Indoor Air 2005
www.blackwellpublishing.com/ina
Printed in Singapore. All rights reserved

INDOOR AIR
doi:10.1111/j.1600-0668.2005.00393.x

Review Article

Organic compounds in office environments – sensory irritation, odor, measurements and the role of reactive chemistry

Abstract Sensory irritation and odor effects of organic compounds in indoor environments are reviewed. It is proposed to subdivide volatile organic compounds (VOCs) into four categories: (i) chemically non-reactive, (ii) chemically 'reactive', (iii) biologically reactive (i.e. form chemical bonds to receptor sites in mucous membranes) and (iv) toxic compounds. Chemically non-reactive VOCs are considered non-irritants at typical indoor air levels. However, compounds with low odor thresholds contribute to the overall perception of the indoor air quality. Reported sensory irritation may be the result of odor annoyance. It appears that odor thresholds for many VOCs probably are considerably lower than previously reported. This explains why many building materials persistently are perceived as odorous, although the concentrations of the detected organic compounds are close to or below their reported odor thresholds. Ozone reacts with certain alkenes to form a gas and aerosol phase of oxidation products, some of which are sensory irritants. However, all of the sensory irritating species have not yet been identified and whether the secondary aerosols (ultrafine and fine particles) contribute to sensory irritation requires investigation. Low relative humidity may exacerbate the sensory irritation impact.

P. Wolkoff, C. K. Wilkins, P. A. Clausen, G. D. Nielsen
National Institute of Occupational Health, Copenhagen Ø, Denmark

Key words: Indoor air quality; Measurements; Odor; Sensory irritation; VOCs.

Peder Wolkoff
Indoor Environment Group
National Institute of Occupational Health
Lersø Parkallé 105
DK-2100
Copenhagen Ø
Denmark
e-mail: pwo@ami.dk

Received for review 7 June 2005. Accepted for publication 27 September 2005.

Practical Implications
Certain odors, in addition to odor annoyance, may result in psychological effects and distraction from work. Some building materials continually cause perceivable odors, because the odor thresholds of the emitted compounds are low. Some oxidation products of alkenes (e.g. terpenes) may contribute to eye and airway symptoms under certain conditions and low relative humidity.

Introduction

Indoor air pollution concerns a large proportion of the working force. It has been estimated to cost society substantially in loss of productivity (Mendell et al., 2002). However, the contribution of indoor air pollution to reported health effects is generally based on assumed causal relationships. The absence of dose-response data for exposure has been ignored, in spite of the indoor concentrations being orders of magnitude below occupational threshold limit values (TLV). Uncertainty about the effects of indoor air pollution (e.g. odors) may, after perception, cause speculation, which could result in reporting of 'symptoms' and expensive remediation. Thus, attention has been focused on the emission of volatile organic compounds (VOCs) from building materials and products, which has resulted in a number of national and international labeling schemes, including the development of certain guidelines/standards (Wolkoff, 2003). As a result, the development of low VOC emitting building materials, products and equipment has followed. However, the positive effects of improvement of the indoor environment by the use of low-emitting building materials, i.e. fewer complaints, is difficult to document (e.g. Tuomainen et al., 2001). Except for a few known airway irritants (e.g. formaldehyde), the typical concentrations of VOCs and MVOCs (microbiological VOCs) cannot explain the reported complaints in the non-industrial working environment (Wolkoff and Nielsen, 2001).

The important criterion for the biological relevance of volatile compounds in indoor air is their dose-response relationships at typical indoor concentrations (cf. Seifert, 1995). The demonstration of an increase of a given complaint (i.e. symptom or sign as a result of an increase of exposure to a given pollutant) is essential for the subsequent investigation. Symptoms are often complex. For example: Do we know what the symptoms related to 'eye irritation' in offices really mean? Do we have established documentation for dose-response relationship thereof? (see Wolkoff et al., 2003). In relation to exposure, an important question is whether we are measuring all the relevant species.

The purpose of this overview is to evaluate and update pertinent literature published as our previous reviews on volatile compounds in indoor air with focus on their influence on perceived indoor air quality and their physiological effects during exposures of short duration (Wolkoff and Nielsen, 2001; Wolkoff et al., 1997). Sensory irritation and odor, including (psychological) discomfort, dominate these effects.

Sensory irritation and odor

Eye/airway irritation and odor are important components included in the classic 'sick building syndrome' in non-industrialized buildings (Burge, 2004; Hodgson, 2002; Redlich et al., 1997). They are common symptoms (complaints) that may be experienced simultaneously and thus may interact with each other. Thus independent evaluation may be difficult, if not impossible (Dalton, 2003). For this reason, it is important to understand the characteristics and contributions of sensory irritation and odor to the overall perception and reporting of the indoor air quality. Perceived indoor air quality, in this paper, refers to the overall perception of sensory irritation symptoms and odor that accumulates during a working day. This is to be opposed to the 'immediately' perceived experience when entering a building or room from the outside (or short-term sensory perception of material emissions in climate chambers). The distinction is relevant for the development of practical guidelines for sensory irritation and odor annoyance in the indoor climate (cf. World Health Organization, 1989).

Eye and upper airway sensory irritation

Both eye and upper airway irritation are common symptoms in indoor environments; however, data collection is problematic (Brightman and Moss, 2000). Differences in design of the questionnaires including symptom type, the use of different recall periods and frequency categories of symptoms may explain the large differences from study to study. For example, in 56 European buildings in nine countries, the mean prevalence of dry eyes was 39% expressed as at least once the preceding month, this dropped to 26% by asking as 'experienced at work at this moment' (Bluyssen et al., 1996). Two studies have administered sequential questionnaires over an extended period. One such study showed a remarkable reduction of the prevalence of eye symptoms within a period of 4–12 months (Chao et al., 2003). A similar time trend has been found within a period of 6 weeks (Tamblyn et al., 1992). The possible causes of this decline are not entirely clear. The mean prevalence of eye-related symptoms is considerably lower if the complaint frequency is often or constant (Doughty et al., 2002), but substantially above an estimated background prevalence of 5% for eye irritation (Wolkoff et al., 2003).

Different terminology has been used to characterize the sensory perception evoked by airborne chemicals, especially as they refer to exposures close to TLV levels (cf. Doty et al., 2004). For example, 'the common chemical sense', which describes mucosal sensitivity to chemicals and more recently pungency and chemesthesis ('chemical irritation'), both encompass mucosal and dermal sensations, but not odor. Pungency refers to nasal and oral chemosensation responses mediated through the trigeminal nerve (fifth cranial nerve). 'Sensory irritation' is a general term, comprising specifically eye and upper airway irritation, used by indoor air scientists and airway toxicologists.

Many symptoms and signs have been used for the characterization of sensory irritation (Doty et al., 2004). Some of these are conceptually overlapping in questionnaires, which adds to the overall confusion (Doughty et al., 2002; Rolando et al., 1998; Wolkoff et al., 2003). For example, one of the most common symptoms in indoor environments, 'dry eyes' has been equated to and associated with complaints of irritated eyes, and in some cases, the combination 'dry, itching, or irritated eyes' is used (cf. Guillon, 2002). The large number of different symptoms for eye irritation (e.g. dry or smarting) or clusters thereof may reflect different ocular mechanisms that are difficult to differentiate (Wolkoff et al., 2005a). For example, the symptoms itching, irritating, grating and sandy have been found to cluster together (Lundin, 1991). In another study, the three symptoms 'dryness, smarting and itching' were found to be occupationally related (Aronsson and Strömberg, 1995).

Sensory irritation symptoms have been reported with intensity from severe, such as pain, smarting, burning or irritating, to less severe, such as itchy eyes, dry eyes or discomfort in the eye (cf. Hedge et al., 1996; Norn, 1992). However, descriptors of eye irritation have so far not included details about its location (i.e. the inner and exterior eyelids vs. the eyeball itself), diurnal variation, onset, duration, or alleviating factors (cf. Gilbard, 1999). In addition, the same symptom(s) may arise from different diseases, for example dry eyes and inflammation of the Meibomian glands (Meibomian dysfunctions) both result in sandy-gritty irritation, and the symptoms are insidious in onset (Gilbard, 1999); similarly, dry eyes and allergic conjunctivitis are difficult to differentiate. Further, individuals with perfume contact allergy or allergic rhinitis are likely to report sensory irritation more frequently and more severely following VOC exposure than those without (e.g. Elberling et al., 2004; Shusterman et al., 2003).

