

Criteria for allergenic building materials

Friedhelm Diel*, Hans-Jürgen Schubert, Michael Fischer, Thomas Schütz, Klaus-Michael Weber, Michael Gagelmann, Hugo Boonen, Andreas Steneberg, Michaela Axt-Gadermann, Roman Khanferyan**, Eva Diel

*Institute of Environment and Health (IUG) and University of Applied Sciences FH Fulda, Germany

**Institute for Allergy and Asthma, Sedin 4, Krasnodar, Russia

Abstract

Allergenic building materials are increasingly problematic. This is true not only in occupational health, but can also be the reason for the increasing prevalence of indoor allergies. Particularly individuals with family heredity of increased sensitizing potential are in need of special protection and practical criteria for the assessment of allergens in building materials. This article attempts to present a point scale scoring the allergenic potential of e.g. wooden chipboard containing formaldehyde, fixed virgin wool fitted carpet and/or loamy plaster containing nickel.

Four easily understandable scores that are practical for patients as well as building experts are suggested: **No or low - relevant - increased - and highly increased allergenic potential.**

“Direct allergens” have to be differentiated from the “indirect allergens”. Direct allergens are defined as (pseudo-) allergenic compounds, which are emitted from building materials into the indoor air. “Indirect allergens” are defined as spores from moulds, excrements from house dust mites and animal epithelia. These allergens are induced by building defects like increased humidity and anthropogenic facilities. Structure-response-analytical knowledge and occupational hazard management serves as basic data for the assessment of indoor air allergenic potential.

Keywords: Allergens, building material, indoor air; environmental health, hazard assessment

UMWELT & GESUNDHEIT 1 (2003) 6-12

Zusammenfassung

Kriterien allergene Baustoffe

*Allergene Baustoffe stellen nicht nur im Arbeitsschutz ein zunehmendes Problem dar, sondern sind mehr und mehr auch die mögliche Ursache für innenraumbedingte Allergien. Insbesondere familiär vorbelastete Menschen mit einem erhöhten Sensibilisierungsrisiko bedürfen eines besonderen Schutzes sowie praktischer Kriterien zur Beurteilung der Allergenität von Baustoffen. In der vorliegenden Arbeit wird erstmals der Versuch unternommen, mittels eines Punktescores zum Beispiel die formaldehydhaltige Holzspanplatte, einen verklebten Schurwolleteppich oder den nickelhaltigen Lehmputz zu beurteilen. Daraus ergeben sich für Betroffene (Allergiker), wie auch für Baufachleute vier einfach verständliche Beurteilungskategorien: **Keine beziehungsweise geringe, relevante, erhöhte und stark erhöhte Allergenität.** Unterschieden wird zwischen direkter Allergenität, also (pseudo-) allergene Stoffe, die aus den Baumaterialien in die Innenluft emittieren und über die Atemwege aufgenommen werden, sowie indirekter Allergenität wie Schimmelpilz-Sporen, Hausstaubmilben-Exkrementen und Tierepithelien, die also nicht direkt aus Baumaterialien stammen, sondern durch Konstruktionsmängel, wie erhöhte Luftfeuchtigkeit eine allergene Belastung entwickeln können. Struktur-wirkungsanalytische Stofflisten und der Gefahrstoffverordnung müssen auf die umweltmedizinischen Beurteilungen innenraumbedingter Allergenität übertragen werden.*

Schlüsselworte: Allergene, Baustoffe, Innenraumluft, Umweltmedizin, Gefahrstoff-Prüfung

Introduction

Allergens in building materials have been a main topic in occupational health a long time. Especially the resorption of occupational allergens via skin, - as it is known e.g. with chromates in the case of bricklayers which led to minimizing the Cr-concentrations in cement, but also to increased efforts in personal occupational care like wearing protective work clothing. Currently the main focus of interest lies on the air-born indoor allergens which are chronically emitted and inhaled. It must be distinguished between Occupational Medicine/Industrial Safety = relatively high exposure, often short term, for certain clients: healthy adult workers working for eight hours - and Environmental Medicine/Environmental Protection = relatively low pollution, but frequently long-term 24 hours a day chronically incorporated indoor allergens, difficult to quantify: all subgroups of the population and riskgroups. This is especially true for 25 - 30 % atopics in the German population. Last but not least, due to the complicated processes, which the German MAK-List outlines: “Currently it is not possible to set the threshold values for the induction of an allergy (sensitization) or the initiation of an allergic reaction in sensitized subjects.” (DFG 2000) The MAK-list distinguishes between “H” (Hautreaktion = skin reaction) and “S” (Sensitizing) and particularly “Sa” (respiratory sensitizing) and “Sh” (skin sensitizing), “Sha” (both) and “SP” (photosensitizing). The “Senatskommission” at the “DFG” assesses the sensitizing responses, even in cases where the pathomechanisms are largely unknown and/or in cases of pseudo-allergic responses. Pseudo-allergic responses are not based

on antigen-antibody recognition. This is observed in small molecules like sulfite, benzene acid, acetyl salicyl acid as well as triazine and their derivatives. Interestingly the "DFG-Senatskommission" accepts structure-response-analyses as well as human and animal tests in the allergy assessment. A distinction is made between the sensitizing potential and the sensitizing frequency of a substance. The sensitizing potential in the work place is much more important than in the "private environment". Cases reported demonstrate that building materials like concrete are dangerous during processing. However, after the house is finished, the special hazard risk - e.g. chromate sensitizing - is diminished.

