+	–	–	nd	×	×	+	×	+	×	IgE	+	Immunoblot: strong IgE binding 16 kDA
”	C	125	–	+	6%*	–	+	52%	×	×	15% of 118	nd		nd			*:Asthma
Spiramycin	CR	2	–	–	+	+	–	nd	×	×	–	×	100%	nd			

TABLE I. (*Continued*)

Substances	Abbreviation	Formula	MW	CAS-Number	TLV-TWA (USA)	EU Label	TLV-TWA (Germany)	Sa Sah	Reference
Spiramycin									Malo, Cartier [1988]
Tetrachloroisophthalonitrile				1897-45-6					Honda, Kohrogi et al. [1992]
Tetracycline		$C_{22}H_{24}N_2O_8$	444.4	60-54-8					Menon, Das [1997]
Tributyl tin oxide		$C_{24}H_{54}OSn_2$	596.08	56-35-9			0.002 ppm; 0.05 mg/m^3		Shelton, Urch et al. [1992]
Tylosin tartrate		$C_{46}H_{77}NO_{17}.C_4H_6O_6$	1066.2	74610-55-2					Lee, Wang et al. [1989a]
Plastics (incl. their monomers)									
95% alkyl aryl polyether alcohol and 5% polypropylene glycol				Polypropylene glycol: 25322-69-4					Stevens [1976]
Alkylcyanoacrylate	ECA	$C_6H_7NO_2$	125.1	7085-85-0					Savonius, Keskinen et al. [1993]
Cyanoacrylates (general)									Lozewicz, Davison et al. [1985]
Methylcyanoacrylate	MCA	$C_5H_5NO_2$	111	137-05-3			2 ppm; 8 mg/m^3		Savonius, Keskinen et al. [1993]
Methyl methacrylates	MMA	$C_5H_8O_2$	100.12	80-62-6	100 ppm; 410 mg/m^3		50 ppm; 210 mg/m^3		Lozewicz, Davison et al. [1985]
Plexiglas (dust)									Kennes, Garcia-Herreros et al. [1981]
Polyethylene		$(–CH_2–CH_2–)_n$	polymer	9002-88-4					Gannon, Burge et al. [1992]
"									Stenton, Kelly et al. [1989]
Polypropylene		$(–CH_2CH(CH_3)–)_n$	polymer	25085-53-4					Malo, Cartier et al. [1994b]
Polyvinylchloride	PVC	$(–CH_2–CHCl–)_n$	polymer	9002-86-2			5 mg/m^3		Lee, Yap et al. [1989b]
Styrene		C_8H_8	104.15	100-42-5	(50 ppm; 213 mg/m^3)		20 ppm; 85 mg/m^3		Hayes, Lambourn et al. [1991]
"									Moscato, Biscaldi et al. [1987]
Synthetic textile fibres (rayon, nylon = polyamide, orlon = acryl, terylen = polyester)									Muittari, Veneskoski [1978]

Substances	Study	n	Symptoms: R	Con.	A	Cou.	S	Tot.	Methods: LFT	Skin test		Spec. challenge		Antibodies			Remarks
Spiramycin	C	51	–	–	8%*	+	–	nd	×	×**		×	25% of 12	nd			*:Asthma; **SPT result not interpretable: reactions to 0.1 but not to 1 mg/ml
Tetrachloroisophthalonitrile	I	1	–	–	+	–	–	nd	×	×	+*	×	+	×	IgE	–	*Skin test: patch
Tetracycline	I	1	–	–	+	+	–	nd	×	×	+	×	+	nd			Oral challenge also positive
Tributyl tin oxide	I	1	+	–	+	–	–	nd	×	×	–	×	+*	nd			*Challenge: FEV1 decline by 19%
Tylosin tartrate	I	1	–	–	+	–	–	nd	nd	nd		×	+*	nd			*Challenge: FEV1 decline begins after 2 h, after 5 h, decline more than 50%
Plastics (incl. their monomers)																	
95% alkyl aryl polyether alcohol and 5% polypropylene glycol	I	1	–	–	–	+	–	nd	×	nd		×	+	nd			
Alkylcyanoacrylate	CR	11	+	–	+	–	–	nd	×	nd		×	91%*	nd			Alcylcyanacrylate *:Challenge with adhesive
Cyanoacrylates (general)	S	5	+	–	+	+	–	nd	×	nd		×	100%	nd			See methylmethacrylate
Methylcyanoacrylate	CR	3	–	–	+	–	–	nd	×	nd		×	100%*	nd			*:Challenge with adhesive
Methyl methacrylates	S	2	–	–	+	–	–	nd	×	nd		×	50%	nd			See cyanacrylate in general
Plexiglas (dust)	I	1	+	–	+	+	–	nd	×	nd		×	+	nd			
Polyethylene	I	1	–	–	+	–	–	nd	×	nd		×	+	nd			
"	I	1	–	–	+	+	–	nd	×	nd		×	+	nd			Challenge: late bronchial reaction
Polypropylene	I	1	–	–	+	+	–	nd	×	nd		×	+	nd			Challenge with heated polypropylene. Challenge with formaldehyde negative
Polyvinylchloride	I	1	–	–	+	+	–	nd	×	nd		×	+	nd			
Styrene	I	1	–	–	+	–	–	nd	×	nd		×	+	nd			Challenge: dual bronchial reaction at 12 ppm
"	CR	2	–	–	+	+	+	nd	×	×	–	×	100%	nd			Challenge in 1 case: after immediate bronchial reaction late cutaneous reaction
Synthetic textile fibres (rayon, nylon = polyamide, orlon = acryl, terylen = polyester)	C	136	–	–	+	–	–	nd	nd	×	61% of 76	×	20% of 79	nd			Mixed exposure to natural fibres; type 1 allergy assumed; fibres may function as haptens

TABLE I. (*Continued*)

												Symptoms						Methods								
Substances	**Abbreviation**	**Formula**	**MW**	**CAS-Number**	**TLV-TWA (USA)**	**EU Label**	**TLV-TWA (Germany)**	**Sa Sah**	**Reference**	**Study**	**n**	**R**	**Con.**	**A**	**Cou.**	**S**	**Tot.**	**LFT**	**Skin test**		**Spec. challenge**		**Antibodies**			**Remarks**
Dyes																										
Basic Blue 99 (hair dye)									Wigger-Alberti, Elsner et al. [1996]	I	1	+	+	–	+	–	nd	nd	×	+	nd		nd			SPT positive, patch negative
Carmine	E 120								Stücker, Roggenbuck et al. [1996]	I	1	+	–	+	–	–	nd	nd	×	+	nd		×	IgE	+	IgE antibodies to coloring components of carmine acid
Dyes (dyeing of textile fibres)									Zuskin, Mustajbegovic et al. [1997]	C	135	–	–	6%*	38%	–	nd	×	nd		nd		nd			*: Asthma; in 103 controls occupational asthma prelavance = 0%; exposed subjects: worse LFT
Henna, black (from *Indigofera argentea*)									Scibilia, Galdi et al. [1997]	I	1	+	+	+	+	–	nd	×	×	+	nd		×	IgE	+	SPT+IgE: red henna negative
Lanasol Yellow 4G									Romano, Sulotto et al. [1992]	I	1	–	–	+	–	–	nd	×	×	+	×	+	nd			Challenge: other colors negative
Remazol black B (dyeing of textile fibres)									Nilsson, Nordlinder et al. [1993]	C	162	–	–	+	–	+	11%	×	×	36% of 14	nd		×	IgE	2.5%	IgE: cross-reactivity with many other colors
Other chemicals																										
Ammonium chloride		NH_4Cl	53.49	12125-02-9					see Weir, Robertson et al. [1989]								nd									
Azodicarbonamide		$C_2H_4N_4O_2$	116.08	123-77-3					Normand, Grange et al. [1989]	CR	4	–	–	+	–	+	nd	×	nd		×	100% of 2	nd			Challenge: 1 immediate and 1 late bronchial reaction
"									Slovak [1981]	C	151	29%	25%	19%*	39%	–	nd	×	×	–	nd		nd			Azodicarbonamide is hardly soluble, therefore problems with production of SPT solutions; SPT might be false-negative
1,2-benzisothiazolin-3-one		C_7H_5NOS	151.19	2634-33-5					Moscato, Omodeo et al. [1997]	I	1	+	–	+	+	–	nd	×	nd		×	+	nd			Challenge: immediate bronchial reaction
Captafol		$C_{10}H_9Cl_4NO_2S$	349.1	2425-06-1	0.1 mg/m^3				Royce, Wald et al. [1993]	I	1	–	–	+	–	–	nd	×	nd		×	+	nd			IgE to maleic acid anhydrice (captafol pre-stage not available)
Chloramine T		$C_7H_7ClNNaO_2S$	227.67	127-65-1					Dijkman, Vooren et al. [1981]	S	5	+	–	+	+	–	nd	nd	×	100% of 4	×	100% of 3	nd			Challenge: 1 dual, 2 late bronchial reactions (4 h after challenge)
"									Kramps, van Toorenenbergen et al. [1981]	S	4	–	–	+	–	–	nd	nd	nd		nd		×	IgE IgG	+ –	Antibody comparison with 4 asymptomatic subjects: also IgE to chloramine T-HSA conjugates
"									Kujala, Reijula et al. [1995]	I	1	–	–	+	+	–	nd	×	×	+	×	+	×	IgE	+	
Diazonium tetrafluoroborate									Luczynska, Hutchcroff et al. [1990]	C	45	–	–	+	+	–	78%	nd	nd		×	100% of 2	×	IgE	20%	Correlation between asthmatic symptoms and IgE
"									Graham, Coe et al. [1981]	I	1	–	–	+	–	–	nd	×	nd		×	+	nd			