During exposure, sensory irritation symptoms may be persistent or transient. Their development in the indoor environment is characterized by latency, i.e. the symptom is experienced with delay in contrast to odor perception. This has been reported from studies of city halls and libraries where reported 'irritation symptoms' increased during a working day (Baird et al., 1994; Skov et al., 1989). In a climate chamber study, subjects exposed over the period of hours to butanol and formaldehyde emitted from an acid-curing lacquer reported sensory irritation with considerable delay. In contrast, a naive panel perceived the odor immediately, but no sensory irritation (Wolkoff et al., 1991b). These and similar observations indicate the role of time for the development and perception of irritative symptoms (Bender et al., 1983; Hempel-Jørgensen et al., 1999; Hudnell et al., 1993). The odor masking effect of butanol in the above case is another possibility (cf. Cain and Murphy, 1980; van Thriel et al., 2003). For this reason, published irritation thresholds that are based on subjective evaluation of short-term exposure, are less suited for the evaluation of indoor concentrations, because of longer exposure durations and lower concentrations. In addition, adaptation (physiological process) and habituation (mainly a psychological process, i.e. familiarity with the sensation) are other important confounding factors that may result in overestimated thresholds (Arts et al., 2002). Overall, the sensory irritation symptoms are often reversible after cessation of exposure.

Observations and cautions for the assessment of sensory irritation from organic compounds in the indoor environment:

- Sensory irritation exhibits longer latency in contrast to odor perception.
- Estimated sensory irritation thresholds (equivalent to a majority of TLV values) are generally orders of magnitude higher than their corresponding odor thresholds (Cometto-Muñiz et al., 2004; Wolkoff, 1999), see also Table 1.
- Short-term exposure thresholds for chemically non-reactive VOCs involve relatively high concentrations (10–10^3 ppm) and are of the same order of magnitude for eye and nasal irritation (Cometto-Muñiz and Cain, 1998). However, such thresholds are less suited for the evaluation of indoor settings.
- Certain occupational risk factors (e.g. computer work and low relative humidity) may exacerbate the effect of sensory irritants, for example during the development of eye symptoms (Wolkoff et al., 2005a); under such conditions, thresholds for eye and nasal irritation may differ.

Sensory irritants formed during terpene oxidation reactions

The sensory irritation of the monoterpene oxidation products has been evaluated by a mouse bioassay and a human eye exposure model. The results from the mouse bioassay, which estimates airway irritation from reduction in the respiratory rate, suggested that the R-limonene/ozone (LO; Clausen et al., 2001), α-pinene/ozone (PO; Wolkoff et al., 1999) and isoprene/ozone (IO) reactions generate sensory irritants of known and unknown structures (Wilkins et al., 2001). The sensory irritation effect is significantly higher than that exhibited by the identified reaction products and residual concentration of the reactants. The identified sensory irritants inter alia include formaldehyde, methacrolein, methyl vinylketone and formic and acetic acid (Wolkoff et al., 2000). In a study, male subjects have been exposed in one eye for 20 min with LO, IO, the nitrate radical, methacrolein and residual reactants. The eye blink frequencies of the subjects were recorded as a physiological measure of trigeminal stimulation (Klenø and Wolkoff, 2004; Nøjgaard et al., 2005). Mean blink frequencies increased significantly only during exposure to LOs and methacrolein compared with that of clean air, and the findings coincided with qualitative reporting of weak eye irritation symptoms. The blink frequency showed a decreasing trend with increase of the relative humidity from 20% to 50% for LO mixtures (Nøjgaard et al., 2005). A similar effect was observed in the mouse bioassay in which sensory irritation was highest at low relative humidity (Wilkins et al., 2003). The observed effects may be ascribed to the formation of less irritation species, a more stable mucous membrane, a more stable eye tear film or a combination.

The above findings substantiate that gaseous LO reaction products cause trigeminal stimulation and possibly eye irritation at ozone- and limonene concentrations that are close to high-end values measured in indoor settings (Wolkoff et al., 2000). The etiological fraction, explained by such alkene oxidation products, however, remains to be evaluated in the context of other occupational factors, e.g. demanding computer work in combination with low relative humidity (cf. Wolkoff et al., 2005a). The impact of ultrafine particles on short-term symptoms such as eye and upper airway irritation is unknown and their possible role in the development of effects in the lower airways is at present speculative (cf. Rohr et al., 2002, 2003).

It is clear that oxidation reactions between certain unsaturated VOCs and oxidants like ozone produce sensory irritants. This is referred to as '*the reactive*

Table 1 Estimated threshold limit values (based on sensory irritation), indoor air norm values for sensory irritation, human sensory irritation threshold, odor threshold and reported concentration of selected common organic compounds in indoor air

Organic compound	$0.03 \times RD_{50}$ TLV (mg/m^3)	Estimated indoor air guideline[1,2] [$0.03 \times RD_{50}/40$ (TLV/40)mg/m^3]	Human sensory irritation threshold [ref 3, if not otherwise stated (mg/m^3)]	Odor threshold ($\mu g/m^3$)	Indoor concentrations reported after year 2000 [mean–max ($\mu g/m^3$)]
Decane	>129 (based on $0.2 \times RD_0$)[4]	>3		43,700[5] 3087[6]	9–29[7]; 3–2370[8]
Toluene	389[9]	10		600[10] 1239[6] 6000[5]	30–44[7]; 28–9500[8]; 22[11]
p-xylene	176[9]	4		1410[5] mixt. of m-/-p 78[10] p-isomer161[6]	10–59[7]; 15[11]
(+)-α-pinene	350[12]	9	20	100[6]	23–44[7]; 13–2952[8]; 7[11]
(+)-limonene	180[13]	4	440[14]	211[6]	33–65[7]; 8–24901[8]; 16[11]
2-ethylhexanol	7[9]	0.2	2	500[10]	5–34[8]
2-butoxyethanol	409[9]	10		207[6]	<3–366[8]
2-butoxyethoxyethanol			Disregarded	9[10]	<3–621[8]
Butanone	795[9]	60		1300[6] 870[10]	3–243[8]
Formaldehyde	0.15[15]	0.004	0.1[16]	1000[10] 600[6]	38–310[8]
Acrolein	0.07	0.002		407[5] 8[6]	Oxidation product
Methacrolein	0.9[17]	0.03		24[6]	Oxidation product of isoprene
Hexanal	129[9]	3	3	58[5] 1[6]	34–520[8]
2-decenal				~4[18]	Emitted from linoleum[19]
Acetic acid	23[20]	0.6	2.5	363[5] 43[10] 15[6]	Emitted from wood products
Hexanoic acid				60[10] 3[6]	Emitted from linseed-based products
Tetrachloethylene				42700[5] 5217[6]	5–15[7]; <1–5540[8]; 3[11]
Ozone	No sensory irritation[21]			6[6]	10–300[22]
Nitrogen dioxide				355[5] 225[6]	300–3000[22]

1: Nielsen et al. 1995. 2: Nielsen et al. 1997. 3: Nielsen, 1996a. 4: Kristiansen and Nielsen, 1988. 5: Devos et al., 1990. 6: Nagata, 2003. 7: Schlink et al., 2004. 8: Schleibinger et al., 2001. 9: Schaper,1993. 10: Woodfield and Hall, 1994. 11: Sexton et al., 2004. 12: Nielsen et al., 2005. 13: Larsen et al. 2000a. 14: Falk-Filipsson et al., 1993. 15: Nielsen et al., 1999. 16: World Health Organization, 2000. 17: Larsen et al., 2000b. 18: Boelens and Gemert, 1987. 19: Jensen et al., 1995. 20: Nielsen et al., 1996b. 21: Nielsen et al., 1999. 22: Wolkoff et al., 2000. 23: Schieberle et al., 1991.

chemistry'–hypothesis (Weschler and Shields, 1997b; Wolkoff and Nielsen, 2001). Some epidemiological studies have indicated that the sum of detectable VOCs may be lower in an office building classified as 'sick' as compared with a similar building classified as 'healthy' (cf. Berglund et al., 1993; Groes et al., 1996; Höppe et al., 1995; Lundin, 1993; Subramanian et al., 2000; Sundell et al., 1993; Willers et al., 1996). In a study of buildings in California, it was found that cleaning products and water-based paints accounted for a significant proportion of the observed association of irritation symptoms (Ten Brinke et al., 1998). Citrus and pine oils, in which terpenes (unsaturated VOCs) are major constituents, are common ingredients in such US products (Nazaroff and Weschler, 2004). In addition, one study has shown an association between terpene concentrations and deteriorated lung functions; however, an interpretation is hampered, because of other risk factors (Norbäck et al., 1995).