Apart from the possibility of an allergic reaction, not only the penetration of (allergic) pollutants (through skin and mucosa) but also the form of the building materials (in this case water soluble compounds like Chromium VI) are of importance. In the long run, the aging and abrasion in private houses can lead to chronic intake of subconcentrated hazards. Consequently the frequency of sensitization may be higher in private houses than is generally assumed. A relatively high number of unknown cases also has to be considered because epidemiological investigations are difficult in this complicated field. Obviously the area of hobbies has to be inspected.

What type of risks have to be considered when houses are built privately? How well is personal working safety controlled? On the other hand, little is known currently about chronic mechanisms of sensitization when allergens in building materials come in contact with human skin immune factors and immune competent body cells. The problem becomes even more complex when allergens are absorbed at airborne carriers like house dust and penetrated through the mucosa of the inhalative or the sensory organs.

One of the most predominant cases not directly associated with the construction field which demonstrates the overlap between occupational and environmental protection is as follows: Occupational baker's asthma or baker's eczema show that after familiar heredity, many young bakers stop their training after noticing that they have been sensitized against the well-known allergens in the bakery work places. Every morning when they

come into the bakery they suffer from attacks of hay fever, asthma and skin irritation. Not only the risk of contamination in the work place (e.g. flour dust in the bakery work place) but furthermore the predisposition (atopy) are main causes for changing professions. The number of unregistered cases is high.

In spite of the fact that it is difficult to define responses and threshold values for indoor pollutants, particularly in the field of environmental medicine, the attempt is undertaken to present a system for the allergenic potency of building materials and compounds.

This is based on the increased prevalence of allergies as mentioned at the beginning, as well as the redundantly references to indoor allergens like **molds, house dust mite, and cats and pats epithelia**. However, more attention should be paid to the increasing (pseudo-) allergenic potency of indoor pollutants in building materials. Therefore direct allergens (compounds incorporated directly from the building materials) will be distinguished from indirect allergens (e.g. molds after humidity).

After this, summaries of currently known relevant allergen groups will be outlined and a first attempt will be made to define threshold values for allergens in building materials. The tolerance values can not be proven allergotoxicologically, but they are recommended by the Institut für Umwelt und Gesundheit (Institute of Environment and Health - IUG) in Germany based on 20 years of indoor assessments. In the case of allergens like formaldehyde, (Diel et al. 1998a, 1998b) nickel, (Schubert et al. 1989) pyrethrum, (Brumi 1995) terpenes, (Seifert 1990) and isocyanates, (Weis 1994) the expert literature is referred to. Based on specific studies on the effects of pyrethroids on the human immune system, "no observed effect levels" (NOEL) are indicated in relation to changes of the signal transduction in human lymphocytes. (Diel 1996, Diel et al. 1998a, 1998b, 1999a, 1999b) Considering the limited research in this field further development of mechanistic models of building related allergen-material responses requires more time and the recommendations presented in this paper will have to be modified in the future. Similarly, the descriptions of the "allergy assessments of building materials" outlined in the including chap-

ters will have to be adapted to the rapidly developing analytical methods in the allergotoxicological determination techniques. Without any claim to finality and/or totality, the authors present a point scale which allows the definition of four classes of the building material allergenic potency allergenicity:

- 1 No or little allergenic potency
- 2 Relevant allergenic potency
- 3 Increased allergenic potency
- 4 Highly increased allergenic potency

This score may be helpful for anyone who uses building materials. This includes construction experts such as architects, engineers or producers, tradesmen or patrons, building supervisors or officials. In the spirit of interdisciplinary environmental medicine, it is the aim that physicians and chemists, as well as toxicologists and construction experts reach an agreement that would offer standards for the better mutual understanding of the people in the construction industry. In this extent it could initiate a new profession - the **indoor expert**. This profession must mainly be grounded on the development of the construction market and consumer care.

I. Direct allergic potency

With relation to the German hazard decree (GefStoffV, Anhang I and TRGS 540) (Rühl, Kluger 1998) and the announcements of the Hazard-Commission (AGS) the following criteria of building material are outlined in respect to their allergenicity. In this context the range of the user's atopy (= risk for sensitization) is of particular importance. The clinical definitions of "allergy" are outlined by J. Ring in his book "Angewandte Allergologie" (Ring 1988) and serve as a basis to explain the so-called familiar predisposition. Total IgE serum concentration is the main correlate to allergies of respiratory lung airways. Normal values for adults are in the range < 100 IU. In the case of allergic skin diseases IgE-levels can be considered normal in a large range. But specific hyperreactivity can be observed against specific compounds (allergens). These can be measured partly with blood tests. Skin tests are, however, easier, safer, and cheaper (epicutantest, pricktest etc.). Furthermore it can be stated, that a major percent of the population does not