TABLE I. (*Continued*)

Substances	Abbreviation	Formula	MW	CAS-Number	TLV-TWA (USA)	EU Label	TLV-TWA (Germany)	Sa Sah	Reference	Study	n	Symptoms R	Con.	A	Cou.	S	Tot.	Methods LFT	Skin test	Spec. challenge	Antibodies	Remarks
EPO 60									Lambouen, Hayes et al. [1992]	I	1	–	–	+	–	–	nd	×	nd	× +	nd	Challenge: late bronchial reaction
Ethylcyanoacrylate									Kopp, McKay et al. [1985]	I	1	+	–	+	+	–	nd	×	nd	× +	nd	Challenge: maximal bronchial reaction after 11 h
Ethyleneimine		C_2H_5N	43.1	151-56-4			0.5 ppm; 0.9 mg/m^3		Kanerva, Estlander et al. [1995]	CR	9	–	–	+	–	+	nd	×	× 80% of 5	× 88% of 8	× IgE –(in 5)	Challenge: 1 immediate, 1 dual, 5 late bronchial reactions. patch: 83% positive
Ethylene oxide		C_2H_4O	44.05	75-21-8	1 ppm; 2 mg/m^3		1 ppm; 2 mg/m^3		Verraes, Michel [1995]	I	1	–	–	+	–	+	nd	nd	nd	nd	× IgE +	Ethylene oxide binds to powder (similar to latex allergens)
Formaldehyde		CH_2O	30. Mrz	50-00-0			0.5 ppm; 0.6 mg/m^3		Lemiere, Desjardins et al. [1995]	CR	3	+	–	+	+	–	nd	×	nd	× 100%	nd	Challenge: 2 subjects reacted only to dust, 1 to dust and gas
"									Burge, Harries et al. [1985]	S	15	+	–	+	+	–	nd	×	nd	× 47%	nd	Non-specific challenge with histamine correlates with specific challenge
Freon®									Malo, Gagnon et al. [1984]	I	1	–	–	+	–	–	nd	×	nd	× +	nd	Challenge: only bronchial reaction to heated Freon
Furfuryl alcohol		$C_5H_6O_2$	98.1	98-00-0	10 ppm; 40 mg/m^3		10 ppm; 40 mg/m^3		Cockcroft, Cartier et al. [1980]	I	1	–	–	+	–	–	nd	×	nd	× +	× IgE –	
Glutaraldehyde		$C_5H_8O_2$	100.12	111-30-8		R 42/43	0.1 ppm; 0.4 mg/m^3		Curran, Burge et al. [1996]	S	20	+	–	65%*	–	–	nd	nd	nd	× 88% of 8	× IgE 28% of 18	*Asthma IgE: comparison to controls. High total IgE interferes
"									Gannon, Bright et al. [1995]	S	8	–	–	+	–	–	nd	×	nd	× 88%	nd	Challenge: mostly late bronchial reactions; 3 subjects reacted to formaldehyde
Hexachlorophene		$C_{13}H_6Cl_6O_2$	406.92	70-30-4					Nagy, Orosz [1984]	I	1	+	–	+	–	–	nd	nd	× –	× +	nd	
Isothiazolinone									Bourke, Convery et al. [1997]	I	1	–	–	+	+	–	nd	×	nd	× +	nd	Challenge: in the workplace
Metabisulphite		$O_5S_2^{2-}$		16731-55-8 7681-57-4					Malo, Cartier et al. [1995]	I	1	–	+	+	–	–	nd	×	× –	× +	nd	Challenge: immediate bronchial reaction to low dose (no irritative reaction)
Ninhydrin		$C_9H_6O_4$	178.14	485-47-2					Hytonen, Martimo et al. [1996]	I	1	+	–	–	–	–	nd	nd	× +	× +	× IgE +	Challenge: no lung function parameters; blocked nose
"									Piirila, Estlander et al. [1997a]	I	1	+	–	(+)	–	–	nd	×	× –	× +	× IgE +	
Sodium iso-nonanoyl-oxibenzene-sulphonate				123354-92-7					Stenton, Dennis et al. [1990]	CR	3	+	+	+	–	–	nd	×	nd	× 100%	nd	Challenge: late reaction (>2 h)
"									Hendrick, Connolly et al. [1988]	I	1	+	–	+	+	–	nd	×	nd	× +	× IgE –	Challenge: late bronchial reaction; antibody test difficult since positive controls not available
Tetrazene		$C_2H_8N_{10}O$	188.2	31330-63-9					Burge, Hendy et al. [1984]	I	1	+	–	+	+	+	nd	×	nd	× +	nd	Challenge: late bronchial reaction

TABLE I. *(Continued)*

Substances	Abbreviation	Formula	MW	CAS-Number	TLV-TWA (USA)	EU Label	TLV-TWA (Germany)	Sa Sah	Reference
Triglycidyl isocyanurate	TGIC	$C_{12}H_{15}N_3O_6$	297.3	2541-62-9					Piirila, Estlander et al. [1997b]
Persulphate salts									
Potassium persulphate, sodium persulphate		$K_2O_8S_2$ $Na_2O_8S_2$	270.33 238.09	7727-21-1 7775-27-1					Parra, Igea et al. [1992]
"									Pankow, Hein et al. [1989]
ANIMALS									
Mites									
Grain mites (*Tyrophagus longior, T. putrescentiae, Glycyphagus destructor, G. domesticus, Acarus siro*)									Musk, Venables et al. [1989]
Grain mites (*G. destructor, G. domesticus, T. putrescentiae, A. siro, A. farris*)									Blainey, Topping et al. [1989]
Grain mites (*Lepidoglyphus destructor*)									van Hage-Hamsten, Ihre et al. [1988]
House dust mites (*Dermatophagoides pteronyssinus, D. farinae*)									Oertmann, Müsken et al. [1995]
Poultry mites (*Ornithonyssus sylviarum*)									Lustsky, Teichtahl et al. [1984]
Red spider mites (*Tetranychus urticae*)									Burches, Pelaez et al. [1996]
"									Delgado, Orta et al. [1997]
Insects									Dyne, Campion et al. [1996]
Bee moth (*Galleria mellonella*; fish bait)									Siracusa, Bettini et al. [1994]
Cockroach (*Blatella germanica*)									Steinberg, Bernstein et al. [1987]
Cricket, locust									Bagenstose, Mathews et al. [1980]