Observations and cautions for the assessment of formation of sensory irritants in the indoor environment:

- Unidentified species for which sampling techniques are unavailable may be partly responsible for sensory irritation effects (Weschler and Shields, 1997b; Wolkoff et al., 1997).
- The ozone (outdoor and indoor) and formaldehyde concentrations should be measured in environments suspected to have strong sources of terpenes.
- High relative humidity may alleviate sensory irritation effects of alkene oxidation products.

Odor

Odor perception is omnipresent in our daily life, including work. Odor as opposed to sensory irritation is immediate with steep time-response curves (Berglund and Lindvall, 1992). The character of odors represents a large variety from pleasant (e.g. perfumes, flowers) to unpleasant (malodors; Distel et al., 1999; Duffee and O'Brien, 2000), but the interaction between odor and a person's psychological state (e.g. emotion/mood) is complex, and cultural differences exist (Ayabe-Kanamura et al., 1998).

The step from odor to the cognitive evaluation of the odor (e.g. annoyance, Berglund et al., 1999) is influenced by a number of personal factors including adaptation, habituation, exposure history, expectation and beliefs about health risk (i.e. informational bias), personal psychological variables and social factors (e.g. personal bias) (Dalton, 2002), and environmental factors (Sucker et al., 2001). In particular, belief concerning health risk has a strong influence, because 'it creates a context through which perception is filtered' (Bell and Paton, 2001). However, a major limitation is that most of the research on odors has been carried out at industrial concentrations close to threshold limit values, and its relevance to indoor air settings is questionable. In any case, habituation would be expected to diminish any concern about health risk (cf. Distel et al., 1999).

There is no evidence that malodors *per se* are associated with objective adverse health effects (Cavalini et al., 1991; Rosenkranz and Cunningham, 2003). However, malodors (as perceived in industrialized cultures, cf. Ayabe-Kanamura et al., 1998) are generally undesirable in the indoor environment. Generally, odor perception provides an adequate warning for the onset of eye/airway irritation (Cometto-Muñiz and Cain, 1995). Some odors appear to influence the pattern of reporting symptoms, for example self-reported health, productivity and mood (cf. Gilbert et al., 1997; Gijsbers van Wijk and Kolk, 2001; Knasko, 1996). For example, it has been found that visual contact to the odor source, e.g. the smoker, enhances the intensity of reporting tobacco smoke (Moschandreas and Relwani, 1992). Exposure to a malodor resulted in startle potentiation, which may be interpreted that the odor triggers a negative emotion (Miltner et al., 1994). When the odor source is unidentified, the level of negative emotion could increase and this would decrease the hedonic quality (pleasantness or acceptability) and increase the arousal level. Provision of information about the odor source could thus decrease the level of negative emotion and increase the hedonic quality; this may reduce the general arousal level.

Certain 'vulnerable' subjects may experience health effects in form of somatic symptoms (Segala et al., 2003; Steinheider, 1999). Combined mechanisms of panic disorder and cognitive mediated fear response have been proposed for explanation (Staudenmayer et al., 2004). Environmental awareness and belief through warning about both pleasant odors and malodors facilitates learning about subjective health symptoms such as airway irritation, i.e. learned aversions (Devries et al., 2004; Van den Bergh et al., 2002; Winters et al., 2003). For example, self-selected healthy subjects reported six times more eye irritation when exposed for 1 h to diluted air from a swine confinement than from clean air, this despite measured compounds were well below known irritation thresholds (Schiffman et al., 2005). The authors suggest combined effects of pollutants or learned aversions are responsible for this. Co-pollutants that are part of an odorant mixture (e.g. microbiological species from water-damaged materials) could also cause health effects.

Results from experiments that involve the presentation of certain odors, like lavender and rosemary, under controlled laboratory conditions suggest that their effects are mainly psychological (Ilmberger et al., 2001; see below). These exposures may alter a number of psychological conditions such as mood, alertness and performance (associated with alertness/arousal/vigilance) relative to clean air conditions, but the effects differ depending on concentration, repetition of odor stimuli, type of task and possibly the individual arousal (motivation towards a change) level prior to exposure. The complexity is reflected in the Yerkes–Dodson law, which describes the association between arousal (e.g. stress reflected as odor) and performance as an inverted U-curve (Yerkes and Dodson, 1908). This relationship predicts that as arousal increases, performance of a task improves, but only to a point where it then starts to decrease. Exposure to a sedative odor (e.g. lavender) or an 'alerting' odor (e.g. peppermint or jasmine) will cause a decrease of the performance (see e.g. Degel et al., 2001). It is quite clear that mood and alertness (attention) influence the mental and cognitive state, and perhaps mental creativity; however, for how long and what concentration(s) are required is unknown. Based on an extensive review, it was concluded that 'weak and even unnoticed concentrations of odors often exert a stronger influence on human behaviour than stronger and explicitly perceived ones' (Köster and Degel, 2001), but the effects under laboratory conditions appear to be modest (e.g. Baron, 1990); quantified implications for the performance at the actual workplace is difficult to predict.

Reported odor detection thresholds of VOCs are generally one to four orders of magnitude lower than estimated thresholds for irritation effects of the upper airways (Cometto-Muñiz et al., 2004; Wolkoff, 1999), see also Table 1. In addition, many reported odor thresholds are too high, sometimes by orders of magnitude. A likely explanation is errors associated with the olfactometric measurements; only recently, an international standard procedure has been developed for odor threshold determination by dynamic olfactometry and use of butanol as a reference odor (CEN, 2003). A comparison of compiled data of older odor thresholds (Devos et al., 1990) with newer data from (Woodfield and Hall, 1994) and (Nagata, 2003) shows the trend of lower thresholds for a number of chemical classes; see also examples in Table 1 (note that the odor threshold of butanol in the two latter compilations is about the same, 40 ppb). The possible influence of temperature and relative humidity on odor threshold determination appears not to be known.

At VOC concentrations that are well below their irritation thresholds, but above their corresponding odor thresholds, reports of perceived irritation most likely is a result of odor annoyance, and possibly accompanied by concern for toxicity (Dalton, 2003). These reactions are probably psychological in nature, possibly a reaction to an 'unknown' airborne chemical. It is plausible that a similar mechanism also exists for indoor levels. However, it is unlikely that individual odors emitted from building materials, office equipment or the ventilation system can be differentiated from odors originated from other sources. Exceptions, however, include ozone and nitrogen oxides emitted from photocopiers and certain odors from mold growth.

Clearly, mold odor is a sign of moisture damage of building materials. This might be interpreted as uncontrolled risk of exposure to elevated concentrations of indoor pollutants, e.g. VOCs and particles, thus possibly triggering a psychological process towards more negative reporting of the indoor air quality.

Reduced air quality because of emission of organic compounds from an old carpet or office equipment in field laboratories has been associated with productivity deterioration, for example slower text typing speed and more typing errors (Bakó-Biró et al., 2004; Wargocki et al., 1999). Two different explanations have been proposed: (i) perception of poor air quality caused headache (carpet study, only), which reduced the effort exerted by the subjects, thus lowering the speed of typing. (ii) Unidentified organic compounds caused the decrements (office equipment study). Headache itself can be the result of depression of breathing caused by perceived odors (cf. Danuser et al., 2003; Schiffman and Williams, 2005). However, a more general explanation could be that nearly perceptible odors of the emitted organic compounds cause mental and cognitive distraction of the subjects (e.g. by extension of the reaction time), which results in reduced performance, especially if the odor were perceived as unpleasant or unrecognizable (Danuser et al., 2003; see also Herz, 2002). The etiological fraction of performance alteration that is caused by odors (e.g. material emissions) needs analysis in context of other important occupational factors in the office environment.