Schwerpunkt

have elevated IgE- values, but is hyper-reactive to single substances. These can also be measured serodiagnostically. In representative studies of German health insurance companies the prevalence of any type of allergy is as much as 30 % with increasing tendency, affecting more children than adults. In a recent publication it is suggested that currently one of every two human beings suffers from an allergy against at least one substance. (Frenkel et al. 2000)

The fact that some allergens obtain additional cancerogenic potential makes it difficult to elucidate the special risk of danger. Indoor formaldehyde is a prominent example, where at least higher concentrations can lead to nasal cancer in animal tests. The relatively small formaldehyde molecule shows high chemical reactivity but is not an antigen of itself. Only after interaction with protein side chains, can the derivated structure be recognized as an immunogen by the human immune system. Heavy/colour-metals like nickel, chromium and palladium also obtain allergen potential. This depends on the oxidation level. Chromium penetrates the skin by an oxidation level VI. However, the dangerous and cancerogenic response of chromium is oxidation level III. The following Table I outlines the overlapping toxicology.

The prognoses for the allergen pollution in indoor-air or house-dust and material/product-abrasion is based on experiences during indoor assessments, which are

Table 1: Indoor Allergenicity – Schematic Classification and Examples

1	Allergens with other additional toxic potential (particularly cancerogenicity) e.g. Epoxide, Azo-colours (Fischer et al. 2000)
2.	Sensitizing and Contact-Allergens (Type I and Type IV) e.g. Formaldehyde (Coombs, Gell 1963)
3.	Sensitizing Allergens (only Type I) (Coombs, Gell 1963) e.g. Caseine in Nature-colours, from animals and plants
5.	Primarily Contact-Allergens (Type IV) (Hausen et al. 1992) e.g. Ni in fittings, Amines (Hannuksela 1989)
6	Pseudoallergens e.g. diverse so-called Histamine-liberators like alkaline peptides and ionophores (Diel 1993)

published and discussed by the Institute for Environment and Health (IUG). (Diel F 1993, Diel E 1993, Diel F, Diel E 1996, Diel et al. 1998a, 1998b, Fischer et al. 2000, Grün 1993)

The following priority should be mentioned: (Tab. 1)

Regarding allergic reaction/response, the most important allergens are those which affect **anaphylactic** immediate reaction like shock, urticaria, hay fever or bronchial asthma, but also late reactivity in eczema attacks etc. following the sensitization period. (Type I) (Coombs, Gell 1963) From a clinical perspective this type of allergic reactivity composes about the range 70 % of all cases. Sensitivity is only possible, if the human immune system is able to recognize the allergenic molecule and after receptor interaction at the cell surface of immune competent cells a signal transduction can initiate the regulatory downstream influencing nuclear factors at the DNA-level. Two criteria are preconditional:

1 Size of the molecule (Mr > 500)

2 The specific allergenic site of the molecule (determinant)

Further immunogen factors influence the intensity of the reaction: Secondary chemical factors (e.g. azo-colours develop allergenic amines, metals develop allergenic organic metal complexes, aldehydes interact with body-proteins and develop antigens etc.); mitogenic factors (for instances, in the presence of lipopolysaccharides or plant alkaloids where e.g. house dust can further aggravate allergies); and carriers (antigens e.g. pollen are absorbed by dust, proteins or other aerosols which then reach the irritated mucose of the bronchial/lung). The most dangerous lipophilic hazards are definitely epoxides (e.g. rest-monomeres in plastics) and azo-colours, which can penetrate down to the nucleus and initiate a long-term effect on the DNA-level (e.g. cancerogens). Caseins are exclusively sensitizing (aero-) allergens in natural colourants. Once painted and dried, it can be considered that they lose their ability to be incorporated into the human body. However, dependent on the surface properties corrosion and rub-off can develop a dangerous mixture which can be inhaled. This is

true for natural textile surfaces (e.g. cotton carpets) or thatched roofs (thatch, sisal, bamboo etc.).

Contact allergens (Type IV) (Coombs, Gell 1963) are habitually listed in occupational health and can be characterized as relatively small molecules. Ni in corroded alloys with the oxidation level II and formaldehyde in chipboards are included in this group. As mentioned earlier, both substances contain additional sensitizing potential, which can be explained by the high chemical reactivity during interaction with foreign or bodily proteins.

Contact allergens can initiate a delayed response which typically manifests allergic symptoms two days after contact. The causal allergen can be detected via skin test (epicutan test).

Pseudo-allergens are substances which stimulate allergic symptoms like true allergens. They are defined as **anaphylactoid** as opposed to anaphylactic reactions. Most of these substances are not able to sensitize the organism and therefore cannot induce the typical long-term sensitizing effect. (Diel E 1993) Anaphylactoid responses bypass the immunological reaction chain provoking the mediator cells (mast cells, basophils) directly. Furthermore, there are hazards which can mimic the mast cell mediators like histamine. These and other mediators stimulate immediate symptoms in any individual levels of intensity. Pseudo-allergens include volatile acids, ketones, or amines; particularly basic peptides; but also formaldehyde - which belongs to all groups in Table 1. Pre-conditionally the contaminants can be incorporated and penetrate the skin. There are also contaminants which stabilize the mediator cells, such as distinct alkalines and carbon monoxide. Table 1 summarizes the substances on a priority score. As it is mentioned earlier, formaldehyde has a relatively high value as (pseudo-)allergen as it belongs to all five groups.