Substances	Study	n	R	Con.	A	Cou.	S	Tot.	LFT	Skin test		Spec. challenge		Antibodies			Remarks
			Symptoms						Methods								
Triglycidyl isocyanurate	I	1	−	−	+	−	+	nd	×	×	−(Prick) +(Patch)	×	+	×	IgE	−	Skin test: patch positive due to contact dermatitis; SPT and IgE negative, perhaps due to bad HSA conjugates
Persulphate salts																	
Potassium persulphate, sodium persulphate	I	1	−	−	+	+	+	nd	×	×	+	×	+	×	IgE, G, M, A	−(all)	Challenge: bronchial reaction after 2 h; pathomechanism unclear
"	I	1	+	+	+	+	−	nd	×	×	+	×	+	nd			Irritative reaction excluded
ANIMALS																	
Mites																	
Grain mites (*Tyrophagus longior, T. putrescentiae, Glycyphagus destructor, G. domesticus, Acarus siro*)	C	279	+	−	+	−	−	25%	×	×	33% of 259	nd		nd			See moulds, *Saccharomyces cerevisiae*
Grain mites (*G. destructor, G. domesticus, T. putrescentiae, A. siro, A. farris*)	C	133	−	−	+	+	−	33%	×	×	25% of 130	×	100% of 1	×	IgE	23% of 128	Various degrees of cross-reactivity with house dust mites
Grain mites (*Lepidoglyphus destructor*)	S	12	−	−	+	−	−	nd	nd	×	100%	×	100%	×	IgE	100%	Healthy exposed farmers (n = 4) in all tests negative
House dust mites (*Dermatophagoides pteronyssinus, D. farinae*)	I	1	+	+	+	−	−	nd	nd	×	+	×	+	×	IgE	+	*Challenge: nasal; mites in hen houses but not in house dust
Poultry mites (*Ornithonyssus sylviarum*)	S	16	+	−	+	−	−	nd	nd	×	63%	×	100% of 1	×	IgE	93% of 14	SPT: all 12 exposed asymtomatic controls negative
Red spider mites (*Tetranychus urticae*)	S	150	+	+	+	−	+	nd	nd	×	36%	×	89% of 54*	×	IgE	100% of 54	*Challenge: conjunctival; cross-reactivity with house dust mite. Sensitization to house dust mite might be a risk factor
"	S	24	+	−	+	−	+	nd	nd	×	66%	×	86% of 14	×	IgE	100% of 16	No cross-reactivity between spider mite and house dust mite
Insects	C	26	−	−	+	−	−	50%	nd	nd		nd		×	IgE	46% of 13	Partial cross-reactivity with different insects
Bee moth (*Galleria mellonella*; fish bait)	S	14	+	+	+	−	−	nd	×	×	15% of 13	×	100% of 1	×	IgE	25% of 12	See also *T. molitor* and *L. caesar*
Cockroach (*Blatella germanica*)	C	6	+	+	−	−	−	50%	nd	×	67%	×	100% of 1*	×	IgE	50% of 4	*Challenge: nasal
Cricket, locust	CR	2	+	+	+	+	−	nd	×	×	100%	×	100%	×	IgE	100%	Prausnitz-Küstner (n = 1); positive

TABLE I. (*Continued*)

												Symptoms						Methods				
Substances	Abbre-viation	Formula	MW	CAS-Number	TLV-TWA (USA)	EU Label	TLV-TWA (Germany)	Sa Sah	Reference	Study	n	R	Con.	A	Cou.	S	Tot.	LFT	Skin test	Spec. challenge	Antibodies	Remarks
Cricket, locust									Tee, Gordon et al. [1988]	C	15	+	–	+	–	+	60%	nd	× 67%	nd	× IgE 73%	Immunoblot with IgE: 7 allergen bands [18-68 kDa]
”									Soparkar, Patel et al. [1993]	C	17	+	–	+	–	+	59%	nd	× 41% of 16	× 100% of 1	nd	A single case was the reason for this study
Echinodorus plamosus larvae									Resta, Foschino-Barbaro et al. [1982]#	I	1	+	+	+	–	–	nd	nd	× +	× +*	× IgE +	*Challenge: FEV1 decrease of about 15%
Fruit flies (*Drosophila melanogaster*)									Spieksma, Vooren et al. [1986]	C	22	–	–	+	–	–	32%	nd	× 41%	× 21% of 14*	× IgE 45%	*Challenge: simultaneously nasal and bronchial; 9 pos. nasal reactions (64%), out of them 3 pos. bronchial reactions
Greenbottle (*Lucilia caesar*; fish bait)									Siracusa, Bettini et al. [1994]	S	14	+	+	+	–	–	nd	×	× 92% of 13	× 67% of 6	× IgE 50% of 12	See also *T. molitor* and *G. Mellonella*
Ground bugs (family *Lygaeidae*)									Garcia Lazaro, Abengozar Muela et al. [1997]	I	1	+	+	+	–	–	nd	×	× +	× +*	× IgE +	*Challenge: conjunctival
Gypsy moth (*Lymantria dispar*)									Etking, Odell et al. [1982]	C	17	–	+	+	–	+	59%	nd	× 88%*	nd	nd	*Skin test: scratch
Honeybee (*Apis mellifera*)									Ostrom, Swanson et al. [1986]	I	1	–	–	+	+	–	nd	nd	× +	× +	× IgE +	RAST inhibition
Mealworm (larva of flour worm *Tenebrio molitor*)									Friedrich [1986]	I	1						nd	nd	× +	× +	× IgE +	
”									Schroeckenstein, Meier-Davis et al. [1990]	I	1	+	+	–	–	–	nd	nd	× +	nd	× IgE +	Cross-reactivity with *Alphitobius diaperinus* in SPT and RAST
”									Siracusa, Bettini et al. [1994]	S	14	+	+	+	–	–	nd	×	× 23% of 13	× 100% of 1	× IgE 8% of 12	See also *L. caesar* and *G. mellonella*
Non-biting midges (*Chironomus thummi thummi*)									Liebers, Hoernstein et al. [1993]	C	225	62%	63%	45%	–	37%	nd	nd	× 54% of 94	nd	× IgE 34% IgG 20%	Association between symptoms and degree of exposure
Sheep blowfly (*Lucilia cuprina*)									Kaufman, Gandevia et al. [1989]	C	53	+	+	+	–	+	28%	nd	nd	nd	× IgE 37%	
Sewer flies (*Psychoda alternata*)									Gold, Mathews et al. [1985]	I	1	+	+	+	–	–	nd	×	× +	× +	× IgE +	Prausnitz-Küstner: positive
Silkworm									Harindranath, Prakasth et al. [1985]	C	243	–	–	17%	–	–	nd	nd	× 22%	nd	× IgE 87%; 80% of 15*	*IgE: 87% to cocoon allergens, 80% to pupal allergens
“Seafood”																						
Clam									Desjardins, Malo et al. [1995]	C	57	7%	–	4%	–	–	nd	nd	× 7%	× 100% of 2	× IgE 7% of 55	See also crabs
Lobster									Lemiere, Desjardins et al. [1996b]	I	1	+	+	+	–	+	nd	×	nd	× +	× IgE +	See also crabs

TABLE I. (*Continued*)