Observations and cautions for the assessment of odors from organic compounds in the indoor environment:

- The degree of annoyance of just perceptible odors greatly depends on personally related differences, i.e. different coping strategies and possibly strong individual associations with a given odor (Dalton, 2002). For example, odors that are perceived as pleasant have a lower annoyance potential than unpleasant ones (Both et al., 2004), and possibly also stronger physiological changes (cf. Danuser et al., 2003).
- A fraction of the population may perceive a given odor at least one order lower than the majority of the population according to the definition of an odor threshold (50% median response fraction).
- Sensory irritation and odor perception may be confused.
- Information, experience and habituation may alter the association of perceived health effects (Devries et al., 2004; Opiekun et al., 2003; Van den Bergh et al., 2002; Winters et al., 2003), and reported odor intensity in some cases (Distel et al., 1999).
- Concentration may not be the best indicator of the impact of an odor, partly because persistence and hedonic value influence its impact (Nicell, 2003), and the relationship between concentration and pleasantness or intensity may be inverse for some compounds (Cocheo et al., 1991; Whelton and Dietrich, 2004).
- Short-term evaluation of the perceived air quality is probably not relevant for the evaluation of symptoms built up during the working day (Bluyssen et al., 1996; Wolkoff et al., 1991b). One exception could be the presence of moldy odor.
- Many reported odor thresholds are too high (comparison of data from Devos et al., 1990, with the data from Nagata, 2003; Woodfield and Hall, 1994).
- Some odor thresholds may be too low because of trace amounts of impurities (e.g. formed by oxidation of the compound) that have much lower thresholds than the unaltered compounds.
- The immediately perceived odor of VOCs emitted from some building materials is influenced by thermal factors, and in particular high relative humidity may deteriorate the sensory perception (Cain et al., 2002; Fang et al., 1998).
- Productivity reduction caused by organic compounds (e.g. from building materials) in climate chambers is encumbered by the complexity and influence of odors on human behaviour. The effect may be only temporary (Danuser et al., 2003).

Sources of organic compounds in the indoor environment

Building materials, products

New building materials may contribute substantially to the indoor air concentrations of VOCs (e.g. Hodgson et al., 2000). Temporarily high concentrations are also obtained during human activity related processes, such as cleaning (Nazaroff and Weschler, 2004; Wolkoff, 1995; Wolkoff et al., 1998). Such concentrations may be above their corresponding odor thresholds and thus contribute substantially to the total odor perception (see Table 1).

Although no standardized test procedure exists worldwide, chemical emission testing and sensory perception of the emission of building materials are common and used in national labeling schemes (Wolkoff, 2003). Two limitations should be recognized. First, emission testing by sensory evaluation based on one or few inhalations, using odor intensity and odor acceptability, is not applicable for extended exposures (a normal working day). Second, there is no documentation that odor *per se* from interior building material emissions is associated with health effects, (cf. Cavalini et al., 1991; Rosenkranz and Cunningham, 2003). In one study, however, headache was reported during text typing tasks, supposedly caused by the odor from an old carpet (Wargocki et al., 1999). Sensory irritation is not likely to be caused by common organic compounds emitted from building materials, except for formaldehyde (Wolkoff and Nielsen, 2001). However, sensory evaluations may be affected by certain building materials that continue to emit (secondary) organic compounds with low odor thresholds, even after a long time (Knudsen et al., 1999; Wolkoff, 1999). Ozone interacts with certain building material surfaces (e.g. textile carpets) to produce and remove odorous compounds (e.g. Morrison and Nazaroff, 2002) thus affecting the perceived odor intensity and odor preference (Knudsen et al., 2003). Such a change may at first be perceived positively, because the odor of ozone at certain low levels is perceived as 'fresh' or it has a masking effect (Boeniger, 1995).

Identification of the odorous organic compounds is difficult, because we know little about the link between the sensory assessment and the 'measured' emitted organic compounds (cf. Jensen et al., 1995). Why many building materials continue to emit odors is not well-understood. Combined chemical and sensory perception testing of common building materials have shown that although the measurable VOCs declined or disappeared within 2 weeks (i.e. below the detection limit), the sensory impact decreased within the same period, but thereafter continued at a nearly constant plateau for months (Knudsen et al., 1999). This is because many materials continue to release VOCs by secondary emission, in particularly those materials that are based on linseed oil or otherwise susceptible to degradation (Wolkoff, 1999). Unsaturated acids in such materials are oxidized by oxygen and ozone to aldehydes with low odor thresholds. Although the corresponding VOC concentrations are in the low $\mu g/m^3$ range or less, the latest reported odor thresholds of many VOCs appear to be considerably lower than previously reported (see Table 1).

The odor threshold of an organic compound depends strongly on its chemical structure. For example, unsaturated and epoxidized C_{10} aldehydes, i.e. presence of carbon-carbon double bonds and an epoxy group, apparently have a large impact on the odor threshold (see Table 2). Such aldehydes are suspected to contribute strongly to the odor intensity of products containing linseed oil. Typically, an odor threshold represents 50% median value, sensitive subjects may detect the odor at one or two orders below the threshold (i.e. $< 1\ pg/m^3$). For this reason, compounds responsible for the odor intensity may not be collected in sufficient amounts during chemical emission testing to be detected by gas chromatographic techniques, only by olfactometry, because it requires analytical quantities in the order of a few picograms for detection.

Some scientists have argued that acute sensory perception of building material emissions (i.e. after a few inhalations) also reflects sensory irritation. This is unlikely, because stimulation of the trigeminal nerve endings (eyes and nose) by organic compounds is characterized by a latency of response, usually in the order of several minutes that depends on the exposure concentration (Hempel-Jørgensen et al., 1999; Hudnell et al., 1993; Wolkoff et al., 1991b).

Observations and cautions for the assessment of sensory evaluation of building materials:

- Nearly all building materials have an odor. Usually, the odor intensity of new building materials decreases within a few weeks to a constant level (Knudsen et al., 1999). However, for some materials the emission profile of VOCs may change over time caused by external factors (Wolkoff, 1999) and these may alter the intensity and perception of the emission (Knudsen et al., 2003).
- Generally, sensory perception (< 1 min) reflects the immediately perceived air quality (odor intensity) and cannot reflect sensory irritation under normal indoor air conditions.
- Organic compounds that are responsible for the odor may be present in such low concentrations that they cannot be collected and/or identified by standard analytical techniques.

Table 2. Odor thresholds for C_{10} aldehydes and required analytical performance in a climate chamber

VOC	Odor threshold (ng/m^3)	Detectability limit for thermal desorption in 2 l of air[d] (pg)
Decanal	1000[a]–3000[b]	2000–6000
2-decenal	~4000[a]	~8000
4,5-epoxy-2-decenal	0.6–3[c]	1–5

a: Boelens and Gemert, 1987; b: Nagata, 2003; c: Schieberle and Grosch, 1991; and d: In a climate chamber with normal loading of material ($1\ m^2/m^3$) and air exchange rate of $1\ h^{-1}$.

- Major emitted organic compounds may not be responsible for the perceived odor.
- Ozone can in some cases alter the odor of a given exposed material (Knudsen et al., 2003); whether this is an effect of ozone, newly formed or declined emissions is unknown.
- The provision of information supplied about building materials may alter the sensory evaluation (Wolkoff et al., 2005b).

Measurements of organic compounds in the indoor environment

The classic definition of VOCs and SVOCs according to their boiling points by WHO (World Health Organization, 1989) is artificial with regard to evaluation of health effects and comfort, because other properties are more relevant. The answer to the question 'What to measure?' depends on the effect of interest. A new definition of organic compounds in indoor air (OCIA) was originally proposed to accommodate the 'reactive chemistry'-hypothesis, but it also accommodates the identification of new species that may be associated with health effects (Wolkoff and Nielsen, 2001). The main idea of this proposal was that organic species/particles other than VOCs may also cause short-term symptoms and health and comfort effects. It now appears salient to distinguish roughly between four types of OCIAs according to their expected health effect, including odor annoyance. These groups are:

- Chemically non-reactive (stable) organic compounds, e.g. octane, toluene and butanol.
- Chemically 'reactive' organic compounds like alkenes (e.g. styrene and limonene) that react with ozone alone or with nitrogen dioxide in presence of light to produce new oxygenated products (Atkinson and Arey, 2003; Weschler, 2000).
- Organic compounds that form chemical bond(s) to receptor-sites in the mucous membranes, i.e. biologically reactive (e.g. formaldehyde and acrolein).
- Organic compounds with (known) toxic properties, e.g. fungicides (e.g. pentachlorophenol); these compounds are characterized by effects developed over long duration of exposure.

Specific compounds may belong to two or more of the above categories. In addition, it should be noted that even non-reactive organic compounds under extreme conditions can be oxidized in air by the OH radical, e.g. formed in ozone/terpene reactions; for example, *p*-xylene can be oxidized to the corresponding *o*-cresol and *p*-tolualdehyde (Fan et al., 2003).

Reported indoor concentrations of individual VOCs are generally below 50 $\mu g/m^3$, with most below 5 $\mu g/m^3$ (Brown, 1999b). Both European and North American studies show that the mean concentration of the majority of single VOCs is generally below 10 $\mu g/m^3$ (e.g. Hippelein, 2004; Schleibinger et al., 2001; Sexton et al., 2004; Shendell et al., 2004). However, heavy traffic, new housing and refurbishing can result in temporarily higher concentrations than normally encountered (e.g. Hodgson et al., 2000; Saijo et al., 2004). Certain human-related activities can also contribute to temporarily higher concentrations, e.g. cleaning, maintenance and food preparation (Nazaroff and Weschler, 2004; Wolkoff et al., 1998).