II. Indirect allergic potency

Classical indoor allergens are/include:

- 1 microorganisms (molds and bacteria)**
- 2 house dust mite (-excrements)**
- 3 animal epithelia, hair and secretions**
- 4 other organic compounds (in the kitchen, indoor plants etc.)**

Schwerpunkt

The indirect allergenic building materials include all materials which allow or stimulate the growth/distribution of microorganisms or other above mentioned classical indoor allergens. The outlined characteristics in buildings and homes can induce these processes:

- cold bridges ► condensed water
- leaks ► water penetration
- allergen penetration
- surface ► large surface
- dirt absorption
- difficult to clean (textile carpets)
- substrates for microorganisms ► after abrasion
- accumulation of dust, animal epithelia ► electrostatic
- others

People who are allergic should avoid use of building materials, which alone or after construction support the growth of germs and germ carriers (bacteria or molds). Furthermore, materials which provide nutrition for the smallest animals should also be avoided; particularly prefabricated wooden houses, which can sometimes invite rodents to gnaw at the wood and get inside the house.

III. Relevant allergen-groups

The presented catalogue does not distinguish between allergens that contact at the inhalation organs, skin, or other target organs. This differs from the GefStoffV in Germany. Obviously, the localization of the point of incorporation can be difficult, for instance as airborne exposure - less via the gas phase than as aerosol particles - simultaneously takes place via skin/mucosa more or less dependent on the inflammatory eczematous status. (Tab. 2)

It is recommended that the allergens outlined in Table 2 should be avoided or minimized in building materials. The current guidelines must be noted e.g. chromate poor cement. Bound metals in concrete or plaster cannot induce allergies even in atopics. This is similar in wood; however, in wooden dust, particularly from tropical timber, are allergens as well as cancerogens. In this case, the special risk can be found when atopic people build their own homes, use wood-material during renovation, and

Table 2. Relevant allergen-groups

Allergen-groups	Examples
Aldehyde/Dialdehyde	- Formaldehyde, - Glutardialdehyde
Anhydride	- 1, 1-Cyclohexanedicarbonsacidanhydride - Phthalateanhydride - 1,2,4,5-Benzynetetra-carbonaciddianhydride - Tetraphthalateanhydride
Metals/Metal-complexes	- organic Hg-compounds - Colour-metals (Cr, Ni, Co complexes)
Amine/Ammonia-compounds/Amide	- p-Aminodiphenylamine - Ammoniapersulfate - 2-Chloracetamine - N-(2-hydroxyethyl)-3-methyl-2-chinoxalin-carboxamid-1,4-dioxid - N-isopropyl-N'-phenyl-4-phenylendiamin
Terpenes	- (epoxidated)
Thiazine/Thiazole	- 2-Chlor -10-(3-dimethyl-aminopropyl)-phenothiazine - MCI/MI (3:1) - 2-Mercaptobenzothiazol - N-cyclohexylbenzothiacylsulfenamid - Benzisothiazolinon
Thiurame	- Tetramethylthiuramdisulfid - Dipentamethylthiuramdisulfid (see also Metal-complexes of Zn)
Nitrile/Cyane/Nitro-/Para-Compounds	- o-Nitro-p-phenylendiamine - 1,2-Dibrom-2,4-dicyanobutan
Triazine	- N,N',N''-tris (2-hydroxyethyl)-hexahydro-1,3,5-triazine
Mixtures	- acrylates - wood (ref. TAGS 907), - Natural latex - Pyrethrum/Pyrethroids - Terpentine oil - Polyurethane (Isocyanate) - Lanoline - Dithiocarbamates - Colourants (Azo- and antrachinon-)

consumers are contaminated with wood dust. Those or other opportunities must be taken into account when assessments of the allergenicity of building materials are carried out.

In the following Table 3, some building material relevant index values are summarized. These values are not quantified by means of immunotoxicological background, but they can be used for atopic and chemical-sensitive consumers according to long-term experiments on indoor assessments by the IUG:

Formaldehyde. It must always be considered that there exist products containing formaldehyde and formaldehyde releasing preservatives, but also indirect formaldehyde emittants like ethoxylated surfactants must be taken in account.