Substances	Abbre-viation	Formula	MW	CAS-Number	TLV-TWA (USA)	EU Label	TLV-TWA (Germany)	Sa Sah	Reference	Study	n	Symptoms: R	Con.	A	Cou.	S	Tot.	Methods: LFT	Skin test		Spec. challenge		Antibodies			Remarks
Shrimp									Lemiere, Desjardins et al. [1996b]	I	1	+	+	+	–	+	nd	×	nd		×	+	×	IgE	+	See also lobster
”									Desjardins, Malo et al. [1995]	C	57	5%	–	4%	–	–	nd	nd	×	16%	×	50% of 2	×	IgE	14% of 55	See also clam
Snow crab									Cartier, Malo et al. [1986b]	C	303	?	?	?	?	?	?	nd	×	55% of 119	nd		×	IgE	54% of 115	Data collection over several years; no information about symptoms
Water-flea (*Daphnia*)									Meister [1978]#	CR	2	–	–	+	–	+	nd	nd	×	100%	×	100% of 1	nd			
Fish																										
Plaice, salmon, tuna, sardine, trout etc.									Rodriguez, Reano et al. [1997]	CR	2	+	+	+	+	–	nd	×	×	100%	×	100%	×	IgE	100%	Oral challenge: negative
Salmon									Douglas, McSharry et al. [1995]	C	291	–	–	+	+	–	42%	×	nd		nd		×	IgE IgG	8.6% 33%	
Trout									Sherson, Hansen et al. [1989]	S	8	+	–	+	+	–	nd	×	nd		×*	67% of 6	×	IgE	100%	*PEFR measurement in the workplace; high concentrations of endotoxins
Dander, hair, and urine of animals								Sah																		
Cow hair									Hinze, Bergmann [1995]	S	67	+	+	+	+	+	nd	×	×	97% of 61	×	84% of 37	×	IgE	82.5% of 40	
Deer dander									Nahm, Park et al. [1996]	I	1	+	–	+	–	–	nd	nd	×	+	×	+	×	IgE	+	Immunoblot: 5 IgE binding components
Laboratory animals																										
Dust of laboratory animals (guinea pigs, rats, mice, rabbits, hamsters)									Krakowiak, Szulc et al. [1997]	C	60	7%	–	13%	–	–	nd	×	×	54% of 26*	nd		×	IgE	15%	*SPT: all tested subjects (n = 26) were atopics
Urine of laboratory animals (guinea pigs, rats, mice, rabbits)									Venables, Tee et al. [1988	C	138	+	+	+	–	+	44%	nd	×	13% of 133	nd		×	IgE	38% of 130	
Pig urine									Haries, Cromwell [1982]	I	1	–	–	+	–	+	nd	nd	×	+	×	+	×	IgE	+	
Mice									Hollander, Doekes et al. [1996]	C	540	–	–	3%	–	4%	10%	nd	×	9.8%	nd		×	IgE	6.1%	See also rats
Mink urine									Jimenez Gomez, Anton et al. [1996]	I	1	+	+	+	+	–	nd	×	×	+	×	+	×	IgE	–	SPT: mink pelt negative
Rats									Hollander, Doekes et al. [1996]	C	540	–	–	6%	–	11%	nd	nd	×	18%	nd		×	IgE	11%	See also mice
Other animals and their products																										
Casein (main milk protein)									Rossi, Corsico et al. [1994]	I	1	+	–	+	+	–	nd	nd	×	+	×	+	×	IgE	+	
”									Olaguibel, Hernandez et al. [1990]	I	1	+	–	+	+	–	nd	nd	×	+	×	+	×	IgE	+	Oral challenge: patient tolerated cow milk

TABLE I. (*Continued*)

												Symptoms						Methods								
Substances	**Abbreviation**	**Formula**	**MW**	**CAS-Number**	**TLV-TWA (USA)**	**EU Label**	**TLV-TWA (Germany)**	**Sa Sah**	**Reference**	**Study**	**n**	**R**	**Con.**	**A**	**Cou.**	**S**	**Tot.**	**LFT**	**Skin test**		**Spec. challenge**		**Antibodies**			**Remarks**
Egg powder (egg white, ovalbumin, ovomucoid, lysozyme, conalbumin)									Bernstein, Smith et al. [1987]	C	25	–	–	+	–	–	?	×	×	32%	×	24%*	×	IgE	16%	*PEFR measurement in the workplace. Number of symptomatic subjects not given
"									Smith, Bernstein et al. [1990]	C	188	–	–	+	–	–	31%	nd	×	34% of 86	×	22%*	×	IgE	26% of 87	*PEFR measurement in the workplace
Frogs									Armentia, Martin-Santos et al. [1988]	I	1	+	+	+	–	–	nd	nd	×	+	nd		×	IgE IgG	+ –	Venom of frog skin glands was identified to be the allergen. Prausnitz-küstner: pos.
Ivory									Armstrong, Neill et al. [1988]	I	1	–	–	+	–	–	nd	×	×	–	×	+	×	IgE	–	Although IgE and SPT were negative a type I reaction is suspected
Lactoalbumin									Rossi, Corsico et al. [1994]	I	1	+	–	+	+	–	nd	nd	×	+	nd		×	IgE	+	See also casein
Poultry (feather extract)									Perfetti, Cartier et al. [1997]	CR	4	+	+	+	–	–	nd	×	×	100%	×	100%*	nd			*FEV1 measurement in the workplace: decrease 20%
Plants																										
Amaryllis (family *Amaryllidaceae*, order *Hippeastrum*)									Jansen, Visser et al. [1996]	I	1	+	–	+	–	–	nd	×	×	+	×	+	×	IgE	+	
Anis seed (*Pimpinella anisum*)									Fraj, Lezaun et al. [1996]	I	1	–	–	+	+	–	nd	×	×	+	×	+	×	IgE	+	SPT: 12 other spices neg.
Asparagus (*Asparagus officinalis*)									Lopez-Rubio, Rodriguez et al. [1998]	I	1	+	+	+	+	–	nd	×	×	+	×	+	×	IgE	+	SPT, challenge, IgE test with raw asparagus pos.; neg. with cooked aspar.
"Baby's breath" (*Gypsophila paniculata*)									Antepara, Jauregui et al. [1994]	I	1	+	–	+	+	–	nd	×	×	+	×	+	×	IgE	+	Immunoblot: 3 IgE binding regions (20–40 kDa)
Buckwheat flour									Park, Nahm [1996]	I	1	+	–	+	–	–	nd	nd	×	+	×	+	×	IgE IgG4	+ +	Immunoblot: 8 IgE binding regions
Cacao beans									Perfetti, Lehrer et al. [1997]	I	1	+	–	+	+	–	nd	×	×	+	×	+	×	IgE	+*	*IgE: weak binding
3-Carene (terpene)									Eriksson, Levin et al. [1997]	C	38	–	+	+	–	–	21%	×	nd		nd		nd			
Castor beans								Sa	Merget, Heger et al. [1994]	I	1	+	–	+	–	–	nd	×	×	+	×	+	×	IgE	+	
"									Baur, Chen et al. [1998]	I	1	+	+	+	–	–	nd	×	×	+	nd		×	IgE	+	
Chicory (*Cichorium intybus*)									Nemery, Demedts [1989]	I	1	+	–	+	+	+	nd	×	×	+*	nd		nd			*Skin test: patch
Decorative flowers (freesias, chrysanthemums, tulips)									Piirila, Keskinen et al. [1994]	CR	4	+	+	+	–	+	nd	×	×	50%	×	100% of 3	×	IgE	100% of 3	
Dried flowers (*Limonium tataricum*)									Quirce, Garcia-Figueroa et al. [1993]	I	1	+	+	+	–	+	nd	×	×	+	×	+	×	IgE	+	SPT also positive with grass
Entada gigas seed									Rubin, Duke [1974]#	I	1	+	+	+	–	–	nd	nd	×	+	nd		nd			
Garlic dust									Falleroni, Zeiss et al. [1981]	I	1	+	–	+	–	–	nd	×	×	+	×	+	×	IgE	+	Additional reaction to onion dust

TABLE I. (*Continued*)

Substances	Abbre-viation	Formula	MW	CAS-Number	TLV-TWA (USA)	EU Label	TLV-TWA (Germany)	Sa Sah	Reference
Ginseng (brazil; *Pfaffia paniculata*)									Subiza, Subiza et al. [1991]
Gluten derivative (AHGD: alkaline hydrolysis wheat glutene derivative)									Lachance, Cartier et al. [1988]
Grain dust									Massin, Bohadana et al. [1995]
Green bean									Igea, Fernandez et al. [1994]
Green (raw) coffee beans (dust)									Larese, Fiorito et al. [1998]
"									Zuskin, Kanceljak et al. [1985]
"									Jones, Hughes et al. [1982]
Herbs (thyme, rosemary, bay leaf, garlic)									Lemiere, Cartier et al. [1996a]
Hops									Newmark [1978]
Mushrooms									Symington, Kerr et al. [1981]
Natural textile fibres (cotton, flax, jute)									Muittari, Veneskoski [197
Pea (*Lathyrus odoratus*)									Jansen, Vermeulen et al. [1995]
Pea flour									Bhagat, Swystun et al. [1995]
Pectin (carbohydrate of plant cells)									Cohen, Forse et al. [1993]
Poppy (*Papaver somniferum*)									Moneo, Alday et al. [1993]#
Roasted coffee beans									Lemiere, Malo et al. [1996c]