The profiles of organic compounds may have changed during the last decade with the introduction of new VOCs and SVOCs. This is partly because of the introduction of new building and household products with higher boiling VOCs and the replacement of aliphatic and aromatic solvents with oxygenated solvents (cf. Schleibinger et al., 2001). Still, it is difficult to explain the complaints of sensory irritation by the VOC levels reported (cf. Meininghaus et al., 2003; Wolkoff and Nielsen, 2001), nor by reported MVOCs (Pasanen et al., 1998), because their concentrations are far below thresholds required for eye/airway irritation (cf. Wolkoff, 1999). This is one of the reasons why the possible role of radicals in indoor environments in the context of the 'reactive chemistry hypothesis' has been proposed as a new research field (Carslaw, 2003).

Oxidation of alkenes and unvented combustion (gas, kerosene and wax) produce radicals in indoor environments (de Kok et al., 2004; Sarwar et al., 2002; Weschler and Shields, 1997a). For example, alkenes, like monoterpenes (i.e. chemically reactive) react with ozone to produce the hydroxyl radical (Atkinson and Arey, 2003; Weschler and Shields, 1997a). Monoterpenes are common and relatively abundant compounds indoors emitted from wood (furniture), plant and fruits and their extracts (e.g. citrus and pine oils). In addition, monoterpenes and monoterpene derivatives are common fragrances used in cleaning agents, household products, including personal care products (Nazaroff and Weschler, 2004). The abundance of and hence the exposure to terpene oxidation products indoors, depends on the identity and concentration of the reactants (e.g. limonene and ozone), their reaction rate and the air exchange rate, both of which determine the build-up of reaction products (Weschler and Shields, 2000). Ozone has been measured in concentrations from a few ppb to hundreds of ppb, and is typically 20–70% of outdoor levels (Weschler, 2000); however, additional contributions from use of photocopiers may create locally high concentrations during operation (Brown, 1999a).

From terpenes a number of different oxidation products are formed, in both gaseous and aerosol form, carboxylic acids, diacids, aldehydes, ketones and mixed combinations thereof, and hydroperoxides (e.g. Docherty et al., 2005; Glasius et al., 2000). The products are formed via intermediary Criegee biradicals (Atkinson and Arey, 2003), and other unstable species. The reaction may also involve nitrogen dioxide and form N-containing products that may be sensory irritating (cf. Wilkins et al., 2001). For example, peroxybenzoyl nitrate, formed in the presence of styrene, ozone and nitrogen dioxide (cf. Weschler and Shields, 1997b), has been reported to be a strong eye irritant (Glasson and Heuss, 1977). In addition to radicals, ultrafine particles are also formed in oxidation reactions of monoterpenes (Long et al., 2000; Wainman et al., 2001; Weschler and Shields, 1999) and in all combustion processes.

Observations and cautions for measurements of organic compounds in the indoor environment:

- The concentration of organic compounds depends on the source emission rate(s), the air exchange rate in a room, the sorption properties of the room and potential chemical reactions.
- Many indoor compounds show substantial seasonal dependence, concentrations are generally higher in the spring and summer season (Schlink et al., 2004; Wolkoff et al., 1991a).
- Some compounds, for example monoterpenes, may be underestimated in ozone enriched environments because of reactions during sampling (e.g. Calogirou et al., 1996). Furthermore, indirect sampling methods without oxidant scrubbing may be inadequate in the presence of oxidants, for example determination of aldehydes on solid sorbents.
- Some organic compounds may be undetected, because of rapid reactions with either ozone or the OH radical. For example, chemically reactive compounds may disappear during canister and bag sampling, because of reactions or sorption and thus leading to calibration problems.
- Traditional sampling techniques are inadequate to trap labile species (e.g. radicals).
- The limit of detection may be too high for organic compounds with low odor thresholds.

Conclusion

As there is a possibility of confusion of odor with sensory irritation, compounds with low odor thresholds may contribute to the overall perception of the indoor air quality. However, another possibility is that even unrecognizable levels of odors can cause annoyance and mental distraction, which may alter the work performance at indoor air conditions. It should be acknowledged that both the perception of odor and sensory irritation is influenced by psychological factors. New olfactometric techniques indicate that odor thresholds for many VOCs probably are considerably lower than previously reported. This may explain why many building materials continue to emit odors, although the concentrations of the detected organic compounds are below the hitherto reported odor thresholds. Ozone reacts with certain VOCs to form gaseous oxidation products and secondary aerosols (fine and ultrafine particles), which may contribute to sensory irritation. However, the identities of some major sensory active species are still unknown; these may include radicals. It is clear, however, that long-term exposure (hours) to low concentrations of formaldehyde (10–50 ppb) is necessary to enable evaluation of the sensory impact of alkene oxidation reactions, because formaldehyde is a major product. Both a bioassay and a human eye exposure study indicate that low relative humidity exacerbates the sensory irritation impact.

The pursuit of the ‘reactive chemistry’ hypothesis should be continued in search of plausible explanations for sensory irritation in office environments; however, this should be carried out in combination with both climate and work-related factors.

Acknowledgements

We thank Drs E. Cometto-Muñiz, M. Hodgson and M. Mendell for constructive comments. We also appreciate the useful comments and suggestions from one referee.

References

Aronsson, G. and Strömberg, A. (1995) Work content and eye discomfort in VDT work, *Int. J. Occup. Safe. Ergon.*, **1**, 1–13.

Arts, J.H., Mojet, J., Gemert, L.J., Emmen, H.H., Lammers, J.H., Marquart, J., Woutersen, R.A. and Feron, V.J. (2002) An analysis of human response to the irritancy of acetone vapors, *Crit. Rev. Toxicol.*, **32**, 43–66.

Atkinson, R. and Arey, J. (2003) Gas-phase troposheric chemistry of biogenic volatile organic compounds: a review, *Atmos. Environ.*, **37**, S197–S219.

Ayabe-Kanamura, S., Schicker, I., Laska, M., Hudson, R., Distel, H., Kobayakawa, T. and Saito, S. (1998) Differences in perception of everyday odors: a Japanese–German cross-cultural study, *Chem. Senses.*, **23**, 31–38.

Baird, J.C., Berglund, B. and Esfandabad, H.S. (1994) Longitudinal assessment of sensory reactions in eyes and upper airways of staff in a sick building, *Environ. Int.*, **20**, 141–160.

Bakó-Biró, Z., Wargocki, P., Weschler, C.J. and Fanger, P.O. (2004) Effects of pollution from personal computers on perceived air quality, SBS symptoms and productivity in offices, *Indoor Air*, **14**, 178–187.

Baron, R.A. (1990) Environmentally induced positive affect. Its impact on self-efficacy, task performance, negotiation, and conflict, *J. Appl. Soc. Psychol.*, **20**, 368–384.

Bell, G.A. and Paton, J.E. (2001) Verbal-cognitive strategy can influence odour judgement, *Aroma Chol. Rev.*, **IX**, 3–9.

Bender, J.R., Mullin, L.S., Graepel, G.J. and Wilson, W.E. (1983) Eye irritation response of humans to formaldehyde, *Am. Ind. Hyg. Assoc. J.*, **44**, 463–465.

Berglund, B. and Lindvall, T. (1992) Theory and method of sensory evaluation of complex gas mixtures, *Ann. N. Y. Acad. Sci.*, **641**, 277–293.

Berglund, B., Johansson, I. and Lindvall, T. (1993) Variability in VOC-concentrations over time in a large building and their relationship with some characteristics of the indoor environment. In: *Proceedings of Indoor Air* '93, vol. 2, 21–26.

Berglund, B., Bluyssen, P., Clausen, G., Garriga-Trillo, A., Gunnarsen, L., Knöppel, H., Lindvall, T., Mølhave, L. and Winneke, G. (1999) *Sensory Evaluation of Indoor Air Quality*, Report No. 20, European Commission, Joint Research Centre. Luxembourg, Environment Institute.

Bluyssen, P.M., De Olivera Fernandes, E., Groes, L., Clausen, G., Fanger, P.O., Valbjørn, O., Bernhard, C.A. and Roulet, C.A. (1996) European indoor air quality audit project in 56 office buildings, *Indoor Air*, **6**, 221–238.

Boelens, M.H. and Gemert, L.J. (1987) Organoleptic properties of aliphatic aldehydes, *Perfumer Flavorist*, **12**, 31–43.