Complaints caused by the use of formaldehyde-emitting materials in e.g. school buildings are clearly demonstrated. A significant dose related sensitization rate was seen in Guinea Pig Maximization test after induction with formaldehyde. Currently an OEL (occupational exposure limit) 0.3 ppm was recommended. The authors calculate one tenth of this level- 0.03 ppm (= 0.36 mg/kg) - as a safety range in environmental health. (Tab. 3)

Nickel (Ni). Adolescents still suffer from atopic dermatitis and the risk of developing allergic contact dermatitis seems to be large. (Martz et al. 1997) Allergic contact stomatitis induced by contaminated drinking water and/or food must also be taken in consideration, as well as other chemically neighbourhood

metals like cobalt, mercury, and chromium (O'Connor et al. 1997) The influence of atopy on delayed type hypersensitivity still remains unclear, and it is suggested that both T helper lymphocyte-1 (Th1) and T helper lymphocyte-2 (Th2) type cytokines are involved in the immunopathogenesis of contact allergy. But no significant differences between nonatopics and atopics could be elucidated after Ni challenge. (Szepietowski et al 1997, Goebeler et al. 1995) Threshold values were calculated in accordance of patch test experiments using 5 % Nickel chloride solution. (Tab. 3)

Pyrethrum/Pyrethroids. Improper use of pyrethroid insecticides in supermarkets, schools, kindergarten, aeroplanes, and private dwellings lead to the specific pyrethroid syndromes Type I and II. (Fischer, Eikmann 1996) These effects can be aggravated by its synergist piperonyl butoxide and other combined chemicals. (Diel et al. 1999a, 1999b, Fischer, Eikmann 1996) Long-term effects may influence the immune system and transmembrane signal-transduction affecting transcriptional nuclear factors. (Diel et al. 2000) Atopics seem to be more sensitive to pyrethroids than nonatopics. (Diel et al. 1998a, 1998b) Threshold values 3 mg/kg are estimated based on the predicted NOEL's in the range 10 - 1000 mg/kg which effective in human blood lymphocyte tests *ex vivo*. (Tab. 3)

Table 3. Indices for allergens in building materials*

Allergen	Building substance	Index (for atopics)
Formaldehyde	Acryl-, Phenyl-resin, chipboards etc.	30 µg/m ³ (0,025 ppm) (IUG 1998)
Ni and other colour-metal	Alloys, drinking-water pipes	free or 10 mg/kg Material
Pyrethrum/Pyrethroids	Wood, textile carpets	3 mg/kg (BRUMI 1995)
Terpenes	Wood, fixatives	max. 30 µg/m ³ (Seifert 1990)
Isocyanates	PU-foams, Polyurethane-fittings	0,14 µg/m ³ (0,02 ppb) (Weis 1994)

* first recommendations

Terpenes. Terpenes are relevant indoor air pollutants emitted by different sources and building materials. Mainly d-limonene, d-3-carene, a-terpinene, and a-pinene were investigated to cause especially chronic effects on the airways. However, oxidative processes like ozone/terpene reactions may occur and can be a significant source of submicron particles in indoor air. (Weschler, Shields 1999) Although terpene exposures up to 214 µg/m³ did not cause any changes in lung function (Eriksson 1997), the threshold level of 30 µg/m³ - that is one fifth of the Swedish OEL (150 µg/m³) is recommended. (Seifert 1990)

Isocyanates. The derivatives of isocyanates have been reported to be potent chemical sensitizers specific and unspecific (irritant) responses are important in allergic asthma diseases. The most important source of building materials which release isocyanates are epoxy resins. On the other hand isocyanates are not volatile. Therefore, the recommendation of indoor air threshold concentrations seems to be difficult. (Fischer et al. 2000, Weis 1994) Based on current investigations the index of 0.14 ml/m³ is recommended. (Tab. 3)

IV. Procedure of the allergen assessment of building materials

The allergen tests of building materials are performed as follows:

- 1 Relevance of function and exposition
- 2 Availability of data and substance characteristics (safety data sheet etc.)
- 3 Tests of allergenity:
 - allergotox - IV 1
 - immunological *ex vivo* - IV 2
 - contact-allergological potential - IV 3
 - immunological *in vivo* - IV 4

The procedure of the indoor assessment is described in various works. (Diel F 1993) The testing institute notes the contaminations in reference to the manifold of the allergens, as well as the mitogenity or adjuvant characteristics of carrier materials (e.g. house dust). This can lead to a devaluation of the building material. Metabolites of the incorporated allergens must be included in the assessment following the roles of good laboratory practice. This may be true for split off of formaldehyde or paranitrophenyls from resins or other inhaled antigens. The same is true for known combination re-

sponses if any synergist, e.g. piperonyl butoxide in pyrethroid treated wood materials exists. As in different sectors, structure-response analytical assessments have to be performed, as well as toxicokinetic and toxicodynamic tests. Photoallergic sensitization must also be considered, as well as the specific cross-reactivity potentials of allergens. In case of doubt assessments have to be carried out in accordance to the chemical laws such as the German ChemG.