Substances	Study	n	Symptoms: R	Con.	A	Cou.	S	Tot.	Methods: LFT	Skin test		Spec. challenge		Antibodies			Remarks
Ginseng (brazil; *Pfaffia paniculata*)	I	1	+	+	+	–	–	nd	×	×	+	×	+	×	IgE IgG	+ –	No hypersensitivity reaction to Korean ginseng (Panax ginseng)
Gluten derivative (AHGD: alkaline hydrolysis wheat glutene derivative)	I	1	+	+	+	–	–	nd	×	×	+	×	+	×	IgE	+	
Grain dust	C	118	–	–	5%	30%	–	nd	×	nd		nd		nd			Significantly more symptoms in exposed subjects than in controls (n = 164). LFT in controls better than in exposed subjects
Green bean	I	1	+	+	+	–	+	nd	×	×	+	×	+	×	IgE	+	SPT: cooked beans: neg. No problems after bean consumption
Green (raw) coffee beans (dust)	C	31	+	+	+	–	–	19.4%	×	×	26%	nd		nd			
"	S	9	+	–	+	+	–	nd	×	×	78%*	×	45%	nd			*Skin test: intradermal
"	C	372	–	–	+	+	–	nd	×	×	10% of 362	nd		×	IgE	7% of 341	The average FEV1 decreased with the duration of occupation
Herbs (thyme, rosemary, bay leaf, garlic)	I	1	–	–	+	+	–	nd	×	×	+	×	+	×	IgE	+	No problems after herb consumption
Hops	I	1	+	+	+	–	+	nd	nd	×	+*	nd		nd			*Skin test: scratch
Mushrooms	S	8	+	–	+	–	–	nd	×	×	63%	×	50%	nd			
Natural textile fibres (cotton, flax, jute)	C	136	–	–	+	–	–	nd	nd	×	54% of 104	×	19% of 108	nd			Mixed exposure to synthetic fibres as well as to wool and silk
Pea (*Lathyrus odoratus*)	I	1	+	+	+	–	–	nd	×	×	+	×	+*	×	IgE	+	*Challenge: PEFR measurement before and after work: FEV1 decrease >20%
Pea flour	I	1	–	–	+	+	–	nd	×	×	+	nd		nd			Non-specific challenge with histamine: positive
Pectin (carbohydrate of plant cells)	I	1	+	–	+	–	–	nd	×	×	+	×	+*	nd			*Challenge: PEFR measurement before and after work: FEV1 decrease of 16%
Poppy (*Papaver somniferum*)	C	28	?	?	?	?	?	21%	nd	×	21%	×	100% of 4	×	IgE IgG	21% –	Immunoblot: IgE binding in the region of 52 kDa. Allergens may be polyphenols
Roasted coffee beans	I	1	+	+	+	–	–	nd	×	×	+	×	+	×	IgE	+	

TABLE I. *(Continued)*

Substances	Abbre-viation	Formula	MW	CAS-Number	TLV-TWA (USA)	EU Label	TLV-TWA (Germany)	Sa Sah	Reference	Study	n	R	Con.	A	Cou.	S	Tot.	LFT		Skin test		Spec. challenge		Antibodies		Remarks
												Symptoms						Methods								
Rose hips									Kwaselow, Rowe et al. [1990]	CR	13	+	–	+	–	+	nd	nd	×	62%	×	50% of 4	×	IgE	64%	
Ryegrass juice (*Lolium perenne*)									Subiza, Subiza et al. [1995]	I	1	+	+	+	+	–	nd	×	×	+	×	+	×	IgE	+	SPT with moulds: negative
Saffron (*Crocus sativus*)									Feo, Martinez et al. [1997]	C	50	16%	–	6%	–	8%	nd	nd	×	6%	×	100% of 3	×	IgE	6%	Challenge: 2 conjunctival, 1 bronchial; 4.2% out of 237 controls showed positive SPT (cross reactivity with pollen)
Sarsaparilla root dust (family *Liliacea*, order *Smila*)									Vandenplas, Depelchin et al. [1996]	I	1	+	–	+	–	–	nd	×	×	+	×	+	×	IgE	+	Component of herbal tea
Sesame seeds (*Sesame indicum*)									Keskinen, Ostman et al. [1991]	I	1	+	–	+	+	+	nd	×	×	+	×	+	×	IgE	+	
Sisal									Zuskin, Kanceljak et al. [1994]	C	20	75%	–	10%*	65%	–	nd	×	×	10%	nd		×	IgE	10%	*Asthma
Spices (paprika, coriander, mace)									Sastre, Olmo et al. [1996]	I	1	+	–	+	–	–	nd	nd	×	+	×	+	×	IgE	+	
Sunflower pollen (*Helianthemum annuus*)									Bousquet, Dhivert et al. [1985]	I	1	+	+	+	–	–	nd	×	×	+	×	+	×	IgE	+	SPT with sunflower seed: negative
Sunflower seeds									Vandenplas, Vander Borght et al. [1998]	I	1	+	+	+	–	–	nd	×	×	+	×	+	×	IgE	+	SPT with sunflower pollen: negative
Tea									Cartier, Malo [1990]	S	3	+	–	+	+	–	nd	×	×	– (100%)	×	67%	×	IgE	– (100%)	
Tobacco dust									Baur [1993]	I	1	+	+	+	–	–	nd	×	×	+	×	+*	×	IgE	+	Challenge: nasal
"									Lander, Gravesen [1988]	C	16	–	–	+	–	–	nd	×	nd		×*		nd			*PEFR measurement before and after work: FEV1 variation in exposed subjects significantly greater than in 32 controls
Vetch (*Vicia sativa*)									Picon, Blanco Carmona et al. [1991]	I	1	–	–	+	+	–	nd	×	×	+	×	+	×	IgG	+	Challenge: late bronchial reaction Prausnitz-Küstner: pos.
Weeping fig (*Ficus benjamina*)									Axelsson, Johansson et al. [1987]	C	84	+	+	+	–	+	17%	nd	×	21%	×	100% of 6	×	IgE	21%	Rhinoconjunctival challenge (n = 9): all positive
Vegetable gums																										
Gaur gum (of *Cypamopsis tetragonolobus*)									Malo, Cartier et al. [1990]	C	162	20%	12%	23%	+	11%	nd	nd	×	5%	×	50% of 4	×	IgE IgG	8% 14% of 133	
Karaya gum									Wagner [1980]	I	1	+	–	+	–	–	nd	×	×	+*	×	+	nd			*Skin test: scratch
Latex (natural rubber latex)				9006-04-6				Sah	Grzybowski, Ownby et al. [1996]	C	741	+	+	+	–	+	60%	nd	nd		nd		×	IgE	9%	
"									Baur, Chen et al. [1995a]	C	111	11%	9%	4%	–	23%	nd	nd	nd		nd		×	IgE	15.3%	

TABLE I. (*Continued*)

Substances	Abbre-viation	Formula	MW	CAS-Number	TLV-TWA (USA)	EU Label	TLV-TWA (Germany)	Sa Sah	Reference	Study	n	Symptoms: R	Con.	A	Cou.	S	Tot.	Methods: LFT	Skin test	Spec. challenge	Antibodies	Remarks
Latex (natural rubber latex)									Yassin, Lierl et al. [1994]	C	224	13%	13%	+	5%	10%	49%	nd	× 17%	nd	nd	Symptoms in SPT pos. subjects significant more frequent than in SPT neg. subjects
Soybean compounds								Sa														
Soybean									Alvarez, Tabar et al. [1996]	S	21	+	–	+	–	–	nd	nd	× 43%	× 56% of 9	× IgE 80% of 5	
Soybean flour									Baur, Sauer et al. [1989]#	S	261	+	+	+	–	–	nd	nd	nd	nd	× IgE 32%	
Soybean lecithin									Lavaud, Perdu et al. [1994]	CR	2	+	–	+	–	–	nd	×	× 100%	× 100%	× IgE 100%	
Grain flour dust				68525-86-0			4 mg/m^3	Sa														
Barley flour									Vidal, Gonzalez-Quintela [1995]	I	1	–	–	+	–	–	nd	×	× +	× +	× IgE +	Oral challenge with beer: positive
Wheat flour									Baur, Degens et al. [1998]	S	193	+	+	+	+	+	nd	×	× 33%	× 55% of 47	× IgE 58%	Also positive reaction to α-amylase and rye flour
"									Houba, Heederik et al. [1998]	C	393	21%	15%	7%	+	–	nd	nd	nd	nd	× IgE 10%	
"									De Zotti, Larese et al. [1994]	C	226	14%	14%	19%	–	–	nd	nd	× 12%	nd	nd	
Rye flour									Baur, Degens et al. [1998]	S	193	+	+	+	+	+	nd	×	× 25%	× 69% of 64	× IgE 42%	Also positive reaction to α-amylase and wheat flour
Wood and wood compounds																						
Abietic acid									Burge, Harries et al. [1980]	S	51	–	–	+	–	–	nd	×	nd	× 100% of 6	nd	Positive reaction after colophonium challenge
Colophonium						R 42/43			Burge, Edge et al. [1981]	C	45	–	–	4%-21%*	–	–	nd	×	× –	nd	× IgE –(in 30)	*:Asthma; Patients were divided into 3 exposure groups
"									So, Lam et al. [1981]	I	1	–	–	+	+	–	nd	×	nd	× +	nd	
"									Burge, Harries et al. [1980]	S	51	–	–	+	–	–	nd	×	nd	× 67%	nd	FEV1 decrease with American colophonium in 83% out of 12 cases lower than with Portuguese colophonium
Plicatic acid																						see red cedar and white cedar
Tall oil									Tarlo [1992]	I	1	+	–	+	–	–	nd	×	× –*	× +	nd	*Skin test: patch with abietic acid, colophonium and pine tar
Wood dust (TRK value)							2 mg/m^3															
Wood dust									Wilhelmsson, Jernudd et al. [1985]#	C	268	–	–	+	–	–	16%	nd	× 13% of 23	× 13% of 23*	nd	*Challenge: nasal
Alnus glutinosa (alder)									Ahman, van Hage-Hamsten et al. [1995]	C	127	+	+	+	+	–	nd	nd	nd	nd	× IgE 0.8%	Discussion, whether for wood SPT is more suitable than IgE detection