Boeniger, M.F. (1995) Use of ozone generating devices to improve indoor air quality, *Am. Ind. Hyg. Assoc. J.*, **56**, 590–598.

Both, R., Sucker, K., Winneke, G. and Koch, E. (2004) Odour intensity and hedonic tone – important parameters to describe odour annoyance to residents?, *Water Sci. Technol.*, **50**, 83–92.

Brightman, H.S. and Moss, N. (2000) Sick building syndrome studies and the compilation of normative and comparative values, In: Spengler, J.D., Samet, J.M. and McCarthy, J.F. (eds) *Indoor Air Quality Handbook*, New York, McGraw-Hill, 3.1–3.32.

Brown, S.K. (1999a) Assessment of pollutant emissions from dry-process photocopiers, *Indoor Air*, **9**, 259–267.

Brown, S.K. (1999b) Occurrence of volatile organic compounds in indoor air, In: Salthammer, T. (ed.) *Organic Indoor Air Pollutants*, Weinheim, Wiley-VCH, 171–184.

Burge, P.S. (2004) Sick building syndrome, *Occup. Environ. Med.*, **61**, 185–190.

Cain, W.S. and Murphy, C.L. (1980) Interaction between chemoreceptive modalities of odour and irritation, *Nature*, **284**, 255–257.

Cain, W.S., Schmidt, R., Leaderer, B.P., Gent, J.F., Bell, D. and Berglund, L.G. (2002) Emission of VOCs from materials used in buildings: analytical and sensory aspects, *ASHRAE Trans.*, **180**, 283–296.

Calogirou, A., Larsen, B.R., Brussol, C., Duane, M. and Kotzias, D. (1996) Decomposition of terpenes by ozone during sampling on tenax, *Anal. Chem.*, **68**, 1499–1506.

Carslaw, N. (2003) Where next with indoor air measurements? *Atmos. Environ.*, **37**, 5645–5646.

Cavalini, P.M., Koeter-Kemmerling, L.G. and Pulles, M.P.J. (1991) Coping with odour annoyance and odour concentrations: three field studies, *J. Environ. Psychol.*, **11**, 123–142.

CEN (2003) Air quality: determination of odor thresholds by dynamic olfactometry, EN 13725, European Committee for Standardization, Brussels, Belgium.

Chao, H.J., Schwartz, J., Milton, D.K. and Burge, H.A. (2003) The work environment and workers' health in four large office buildings, *Environ. Health. Perspect.*, **111**, 1242–1248.

Clausen, P.A., Wilkins, C.K., Wolkoff, P. and Nielsen, G.D. (2001) Chemical and biological evaluation of a reaction mixture of R-(+)-limonene/ozone: formation of strong airway irritants, *Environ. Int.*, **26**, 511–522.

Cocheo, V., Boaretto, C., Quaglio, F., Sacco, P. and Zannetti, R. (1991) Identification by cryofocusing-gas chromatography-mass spectrometry of odorous cyclic acetals emitted from a polyester resin plant, *Analyst*, **116**, 1337–1342.

Cometto-Muñiz, J.E. and Cain, W.S. (1995) Relative sensitivity of the ocular trigeminal, nasal trigeminal and olfactory systems to airborne chemicals, *Chem. Senses.*, **20**, 191–198.

Cometto-Muñiz, J.E. and Cain, W.S. (1998) Trigeminal and olfactory sensitivity: comparison of modalities and methods of measurement, *Int. Arch. Occup. Environ. Health*, **71**, 105–110.

Cometto-Muñiz, J.E., Cain, W.S. and Abraham, M.H. (2004) Detection of single and mixed VOCs by smell and by sensory irritation, *Indoor Air*, **14**, 108–117.

Dalton, P. (2002) Odor, irritation and perception of health risk, *Int. Arch. Occup. Environ. Health*, **75**, 283–290.

Dalton, P. (2003) Upper airway irritation, odor perception and health risk due to airborne chemicals, *Toxicol Lett.*, **140–141**, 239–248.

Danuser, B., Moser, D., Vitale-Sethre, T., Hirsig, R. and Krueger, H. (2003) Performance in a complex task and breathing under odor exposure, *Hum. Factors.*, **45**, 549–562.

Degel, J., Piper, D. and Köster, E.P. (2001) Implicit learning and implicit memory for odors: the influence of odor identification and retention time, *Chem. Senses.*, **26**, 267–280.

Devos, M., Patte, F., Rouault, J., Laffort, P. and van Gemert, L.J. (1990) *Standardized Human Olfactory Thresholds*, Oxford, IRL Press at Oxford University Press, 1–165.

Devries, S., Winters, W., Van Diest, I., De Peuter, S., Vos, G., Van de Voestijne, K. and Van den Bergh, O. (2004) Perceived relation between odors and a negative event determines learning of symptoms in response to chemicals, *Int. Arch. Occup. Environ. Health.*, **77**, 200–204.

Distel, H., Ayabe-Kanamura, S., Martinez-Gómez, M., Schicker, I., Kobayakawa, T., Saito, S. and Hudson, R. (1999) Perception of everyday odors – correlation between intensity, familiarity and strength of hedonic judgement, *Chem. Senses.*, **24**, 191–199.

Docherty, K.S., Wu, W., Lim, Y.B. and Ziemann, P.J. (2005) Contributions of organic peroxides to secondary aerosol formed from reactions of monoterpenes and O_3, *Environ. Sci. Technol.*, **39**, 4049–4059.

Doty, R.L., Cometto-Muñiz, J.E., Jalowayski, A.A., Dalton, P., Kendall-Reed, M. and Hodgson, M. (2004) Assessment of upper respiratory tract and ocular irritative effects of volatile chemicals in humans, *Crit. Rev. Toxicol.*, **34**, 85–142.

Doughty, M.J., Blades, K.A. and Ibrahim, N. (2002) Assessment of the number of eye symptoms and the impact of some confounding variables for office staff in non-air-conditioned buildings, *Opthal. Physiol. Opt.*, **22**, 143–155.

Duffee, R.A. and O'Brien, M. (2000) Response to odors, In: Spengler, J.D., Samet, J.M. and McCarthy, J.F. (eds) *Indoor Air Quality Handbook*, New York, McGraw-Hill, 21.1–21.12.

Elberling, J., Linneberg, A., Mosbech, H., Dirksen, A., Frølund, L., Madsen, F., Nielsen, N.H. and Johansen, J.D. (2004) A link between skin and airways regarding sensitivity to fragrance products? *Br. J. Dermatol.*, **151**, 1197–1203.

Falk-Filipsson, A., Löf, A., Hagberg, M., Hjelm, E.W. and Wang, Z. (1993) d-Limonene exposure to humans by inhalation: uptake, distribution, elimination, and effects on the pulmonary function, *J. Toxicol Environ. Health*, **38**, 77–88.

Fan, Z., Lioy, P., Weschler, C.J., Fielder, N., Kipen, H. and Zhang, J. (2003) Ozone-initiated reactions with mixtures of volatile organic compounds under simulated indoor conditions, *Environ. Sci. Technol.*, **37**, 1811–1821.

Fang, L., Clausen, G. and Fanger, P.O. (1998) Impact of temperature and humidity on the perception of indoor air quality, *Indoor Air*, **8**, 80–90.

Gijsbers van Wijk, C.M.T. and Kolk, A.M. (2001) Sex differences in physical symptoms: the contribution of symptom perception theory, *Soc. Sci. Med.*, **45**, 231–246.

Gilbard, J.P. (1999) Dry eye, blepharitis and chronic eye irritation: divide and conquer, *J. Ophthalmic Nurs. Technol.*, **18**, 109–115.

Gilbert, A.N., Knasko, S.C. and Sabini, J. (1997) Sex differences in task performance associated with attention to ambient odor, *Arch. Environ. Health.*, **52**, 195–198.

Glasius, M., Lahaniati, M., Calogirou, A., Di Bella, D., Jensen, N.R., Hjorth, J., Kotzias, D. and Larsen, B.R. (2000) Carboxylic acids in secondary aerosols from oxidation of cyclic monoterpenes by ozone, *Environ. Sci. Technol.*, **34**, 1001–1010.

Glasson, W.A. and Heuss, J.M. (1977) Synthesis and evaluation of potential atmospheric eye irritants, *Environ. Sci. Technol.*, **11**, 395–398.

Groes, L., Pejtersen, J. and Valbjørn, O. (1996) Perception and symptoms as a function of indoor environmental factors, personal factors and building characteristics in office buildings. In: *Proceedings of Indoor Air* '96, vol. 4, 237–242.