IV.1. Allergotoxic Test

Generally the allergological tests are carried out in standardized test chambers. In total, about 200 single compounds are determined. From these, 50 show allergen and/or pseudo-allergen potential. The measurements are related to the following groups of contaminants:

- 1 Olfactometrical determinations
- 2 VOC and SVOC (in the standardized test chamber)
- 3 Glycols and other polar compounds
- 4 Aldehydes and ketones
- 5 Chemical additives
 - Assessments in regard to the TVOC-concept under particular consideration related to allergens and pseudo-allergens
- 6 Heavy- and colour-metals (from the solid samples)
- 7 Selected biocides

The test chamber method is performed in reference to CEN/TC 264 Air Quality - Indoor Air Quality. The substances are resorbed in special resorption tubes at different air exchange rates in 100 L- and 250 L-high-grade steel test chambers. After resorption, they are separated and analysed on GC-MS (gas chromatography - mass spectrometry). Depending on the sample material metals are determined by ICP-MS (inductively coupled plasma), AAS (atomic absorption spectrometry) or polarography (if there are toxicologically relevant oxidation levels e.g. Cr).

The toxicological values are reported in reference to the recommendations of the AGÖF (Arbeitsgemeinschaft Ökologischer Forschungsinstitute) as well as ChemG (Chemikaliengesetz 1982), GefStoffV (Gefahrstoffverordnung 1986), TRGS (German technical guidelines for hazards) and the relevant reports of the LMBG (Lebensmittel- und Bedarfsgegenständegesetz) ff. respectively.

Schwerpunkt

IV.2. Immunological tests *ex vivo*

Immunological tests are performed for the allergotoxicological assessments using blood cell fractions of atopics and non-atopics in incubates and primary cell cultures. These *ex vivo*-methods are published in peer reviewed international journals. (Diel et al. 1999a, 1999b) These include

- 1 the histamine-liberation-test HLT (which mimicks the anaphylactic and anaphytactoid immediate reaction)
- 2 the lymphocyte-vitality-test (testing the lymphocyte proliferation, "MTT - test" after stimulation using different mitogens like PHA - phytohemagglutinin, LPS-lipopolysaccharide, Con A - concanavalin A etc.)
- 3 the basophile-degranulation-test (pan-optical determination of the degranulated basophils from atopics and non-atopics. This is to recognize the challenge of basophils in atopics and non-atopics.)

The catalogue of allergens in the MAK-BAT-lists of the DFG (Deutsche Forschungsgemeinschaft)-Senatskommission serves as a basis for the assessments. In this case mainly inhalative (contact-) allergens are reported. (DFG 1999)

IV.3. Contact-allergen potential Tests

No *in vitro* test method exists for this. Therefore one has to use the provocation tests with human beings or animals. Normally the animals used in tests are mice and guinea pigs, which are more sensitive than human beings in some cases.

Testing the improvement of the sensitizing potential in humans is forbidden (even for volunteers) in the EU with regard to ethical limits. However in the USA many results exist from relevant studies.

The following animal-tests are usable:

- 1 guinea pig maximisation test (Magnusson, Kligmann 1969)
- 2 lymph node test on mice (Kimber et al. 1986)
- 3 TINA-test on guinea pigs (Ziegler 1977)

A substance has to be reported as **sensitizing after skin contact** ("Sa") when

in the presence of *Freund's* adjuvants > 30 % respond with sensitization of the skin (allergic contact eczema) or typical changes of the lymph nodes respectively. The substance must then be indicated with an "R" in the workplace. (GefStoffV, Anhang 1 No 1.1.2.4.10.-4)

IV.4. Immunological tests *in vivo* (has to be elucidated)

V. Point-Score Allergenicity

As far allergens in building materials are incorporated as aerosols after rub-off or aging a devaluation has to be performed. (see at the beginning @ carriers) The recommendations and definitions in the MAK-publications have to be considered. (DFG 1999, p 157ff) Additionally the mitogenic responses of the carriers from dust, fiber rub-off, foams and emissions must be indicated as ultrafine aerosols obtaining diffusion-equivalent radius < 100 nm.

The following point-scale is recommended for use in the assessment of the allergenicity of building materials (Tab. 4)

Table 4. **Point-Score allergenicity of building-materials**

Allergenicity	Basic points max.
Sensitizing (anaphylactic) + other toxicity (e.g. cancerogen)	5
Sensitizing + contact allergen (Type I + Type IV)	4
Sensitizing (Type I)	3
Contact allergen (Type IV)	2
Pseudoallergenicity (anaphylactoid)	1
Indirect allergenicity (chapter II)	1
Other Type of the allergic responses	1

From this score the maximum number has to be selected and multiplied with the following factors dependent on exposure risk:

	Factor
Inhalative and/or aerosol	2
Combination response (Synergist)	1.5
Aerosols after aging and/or rub-off	1.5
Additional main allergens (Other the allergic symptoms supporting influences*	1.5)

*optional, if more than one of the mentioned influences exist but do not lead to be valued by the factor 1.5

In this scheme, a maximum score of 5 x 2 x 1.5 x 1.5 x 1.5 = 33,75, rounded up to 34, can be calculated (It must be rounded up or down)

1. Example: HCHO. A formaldehyde-containing (> 00.3 ppm) chipboard with terpene (e.g. d,l-limonen) paint suffering from slight abrasion can reach the following point score: (Diel F 1993)