TABLE I. (*Continued*)

												Symptoms						Methods								
Substances	**Abbreviation**	**Formula**	**MW**	**CAS-Number**	**TLV-TWA (USA)**	**EU Label**	**TLV-TWA (Germany)**	**Sa Sah**	**Reference**	**Study**	**n**	**R**	**Con.**	**A**	**Cou.**	**S**	**Tot.**	**LFT**	**Skin test**		**Spec. challenge**		**Antibodies**			**Remarks**
Aningeria robusta (mukali)									Garces Sotillos, Blanco Carmona et al. [1995]	I	1	–	–	+	–	+	nd	×	×	+	×	+	nd			Challenge and SPT: negative with pine and iroko
Balfourodendron riedelianum (pau marfim)									Basomba, Burches et al. [1991]	I	1	+	–	+	–	–	nd	×	×	+	×	+	×	IgE	+	
Chlorophora excelsa (iroko, kambala)									Kersten, von Wahl [1994]	S*	157	?	?	?	?	?	nd	nd	×	5.3%*	×	7.8%*	nd			*Patients claiming for compensation due to occupational asthma. *SPT: 263 tests with 18 wood types. *Challenge: 90 tests with 14 wood types.
Euonymus europaeus (spindle tree)									Herold, Wahl et al. [1991]	I	1	+	+	+	–	–	nd	nd	×	+*	×	+*	×	IgE	+	*Skin test: scratch; *challenge: nasal
Fagus sylvatica (beech)									Oertmann, Bergmann [1993]	S*	55	–	–	+	–	–	nd	nd	nd		×	50% of 2	nd			*Patients claiming for compensation due to occupational asthma
"									Spiewak, Bozek et al. [1994]	I	1	+	+	+	–	–	nd	×	×	–	×	+	nd			See also ash, oak, pine
"									Kersten, von Wahl [1994]	S*	157	?	?	?	?	?	nd	nd	×	6.1%*	×	6.7%*	nd			*Patients claiming for compensation due to occupational asthma. *SPT: 263 tests with 18 wood types. *Challenge: 90 tests with 14 wood types.
Fraxinus excelsior (ash)									Fernandez-Rivas, Perez-Carral et al. [1997]	I	1	+	+	+	+	–	nd	×	×	+*	×	+*	×	IgE	+	*Skin test: intradermal *Challenge: FEV1 decrease: 18%
"									Oertmann, Bergmann [1993]	S*	55	–	–	+	–	–	nd	nd	nd		×	100% of 2	nd			*Patients claiming for compensation due to occupational asthma
"									Spiewak, Bozek et al. [1994]	I	1	+	+	+	–	–	nd	×	×	–	×	+	nd			See also beech, oak, pine
Gaboon									Kersten, von Wahl [1994]	S*	157	?	?	?	?	?	nd	nd	×	5.3%*	×	4.4%*	nd			*Patients claiming for compensation due to occupational asthma. *SPT: 263 tests with 18 wood types. *Challenge: 90 tests with 14 wood types.
Gonystylus bancanus (ramin)									Hinojosa, Losada et al. [1986]	S	2	–	–	+	–	–	nd	×	×	100%	×	–(100%)	nd			Cross-reactivity with obeche (*Triplochiton scleroxylon*)
Khaya anthoteca (african. mahaghoni)									Oertmann, Bergmann [1993]	S*	55	–	–	+	–	–	nd	nd	nd		×	50% of 4	nd			*Patients claiming for compensation due to occupational asthma
Microberlinia (african. zebrawood)									Bush, Yunginger et al. [1978]	I	1	–	–	+	–	–	nd	×	×	+	×	+	×	IgG IgE	– +	

TABLE I. (*Continued*)

Substances	Abbre-viation	Formula	MW	CAS-Number	TLV-TWA (USA)	EU Label	TLV-TWA (Germany)	Sa Sah	Reference	Study	n	R	Con.	A	Cou.	S	Tot.	LFT	Skin test	Spec. challenge	Antibodies	Remarks
												Symptoms						Methods				
Phoebe porosa (imbuia)									Jeebhay, Prescott et al. [1996]	I	1	+	–	+	–	–	nd	×	nd	× +	× IgG +	
Picea abis (spruce)									Oertmann, Bergmann [1993]	S*	55	–	–	+	–	–	nd	nd	nd	× 0% of 2	nd	*Patients claiming for compensation due to occupational asthma
"									Kersten, von Wahl [1994]	S*	157	?	?	?	?	?	nd	nd	× 8.4%*	× 2.2%*	nd	*Patients claiming for compensation due to occupational asthma. *SPT: 263 tests with 18 wood types. *Challenge: 90 tests with 14 wood types.
Pinus sylvestris (pine)									Spiewak, Bozek et al. [1994]	I	1	+	+	+	–	–	nd	×	× –	× +	nd	See also beech, oak, ash
"									Kersten, von Wahl [1994]	S*	157	?	?	?	?	?	nd	nd	× 5.3%*	× 5.6%*	nd	*Patients claiming for compensation due to occupational asthma. *SPT: 263 tests with 18 wood types. *Challenge: 90 tests with 14 wood types.
Prunus avium (cherry tree)									Abendroth, Kalveram et al. [1992]	C	33	51%	–	–	–	–	nd	×	nd	nd	× IgE 80% of 10	See also oak
Quillaja saponaria (Soapbark)									Raghuprasad, Brooks et al. [1980]	I	1	+	+	+	–	–	nd	×	nd	× +	× IgE +	Cross-reactivity with gum acacia and gum tragacanth
Quercus (Oak)									Oertmann, Bergmann [1993]	S*	55	–	–	+	–	–	nd	nd	nd	× 33% of 3	nd	*Patients claiming for compensation due to occupational asthma
"									Malo, Cartier et al. [1995]	CR	3	+	–	+	+	–	nd	×	× – (100%)	× 100%	nd	Challenge: 2 dual and 1 late bronchial reaction
"									Abendroth, Kalveram et al. [1992]	C	33	51%	–	–	–	–	nd	×	nd	nd	× IgE 80% of 10	See also cherry tree
Swietenia mahagoni (Americ. mahagoni)									Kersten, von Wahl [1994]	S*	157	?	?	?	?	?	nd	nd	× 8%*	nd	nd	*Patients claiming for compensation due to occupational asthma. * SPT: 263 tests with 18 wood types.
Tectona grandis (teak)									Oertmann, Bergmann [1993]	S*	55	–	–	+	–	–	nd	nd	nd	× 50% of 2	nd	*Patients claiming for compensation due to occupational asthma
Terminalia superba (limba)									Oertmann, Bergmann [1993]	S*	55	–	–	+	–	–	nd	nd	nd	× 33% of 3	nd	*Patients claiming for compensation due to occupational asthma
Thuja occidentalis (eastern white cedar)									Cartier, Chan et al. [1986a	I	1	–	–	+	+	–	nd	×	nd	× +*	× IgE +*	*Challenge: FEV1 decrease only 12% *IgE to plicatic acid (see there)
"									Malo, Cartier et al. [1994a]	C	43	–	–	+	+	–	58%	×	nd	× 25% of 12*	nd	*Challenge: with plicatic acid (see there)
Thuja plicata (red cedar)								Sah														See plicatic acid