Guillon, J.-P. (2002) Current clinical techniques to study the tear film and tear secretions, In: (ed.) *The Tear Film: Structure, Function and Clinical Examination*, Oxford, Butterworth-Heinemann, 51–81.

Hedge, A., Erickson, A. and Rubin, G. (1996) Predicting sick building syndrome at the individual and aggregate levels, *Environ. Int.*, **22**, 3–19.

Hempel-Jørgensen, A., Kjærgaard, S.K. and Mølhave, L. (1999) Time course of sensory eye irritation in humans exposed to N-butanol and 1-octene, *Arch. Environ. Health.*, **54**, 86–94.

Herz, R.S. (2002) Influences of odors on mood and affective cognition, In: Rouby, C., Schaal, B., Dubois, D., Gervais, R. and Holley, A. (eds) *Olfaction, Taste, and Cognition*, Cambridge, Cambridge University Press, 160–177.

Hippelein, M. (2004) Background concentrations of individual and total volatile organic compounds in residential indoor air of Schleswig-Holstein, Germany, *J. Environ. Monit.*, **6**, 745–752.

Hodgson, M. (2002) Indoor environmental exposure and symptoms, *Environ. Health. Perspect.*, **110**, 663–667.

Hodgson, A.T., Rudd, A.F., Beal, D. and Chandra, S. (2000) Volatile organic compound concentrations and emission rates in new manufactured and site-built houses, *Indoor Air*, **10**, 178–192.

Höppe, P., Praml, G., Rabe, G., Lindner, J., Fruhmann, G. and Kessel, R. (1995) Environmental ozone field study on pulmonary and subjective responses of assumed risk groups, *Environ. Res.*, **71**, 109–121.

Hudnell, H.K., Otto, D.A. and House, D.E. (1993) Time course of odor and irritation effects in humans exposed to a mixture of 22 volatile organic compounds, In: *Proceedings of Indoor Air* '93, vol. 1, 567–572.

Ilmberger, J., Heuberger, E., Mahrhofer, C., Dessovic, H., Kowarik, D. and Buchbauer, G. (2001) The influence of essential oils on human attention. 1: alertness, *Chem. Senses.*, **26**, 239–245.

Jensen, B., Wolkoff, P. and Wilkins, C.K. (1995) Characterization of linoleum. Part 2: preliminary odour evaluation, *Indoor Air*, **5**, 44–49.

Klenø, J. and Wolkoff, P. (2004) Changes in eye blink frequency as a measure of trigeminal stimulation by exposure to limonene oxidation products, isoprene oxidation products, and nitrate radicals, *Int. Arch. Occup. Environ. Health.*, **77**, 235–243.

Knasko, S.C. (1996) Human responses to ambient olfactory stimuli, In: Gammage, R.B. and Berven, B.A. (eds) *Indoor Air and Human Health*, Boca Raton, Lewis Publishers, 107–123.

Knudsen, H.K., Nielsen, P.A., Kjaer, U.D. and Wolkoff, P. (1999) Chemical and sensory characterization of VOC emissions from building products: the impact of concentration and air velocity, *Atmos. Environ.*, **33**, 1217–1230.

Knudsen, H.N., Nielsen, P.A., Clausen, P.A., Wilkins, C.K. and Wolkoff, P. (2003) Sensory evaluation of emissions from selected building products exposed to ozone, *Indoor Air*, **13**, 223–231.

de Kok, T.M.C.M., Hogervorst, J.G.F., Kleinjans, J.C.S. and Briedé, J.J. (2004) Radicals in the church, *Eur. Respir. J.*, **24**, 1069–1070.

Köster, E.P. and Degel, J. (2001) Are weak odors stronger than strong odors? *Aroma Chol. Rev.*, **IX**, 9–11.

Kristiansen, U. and Nielsen, G.D. (1988) Activation of the sensory irritant receptor by C7-Cl1 n-alkanes, *Archives of Toxicology*, **61**, 419–425.

Larsen, S.T., Hougaard, K.S., Alarie, Y., Wolkoff, P., Clausen, P.A., Wilkins, C.K. and Nielsen, G.D. (2000a) Effects of R-(+)- and S-(−)-limonene on the respiratory tract in mice, *Human & Experimental Toxicology*, **19**, 457–466.

Larsen, S.T. and Nielsen, G.D. (2000b) The effects of methacrolein on the respiratory tract in mice, *Toxicol. Lett.*, **114**, 197–202.

Long, C.M., Suh, H.H. and Koutrakis, P. (2000) Characterization of indoor particle sources using continuous mass and size monitors, *J. Air Waste Manage. Assoc.*, **50**, 1236–1250.

Lundin, L. (1991) *On Building-related Causes of the Sick Building Syndrome*, Stockholm, Almqvist & Wiksell Int.

Lundin, L. (1993) Symptom patterns and air quality in a sick library, In: *Proceedings of Indoor Air* '93, vol. 1, 127–132.

Meininghaus, R., Kouniali, A., Mandin, C. and Cicolella, A. (2003) Risk assessment of sensory irritants in indoor air – a case study in a French school, *Environ. Int.*, **28**, 553–557.

Mendell, M.J., Fisk, W.J., Kreiss, K., Levin, H., Alexander, D., Cain, W.S., Girman, J.R., Hines, C.J., Jensen, P.A., Milton, D.K., Rexroat, L.P. and Wallingford, K.M. (2002) Improving the health of workers in indoor environments: priority research needs for a national occupational research agenda, *Am. J. Public. Health.*, **92**, 1430–1440.

Miltner, W., Matjak, M., Braun, C., Diekmann, H. and Brody, S. (1994) Emotional qualities of odors and their influence on the startle reflex in humans, *Psychophysiology*, **31**, 107–110.

Morrison, G.C. and Nazaroff, W.W. (2002) Ozone interactions with carpet: secondary emissions of aldehydes, *Environ. Sci. Technol.*, **36**, 2185–2192.

Moschandreas, D.J. and Relwani, S.M. (1992) Perception of ETS odors: a visual and olfactory response, *Atmos. Environ.*, **26B**, 263–269.

Nagata, Y. (2003) Odor intensity and odor threshold value, *J. Jpn. Air Cleaning Assoc.*, **41**, 17–25.

Nazaroff, W.W. and Weschler, C.J. (2004) Cleaning products and air fresheners. Exposure to primary and secondary pollutants, *Atmos. Environ.*, **38**, 2841–2865.

Nicell, J.A. (2003) Expression to relate population responses to odor concentration, *Atmos. Environ.*, **37**, 4955–4964.

Nielsen, G.D., Alarie, Y., Poulsen, O.M. and Andersen Nexø, B. (1995) Possible mechanisms for the respiratory tract of noncarcinogenic indoor-climate pollutants and bases for their risk assessment, *Scan J Work Environ Health*, **21**, 165–178.

Nielsen, G.D., Hansen, L.F., Andersen Nexø, B. and Poulsen, O.M. (1996a) *Toxicological based air quality guidelines for substances in indoor air*, 1996; 11 E, Helsingfors, Nordic Committee on Building Regulations, NKB.

Nielsen, G.D., Hansen, L.F. and Hammer, M. (1996b) *Eye and Airway Irritation Effects of Organic Acids*, Working Environment Fund, Copenhagen.

Nielsen, G.D., Hansen, L.F. and Wolkoff, P. (1997) Chemical and biological evaluation of building material emissions. II. Approaches for setting indoor air standards or guidelines for chemicals, *Indoor Air*, **7**, 17–32.

Nielson, G.D., Hougaard, K.S., Larsen, S.T., Wolkoff, P., Clausen, P.A., Wilkins, C.K. and Alarie, Y. (1999) Acute airway effects of formaldehyde and ozone in BALB/c mice. *Human & Experimental Toxicology*, **18**, 400–409.

Nielsen, G.D., Larsen, S.T., Hougaard, K.S., Hammer, M., Wolkoff, P., Clausen, P.A., Wilkins, C.K. and Alarie, Y. (2005) Mechanisms of acute inhalation effects of (+) and (−)-α-pinene in BALB/c mice, *Pharmacol. Toxicol.*, **96**, 1–9.