5 (sensitizing and chemical change of body proteins + suggestion of cancerogen activity) x **2** (inhalative) x **1.5** (aerosols after aging of the chipboard - less intensive) x **1.5** (terpenes are violent allergens) x **1.5**
Chipboard: 34 (total count)

2. Example: Ni. A loam paste at the outer wall of a building contains > 500 mg/kg Ni as well as Cr and Co. (Schubert 1985)

2 (contact-allergen) x **1.5** (other non-unresponsive contact-allergens)
Loam paste: 3 (total count)

3. Example: Pyrethrum. A cotton carpet is treated with pyrethrum/PBO and fixed with SVOC emitting fixative. (Fischer et al. 2000)

3.1. Without lanoline (wool-fat allergen)
2 (weak contact-allergen) x **2** (inhaled as aerosol in house dust) x **1.5** (combination response with PBO) (Witte et al. 2000)

Cotton carpet without lanoline: 6 (total count)

3.2. With lanoline
6 (from 3.1) x **1.5** (additional allergen)
Cotton carpet with lanoline: 9 (total count)

In Table 5 the point scale is recommended:

Table 5. **Value scale for the allergenicity of building materials**

Points	score/value
1 - 4	no or weak allergenicity
5 - 10	relevant allergenicity
11 - 20	increased allergenicity
> 20	high allergenicity

Results for the calculated examples from this assessment:

Example 1:
Formaldehyde containing chipboard
→ "high allergenicity"

Example 2:
Colour-metal containing loam paste
→ "no allergenicity"

Example 3:
Insecticide treated cotton carpet
→ "relevant allergenicity"

A basis point score is provided in Table 5 in relation to the priority in Table 1. This can be explained following the generally accepted allergotoxicological considerations. For the assessment of the allergy risk, which can be suffered after the use of building materials containing allergens similar to other harmful contaminants, the type and structure of the molecule is important for the choice of the basic point score. On the other hand, the individual incorporation and sensitivity of target organs is of importance. (Factor)

This can be different than other pollutants, which do not respond as much depending on the individual sensitivity, as other allergens do. The family heredity, the fact of atopy - yes or no - can definitely influence the allergotoxicological assessment scores. In extreme cases, the one and only contamination of an allergen can be relevant in one family, but irrelevant in another. Increased Ni-contaminations can cause elevated chronic digestive diseases with all its complications in a family with predisposition to contact-allergen sensitivity against colour-metals. Sometimes it is difficult to make the proper diagnosis. A different family without any such predisposition may not show any symptoms. How is it possible to standardize the assessment of those building materials?

The recommended scores in the presented paper can give a rough orientation to the matter of consumer care. With long-term experiences in indoor assessment and the study of literature, it can now be suggested that the risk of suffering from an indoor disease caused by the "formaldehyde containing chip-board" is much higher than being harmfully contaminated by the "cotton carpets". In this case, the lanoline could be crucial for increased allergic symptoms. This can only be true, if skin contact or incorporation of dust after rub-off has taken place.

The selected cases should validate the procedure for the proper choice of basic points and factors. It can be elucidated that the inspector and the inspecting institute can make their recommendation within a defined range of consideration. With this, an "after the point-precision" can be avoided. The professional inspector should obtain sufficient knowledge in chemistry, toxicology, and medicine. The allergotoxicological education is the

main content along the way to the profession **Certificated Indoor Inspector**. Currently no final criteria or judgement for the allergotoxicological assessment of building materials or products exist. This may also be excluded because allergies naturally vary depending on age, geo-social and ethnical conditions. The decision whether building materials can be used or how much the allergic potential can be minimized has to be considered on the basis of environmental medical prognoses and the individual family heredity.

Acknowledgement: This work is supported by a grant from the Stiftung VERUM (München).

Diese Arbeit wurde in Auszügen in der Zeitschrift *Med. Immunol.* 2002 auf den Seiten 404-416 veröffentlicht. Die Erstveröffentlichung in deutscher Sprache (*Diel F, Schubert H, Fischer M: Kriterien zur Beurteilung der Allergenität von Baustoffen. UMWELT & GESUNDHEIT* 12 2 (2001) 55-62) wurde aktualisiert.

Prof. Dr. *Friedhelm Diel*,
Head of Biochemistry
Dept. Of Nutrition
University of Applied Sciences FH Fulda
D-36039 Fulda –Germany
Email: friedhelm.diel@t-online.de
Tel.: ++49-661-9640-353
Fax: -399

References:

- BIFAU: Textilallergie. Berliner Institut für Analytik und Umweltforschung e.V., Umweltheft 15 (Berlin 1999)
- Boscolo et al.*: Expression of lymphocyte subpopulations, cytokine serum levels and blood and urine trace elements in nickel sensitized women. *Pharmacol Letters* **63** (1998) 1417-22
- BRUMI. Pyrethroide - Pestizide in Innenräumen. Bremer Umweltinstitut e. V. (Bremen 1995)
- Coombs, Gell*: The classification of allergic reactions underlying disease. In *Gell/Coombs* (Ed) Clinical aspects of immunology. Davis (Philadelphia 1963) 317
- Deutsche Forschungsgemeinschaft (DFG): MAK- und BAT -Werte-Liste. Wiley VCH (Weinheim 1999)
- Diel F*: Innenraumbedingte Allergien und ihre Vermeidung. In *Diel F* (Hrsg.): Innenraumbelastungen. Bauverlag (Wiesbaden 1993) 60-7
- Diel E*: Hausstaub als Allergenpotential und Möglichkeiten der Vermeidung. In *Diel F* (Hrsg.): Innenraumbelastungen. Bauverlag (Wiesbaden 1993) 48-51
- Diel F, Diel E*: Allergien. Moewig Pabel (Rastatt 1996)
- Diel et al.*: Ökologisches Bauen und Sanieren. C.F.Müller (Heidelberg 1998a)
- Diel et al.*: *In vitro* effects of the pyrethroid S-Bioallethrin on lymphocytes and basophils from atopic and non-atopic subjects. *Allergy* **53** (1998b) 1052-59
- Diel et al.*: Pyrethroids and the synergistic PBO affect T-cells and basophils. *Inflamm Res* **48** (1999a) 15-6
- Diel et al.*: Pyrethroids and piperonyl-butoxide affect human T-lymphocytes *in vitro*. *Tox Letters* **107** (1999b) 65-74
- Eriksson*: Monoterpenes from pinewood may affect respiratory function. *Food Chem Tox* **35** (1997) 737
- Fischer et al.*: Textile Bodenbeläge. C.F.Müller (Heidelberg 2000)
- Fischer, Eikmann*: Improper use of all insecticide at a kindergarten. *Toxicol Letters* **88** (1996) 359-64
- Fregert, Grubberger*: Solubility of cobalt in cement. *Contact Dermatitis* **4** (1978) 14-8
- Frenkel et al.*: Early response transcription factors in activated mast cells. *Mod Asp Immunobiol* **1/2** (2000) 57-8
- Goebeler et al.*: Nickel and cobalt, two common haptens leading to contact allergy, directly induced endothelial expression of C-C- and C-X-C-chemokines. *J Invest Dermatol* **105** (1995) 482
- Grün*: Allergene im Innenraum. In *Diel F* (Hrsg.): Innenraumbelastungen. Bauverlag (Wiesbaden 1993) 41-7
- Hannuksela*: Occupational Dermatoses: Appropriate diagnosis and theory. *Allergologie* **12** (1989) 71-4
- Hausen et al.*: Lexikon der Kontaktallergene. *Ecomed* (Landsberg 1992) Loseblattsammlung IUG: IUG-interne Bewertungskriterien (Fulda 1998)
- König, Kollmeyer*: Vorstufen einer verbesserten arbeitsmedizinischen Allergiediagnostik. Wissenschaftsverlag NW (Bremerhaven 1989)
- Kimber et al.*: Development of murine local lymph node assay for the determination of sensitizing potential. *Food Chem Toxicol* **24** (1986) 585-91
- Martz et al.*: The prevalence of eczema and contact allergy in 8th grade school children. *J Europ Acad Dermatol Venerol* **9** (1997) 139
- Magnusson, Kligmann*: The identification of contact allergens by animal assay. The guinea pig maximization test. *J Invest Dermatol* **52** (1969) 268-74
- Maibach, Menne*: Nickel and the skin. *Immunology and Toxicology*. CRC Press Inc. (Boca Raton 1989)
- Menne et al.*: Patch test reactivity to nickel alloys. *Contact Dermatitis* **16** (1987) 255-9
- O'Connor et al.*: Allergic contact stomatitis, a 20 year experience. *J Europ Acad Dermatol Venerol* **9** (1997) 163
- Ring*: Angewandte Allergologie. MMV Medizin Vlg (München 1988)
- Rühl, Kluger*: Handbuch der Bau-Chemikalien. *Ecomed* (Landsberg 1998) Loseblattsammlung
- Schneider et al.*: The nickel status of human beings. In *Anke et al.* (Ed): Spurenelemente Symposium Nickel, VEB-Kongress- und Werbedruck (Jena 1980) 277-83
- Schubert et al.*: Nickel dermatitis in construction workers. In *Frosch et al.* (Ed): Current Topics in Contact Dermatitis. Springer (Berlin 1989) 191-4
- Seifert*: Regulation indoor air. In *Walkinshaw* (Hrsg.): Indoor Air '90, Proceedings of the 5th International Conference on Indoor Air Quality and Climate 5 (Toronto 1990) 35-49
- Szepietowski et al.*: The cytokine profile in nickel-induced contact dermatitis in atopic dermatitis patients and nonatopic individuals. *J Europ Acad Dermatol Venerol* **9** (1997) 119
- Weis*: Toxikologie und Nachweis monomerer Isocyanate in der Innenraumluft. Verlag Shaker (Aachen 1994)
- Weschler, Shields*: Indoor ozone/terpene reactions as a source of indoor particles. *Atmospheric Environment* **33** (1999) 2301-12
- Ziegler*: Der tierexperimentelle Nachweis allergener Eigenschaften von Industrieprodukten. *Dermatol Monatsschr* **163** (1977) 387-91