TABLE I. (*Continued*)

Substances	Abbre-viation	Formula	MW	CAS-Number	TLV-TWA (USA)	EU Label	TLV-TWA (Germany)	Sa Sah	Reference	Study	n	Symptoms: R	Con.	A	Cou.	S	Tot.	Methods: LFT	Skin test		Spec. challenge		Antibodies			Remarks
Plicatic acid (PA, major allergen or red cedar) white cedar contains half the PA amount of red cedar									Cote, Kennedy et al. [1990]	S	23	–	–	+	+	–	nd	nd	nd		×	61%	nd			See red cedar and white cedar
"									Lam, Tan et al. [1983]	S*	206	–	–	+	–	–	nd	×	nd		×	100% of 8	×	IgE IgG	30%* –	*S: Patients with diagnosed red cedar asthma; *IgE to red cedar dust: 25%
"									Chan-Yeung, Desjardins [1992]	S	4	+	–	+	–	–	nd	×	nd		×	100%	×	IgE	75%	
Tieghemella heckeli (macrore)									Oertmann, Bergmann [1993]	S*	55	–	–	+	–	–	nd	nd	nd		×	80% of 5	nd			*Patients claiming for compensation due to occupational asthma
"									Kersten, von Wahl [1994]	S*	157	?	?	?	?	?	nd	nd	×	11.4%*	×	15.6%*	nd			*Patients claiming for compensation due to occupational asthma. *SPT: 263 tests with 18 wood types. *Challenge: 90 tests with 14 wood types.
Triplochiton scleroxylon (obeche)								Sah	Hinojosa, Losada et al. [1986]	S	4	–	–	+	–	–	nd	×	×	100%	×	100%	×	IgE	100%	Cross-reactivity with ramin (*Gonystylus bancanus*)
"									Oertmann, Bergmann [1993]	S*	55	–	–	+	–	–	nd	nd	nd		×	75% of 8	nd			*Patients claiming for compensation due to occupational asthma.
"									Kersten, von Wahl [1994]	S*	157	?	?	?	?	?	nd	nd	×	11.8%*	×	22.2%	nd			*Patients claiming for compensation due to occupational asthma. *SPT: 263 tests with 18 wood types. *Challenge: 90 tests with 14 wood types.
Microorganisms																										
Fungi																										
Aspergillus niger									Seaton, Wales [1994]	C	261	–	–	+	+	–	30%	nd	×	9.6%	nd		nd			After 7 years: 14% of sympt. and 49% of non-symptomatic subjects remained
Aspergillus fumigatus									Allmers, Huber et al. [1997]	I	1	–	–	+	+	–	nd	×	×	+	×	+	×	IgE	+	Diagnosis: ABPA (allergic bronchopulmonary aspergillosis)
Chrysonila sitophila									Tarlo, Wai et al. [1996]	I	1	+	+	+	+	–	nd	×	×	+	×	+*	×	IgE	+	*PEFR measurement in the workplace
Dictyostelium discoideum (slime mould)									Gottlieb, Garibaldi et al. [1993]	I	1	+	+	+	–	–	nd	× *	×	+	nd		×	IgE	+	*LFT before and after working with the mould – > FEV1 decrease of 14%
Neurospora sp.									Cote, Chan et al. [1991]	I	1	–	–	+	–	–	nd	×	×	+	×	+	×	IgE	+	
Paecilomyces sp.									Wilhelmsson, Jernudd et al. [1985] #	C	268	–	–	+	–	–	16%	nd	×	43% of 23*	×	50% of 10*	×	IgG	32%	*SPT: only in symptomatic subjects; *challenge: nasal

TABLE I. (*Continued*)

Substances	Abbre-viation	Formula	MW	CAS-Number	TLV-TWA (USA)	EU Label	TLV-TWA (Germany)	Sa Sah	Reference
Saccharomyces cerevisiae									Belchi-Hernandez Mora-Gonzalez et al. [1996]
"									Musk, Venables et al. [1989]
"									Baldo, Baker [1988]
Mold-containing dust									Musk, Venables et al. [1989]
Aspergillus, Mucor, Cladosporium									Wallenstein, Bergmann et al. [1980]#
Enzymes									
α-Amylase				9000-90-2		R 42		Sa	
α-Amylase of Aspergillus oryzae									Losada, Hinojosa et al. [1992]
"									Quirce, Cuevas et al. [1992]
"									Baur, Chen et al. [1994]
Bromelain (protease of plant family *Bromeliaceae*)				9001-00-7		R 42			Gailhofer, Teubl et al. [1987]#
Cellulase of *Aspergillus niger*				9012-54-8		R 42			Sander, Raulf-Heimsoth et al. [1998]
"									Tarvainen, Kanerva et al. [1991]
"									Losada, Hinojosa et al. [1986]
Esperase® (protease)						(R 42)			Johnsen, Sorensen et al. [1997]
"									Zachariae, Hoech-Thomsen et al. [1981]
Glucoamylase of *Aspergillus niger* (Amyloglucosidase)									Baur, Sauer et al. [1989]#
"									Sander, Raulf-Heimsoth et al. [1998]
Glucose oxidase of *Aspergillus niger*									Baur [1981]

Substances	Study	n	Symptoms						Methods								Remarks
			R	Con.	A	Cou.	S	Tot.	LFT	Skin test		Spec. challenge		Antibodies			
Saccharomyces cerevisiae (Belchi-Hernandez Mora-Gonzalez et al. [1996])	I	1	–	–	+	+	–	nd	×	×	+	×	+	×	IgE	+	
" (Musk, Venables et al. [1989])	C	279	+	–	+	–	–	25%	×	×	1% of 259	nd		nd			See also grain mites, moulds
" (Baldo, Baker [1988])	S	47	+	–	+	–	+	nd	nd	×	66%	nd		×	IgE	68%	Tests were performed with Enolase of *S. cerevisiae* –> an important allergen
Mold-containing dust	C	279	+	–	+	–	–	25%	×	×	2% of 259	nd		nd			See also grain mites, *Saccharomyces c.*
Aspergillus, Mucor, Cladosporium	S	437	?	?	?	?	?	nd	nd	×	95%*	×	4% of 354	nd			*Skin test: intradermal
Enzymes																	
α-Amylase																	
α-Amylase of Aspergillus oryzae (Losada, Hinojosa et al. [1992])	C	83	59%	–	30%	–	–	nd	nd	×	31%	×	43% of 14	×	IgE	52%	Oral challenge: 1 of 5 subjects (20%) positive
" (Quirce, Cuevas et al. [1992])	S	5	+	+	+	–	–	nd	×	×	100%	×	100%	×	IgE	100%	
" (Baur, Chen et al. [1994])	C	89	+	–	+	–	–	48%	nd	×	18%	nd		×	IgE	16%	
Bromelain (protease of plant family *Bromeliaceae*)	CR	2	+	+	+	–	–	nd	nd	×	100%	nd		×	IgE	100%	1 case: anaphylactic shock after ingestion of pineapple
Cellulase of *Aspergillus niger* (Sander, Raulf-Heimsoth et al. [1998])	S	171	+	+	+	–	+	nd	nd	nd		nd		×	IgE	13%	Mixed exposure; cross-reactivity with xylanase
" (Tarvainen, Kanerva et al. [1991])	S	4	+	–	+	–	+	nd	×	×	75%	nd		×	IgE	100%	RAST-inhibition: cross-reactivity with xylanase
" (Losada, Hinojosa et al. [1986])	S	2	+	–	+	+	–	nd	×	×	100%	×	100%	×	IgE IgG	100% –	Prausnitz-Küstner: 100% pos. of 1
Esperase® (protease) (Johnsen, Sorensen et al. [1997])	L	1064	+	–	+	–	+	8.8% (3 J)	×	nd		nd		×	IgE	22% of 653	Mixed exposure; Incidence development 0–15 mon. = 4.9%, 16–27 mon. = 2,8%; 28–39 mon. = 1,1%
" (Zachariae, Hoech-Thomsen et al. [1981])	L	667	+	–	+	+	–	3.3% (10 J)	×	nd		nd		×	IgE	4.7% in 10 Y	
Glucoamylase of *Aspergillus niger* (Amyloglucosidase) (Baur, Sauer et al. [1989]#)	S	261	+	+	+	–	–	nd	nd	nd		nd		×	IgE	5%	Mixed exposure
" (Sander, Raulf-Heimsoth et al. [1998])	S	171	+	+	+	–	+	nd	nd	nd		nd		×	IgE	8%	Mixed exposure
Glucose oxidase of *Aspergillus niger* (Baur [1981])	I	1	–	–	+	–	–	nd	nd	×	+	nd		×	IgE	+	

TABLE I. (*Continued*)

												Symptoms						Methods								
Substances	**Abbreviation**	**Formula**	**MW**	**CAS-Number**	**TLV-TWA (USA)**	**EU Label**	**TLV-TWA (Germany)**	**Sa Sah**	**Reference**	**Study**	**n**	**R**	**Con.**	**A**	**Cou.**	**S**	**Tot.**	**LFT**	**Skin test**		**Spec. challenge**		**Antibodies**			**Remarks**
Hemicellulase of *Aspergillus niger*									Baur, Sauer et al. [1989]#	S	261	+	+	+	−	−	nd	nd	nd		nd		×	IgE	10%	Mixed exposure
Lactase									Muir, Verrall et al. [1997]	C	207	+	+	+	−	−	nd	×	×	31%	nd		nd			
Lysozyme (lysozyme chloride)									Park, Nahm [1997]	I	1	+	−	+	−	−	nd	×	×	+	×	+	×	IgE	+	See peptidase; RAST inhibition: no cross-reactivity
Lysozyme (egg)									Anibarro Bausela, Fontela [1996]	I	1	+	+	+	+	−	nd	×	×	+	×	+	×	IgE	−	See pepsin; RAST inibition: no cross-reactivity
”									Bernstein, Kraut et al. [1993]	I	1	−	−	+	−	−	nd	×	×	+	×	+		IgE	+	
Pancreatin (porcine)									Wiessmann, Baur [1985]	S	14	−	−	+	+	−	nd	×	×	93%	×	100% of 8	×	IgE IgG	75% of 4 14%	Reaction to the single substance α-amylase
Pancreatin (α-amylase of porcine pancreatin)									Aiken, Ward et al. [1997]	I	1	−	−	+	−	−	nd	×	nd		×	+	nd			
Papain of *Carica papaya*				9001-73-4		R 42			Merget, Bergmann et al. [1995]	I	1	+	+	+	−	−	nd	×	×	+	nd		×	IgE	+	
”									Baur, Konig et al. [1982]	C	29	+	+	+	−	+	45%	nd	×	41%	×	89% of 9	×	IgE	40%	
Pepsin				9001-75-6		R 42			Drexler, Beyer [1997]	I	1	−	−	+	−	−	nd	×	×	+	×	+	×	IgE	+	
”									Anibarro Bausela, Fontela [1996]	I	1	+	+	+	+	−	nd	×	×	+	×	+	×	IgE	−	See lysozyme; RAST-inhibition: no cross-reactivity
Peptidase of *Serratia ssp.*									Park, Nahm [1997]	I	1	+	−	+	−	−	nd	×	×	+	×	+	×	IgE	+	See lysozyme; RAST-inhibition: no cross-reactivity
Phytase of *Aspergillus niger*									Straßburger, Bossert et al. [1998]#	C	49	+	+	+	−	−	65%	×	×	34% of 32	×	34% of 32*	×	IgE	31% of 32	*Challenge: nasal
”									Doekes, Kamminga et al. [1999]	C	11	−	−	+	+	−	55%	nd	nd		nd		×	IgE	82%	Significantly evelated IgE level of exposed compared to non-exposed subjects (n = 30)
Suparen® (a rennet of *Endothica parasitica*)									Niinimaki, Saari [1978]	I	1	−	−	+	−	−	nd	nd	×	+*	nd		nd			*Skin test: scratch; skin test with rennet from calf: negative
Trypsin of cow pancreatin				9002-07-7		R 42			Johnsen, Sorensen et al. [1997]	L	1064	+	−	+	+	−	8.8% (3J)	×	nd		nd		×	IgE	11% of 288	Mixed exposure; Incidence development: 0–15 mon. = 4,9%; 16–27 mon. = 2,8%; 28–39 mon. = 1,1%
Trypsin (porcine)						R 42			Colten, Polakoff et al. [1975]	C	14	+	+	+	−	−	29%	×	×	29%*	×	75% of 4	×	IgG	−	*Skin test: scratch; Prausnitz-Küstner: 100% pos. of 2
β-Xylanase									Tarvainen, Kanerva et al. [1991]	CR	2	+	−	+	−	+	nd	×	×	100%	nd		×	IgE	100%	RAST inhibition: cross-reactivity with cellulase

TABLE I. *(Continued)*

Substances	Abbre-viation	Formula	MW	CAS-Number	TLV-TWA (USA)	EU Label	TLV-TWA (Germany)	Sa Sah	Reference
β-Xylanase (*Aspergillus niger*)									Sander, Raulf-Heimsoth et al. [1998]
"									Baur, Sander et al. [1998]
Bacillus subtilis enzymes									
Alkalase® (Subtilisin A) (protease)						R 42			Johnsen, Sorensen et al. [1997]
Proteases (*B.s.*)						R 42			Franz, McMurrain et al. [1971]
Mixture (*B.s.*)									Juniper, How et al. [1977]#
Enzyme dust (mixture)									
Trypsin, chymotrypsin, bromelain, papain = proteolytic enzymes; α-amylase, lipase									Zentner, Jeep et al. [1997]
α-Amylase, cellulase, xylanase									Vanhanen, Tuomi et al. [1996]

Substances	Study	n	Symptoms R	Con.	A	Cou.	S	Tot.	Methods LFT	Skin test		Spec. challenge		Antibodies			Remarks
β-Xylanase (*Aspergillus niger*)	S	171	+	+	+	−	+	nd	nd	nd		nd		×	IgE	11%	Mixed exposure; cross-reactivity with cellulase
"	I	1	+	+	+	−	−	nd	×	×	+	×	+	×	IgE	+	
Bacillus subtilis enzymes																	
Alkalase® (Subtilisin A) (protease)	L	1064	+	−	+	−	+	8.8% (3 J)	×	nd		nd		×	IgE	16% of 799	Mixed exposure; Incidence development: 0–15 mon. = 4,9%; 16–27 mon. = 2,8%; 28–39 mon. = 1,1%
Proteases (*B.s.*)	S	38	−	−	+	−	+	nd	×	×	66%*	×	90% of 10*	×	IgG	48% of 25	*Skin test: intradermal; *challenge; FEV1 decrease of 14–45% Prausnitz-Küstner: 100% pos. of 5
Mixture (*B.s.*)	L	1642	−	−	3%*	−	−	nd	×	×	18%*	nd		×	IgE	°26% of 248	*:Incidence over 7 years °:Alkalase-spec. IgE
Enzyme dust (mixture)																	
Trypsin, chymotrypsin, bromelain, papain = proteolytic enzymes; α-amylase, lipase	S	10	−	+	+	+	−	nd	nd	×	100%	nd		×	IgE	100%	Sensitization to proteolytic enzymes more frequent, SPT: 6 subjects reacted to >3, IgE: 5 subjects reacted to >2 enzymes
α-Amylase, cellulase, xylanase	C	365	+	−	+	+	−	16%	nd	×	5.2%	nd		nd			

Occupational agents which, according to international publications, have proven to be airway sensitizers are presented. Substances are systematically arranged into four groups: chemicals, and those originating from animals, plants or microorganisms. Chemicals are subclassified into isocyanates, anhydrides or amines, metals and their compounds, medicaments, plastics including their monomers, dyes, and other chemicals. Animal categories include mites, insects, seafood, fish, dander, hair and urine of animals, and other animals and their products. Plants and microorganisms are arranged alphabetically and include subgroups of vegetable gums, soybean compounds, grain flour dust, wood and its components. Microorganisms (fungi) and enzymes complete the list.

[a] Modified from: van Kampen V, Merget R, Baur X. 1999. Atemwegssensibilisierende Arbeitsstoffe: Eine Übersicht. Arbeitsmedizin Sozialmedizin. Umweltmedizin. Stuttgart, Germany: Gentner Verlag.

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