Norbäck, D., Björnsson, E., Janson, C., Widström, J. and Boman, G. (1995) Asthmatic symptoms and volatile organic compounds, formaldehyde, and carbon

dioxide in dwellings, *Occup. Environ. Med.*, **52**, 388–395.
Norn, M.S. (1992) Pollution keratoconjunctivitis, *Acta Ophthalmol.*, **70**, 269–273.
Nøjgaard, J.K., Christensen, K.B. and Wolkoff, P. (2005) The effect on human eye blink frequency by exposure to limonene oxidation products and methacrolein, *Toxicol Lett.*, **156**, 241–251.
Opiekun, R.E., Smeets, M.A.M., Sulewski, M., Rogers, R., Prasad, N., Vedula, U. and Dalton, P. (2003) Assessment of ocular and nasal irritation in asthmatics resulting from fragrance exposure, *Clin. Exp. Allergy.*, **33**, 1256–1265.
Pasanen, A.-L., Korpi, A., Kasanen, J.-P. and Pasanen, P. (1998) Critical aspects on the significance of microbial volatile metabolites as indoor air pollutants, *Environ. Int.*, **24**, 703–712.
Redlich, C.A., Sparer, J. and Cullen, M.R. (1997) Sick-building syndrome, *Lancet*, **349**, 1013–1016.
Rohr, A., Wilkins, C.K., Clausen, P.A., Hammer, M., Nielsen, G.D., Wolkoff, P. and Spengler, J.D. (2002) Upper airway and pulmonary effects of oxidation products of (+)-α-pinene, *d*-limonene, and isoprene in BALB/c mice, *Inhal. Toxicol.*, **14**, 663–684.
Rohr, A.C., Weschler, C.J., Koutrakis, P. and Spengler, J.D. (2003) Generation and quantification of ultrafine particles through terpene/ozone reaction in a chamber setting, *Aerosol Sci. Technol.*, **37**, 65–78.
Rolando, M., Macri, A., Carlandrea, T. and Calabria, G. (1998) Use of a questionnaire for the diagnosis of tear film-related ocular surface disease, In: Sullivan, D.A. (ed.) *Lacrimal Gland, Tear Film, and Dry Eye Syndromes 2*, New York, Plenum Press, 821–825.
Rosenkranz, H.S. and Cunningham, A.R. (2003) Environmental odors and health hazards, *Sci. Total. Environ.*, **313**, 15–24.
Saijo, Y., Kishi, R., Sata, F., Katakura, Y., Urashima, Y., Hatakeyama, S., Kobayashi, S., Jin, K., Kurahashi, N., Kondo, T., Gong, Y.Y. and Umemura, T. (2004) Symptoms in relation to chemicals and dampness in newly built dwellings, *Int. Arch. Occup. Environ. Health.*, **77**, 461–470.
Sarwar, G., Corsi, R., Kimura, Y., Allen, D. and Weschler, C.J. (2002) Hydroxyl radicals in indoor environment, *Atmos. Environ.*, **36**, 3973–3988.
Schaper, M. (1993) Development of a database for sensory irritants and its use in establishing occupational exposure limits, *Am Ind Hyg Assoc J*, **54**, 488–544.
Schieberle, P. and Grosch, W. (1991) Potent odorants of the wheat bread crump. Differences to the crust and effect of a longer dough fermentation, *Z Lebensm Unters Forsch*, **192**, 130–135.
Schiffman, S.S. and Williams, C.M. (2005) Science of odor as a potential health issue, *J. Environ. Qual.*, **34**, 129–138.
Schiffman, S.S., Studwell, C.E., Landermann, L.R., Berman, K. and Sundy, J.S. (2005) Symptomatic effects of exposure to diluted air sampled from a swine confinement atmosphere on healthy human subjects, *Environ. Health. Perspect.*, **113**, 567–576.
Schleibinger, H., Hott, U., Braun, P., Plieninger, P. and Rüden, H. (2001) VOC-Koncentrationen in Innenräumen des Grossraums Berlin im Zeitraum von 1988 bis 1999, *Gefahrstoffe Reinhaltung Luft.*, **61**, 26–34.
Schlink, U., Rehwagen, M., Damm, M., Richter, M., Borte, M. and Herbarth, O. (2004) Seasonal cycle of indoor-VOCs: comparison of apartments and cities, *Atmos. Environ.*, **38**, 1181–1190.
Segala, C., Poizeau, D. and Maze, J.M. (2003) Odors and health: a descriptive epidemiological study around a wastewater treatment plant, *Rev. Epidemiol. Sante. Publique.*, **51**, 201–214.
Seifert, B. (1995) Validity criteria for exposure assessment methods, *Sci. Total. Environ.*, **168**, 101–107.
Sexton, K., Adgate, J.L., Ramachandran, G., Pratt, G.C., Mongin, S.J., Stock, T.H. and Morandi, M.T. (2004) Comparison of personal, indoor, and outdoor exposures to hazardous air pollutants in three urban communities, *Environ. Sci. Technol.*, **38**, 423–430.
Shendell, D.G., Winer, A.M., Stock, T.H., Zhang, L., Zhang, J., Maberti, S. and Colome, S.D. (2004) Air concentrations of VOCs in portable and traditional classrooms: results of a pilot study in Los Angeles County, *J. Expo. Anal. Environ. Epidemiol.*, **14**, 44–59.
Shusterman, D., Murphy, M.A. and Balmes, J. (2003) Differences in nasal irritant sensitivity by age, gender, and allergic rhinitis status, *Int. Arch. Occup. Environ. Health.*, **76**, 577–583.
Skov, P., Valbjørn, O., Gyntelberg, F. and DISG (1989) *Rådhusundersøgelsen – Indeklima i kontorer*, Copenhagen, Arbejdsmiljofondet, 1–71.
Staudenmayer, H., Binkley, K.E., Leznoff, A. and Phillips, S. (2004) Idiophatic environmental intolerance. Part 2: causation analysis applying Bradford Hill's criteria to the toxicogenic theory, *Toxicol. Rev.*, **22**, 247–261.
Steinheider, B. (1999) Environmental odours and somatic complaints, *Z. Hygiene Umweltmed.*, **202**, 101–119.
Subramanian, P., Reynolds, S., Breuer, G. and Whitten, P. (2000) Analysis of limonene as an indicator for the assessment of environmental air-quality and health symptoms in office buildings, *J. Environ. Sci. Health A Toxic/Hazard. Subst. Environ. Eng.*, **A35**, 999–1019.
Sucker, K., Both, R. and Winneke, G. (2001) Adverse effects of environmental odours: reviewing studies on annoyance responses and symptom reporting, *Water Sci. Technol.*, **44**, 43–51.
Sundell, J., Andersson, B., Andersson, K. and Lindvall, T. (1993) Volatile organic compounds in ventilating air in buildings at different sampling points in the buildings and their relationship with the prevalence of occupant symptoms, *Indoor Air*, **3**, 82–93.
Tamblyn, R.M., Menzies, R.I., Tamblyn, R.T., Farant, J.-P. and Hanley, J. (1992) The feasibility of using a double blind experimental cross-over design to study interventions for sick building syndrome, *J. Clin. Epidemiol.*, **45**, 603–612.
Ten Brinke, J., Selvin, S., Hodgson, A.T., Fisk, W.J., Mendell, M.J., Kosjland, C.P. and Daisey, J.M. (1998) Development of new volatile organic compound (VOC) exposure metrics and their relationship to sick building syndrome symptoms, *Indoor Air*, **8**, 140–152.
van Thriel, C., Kiesswetter, E., Blaszkewicz, M., Golka, K. and Seeber, A. (2003) Neurobehavioral effects during experimental exposure to 1-octanol and isopropanol, *Scand. J. Work. Environ. Health.*, **29**, 143–151.
Tuomainen, M., Pasanen, A.-L., Tuomainen, A., Liesivuori, J. and Juvonen, P. (2001) Usefulness of the Finnish classification of indoor climate, construction and finishing materials: comparison of indoor climate between two new blocks of flats in Finland, *Atmos. Environ.*, **35**, 305–313.
Van den Bergh, O., Winters, W., Devries, S. and Van Diest, I. (2002) Learning subjective health complaints, *Scand. J. Psychol.*, **43**, 147–152.
Wainman, T., Weschler, C.J., Lioy, P.J. and Zhang, J. (2001) Effects of surface type and relative humidity on the production and concentration of nitrous acid in a model indoor environment, *Environ. Sci. Technol.*, **35**, 2200–2206.
Wargocki, P., Wyon, D.P., Baik, Y.K., Clausen, G. and Fanger, P.O. (1999) Perceived air quality, sick building syndrome (SBS) symptoms and productivity in an office with two different pollution loads, *Indoor Air*, **9**, 165–179.
Weschler, C.J. (2000) Ozone in indoor environments: concentrations and chemistry, *Indoor Air*, **10**, 269–288.
Weschler, C.J. and Shields, H.C. (1997a) Measurements of the hydroxyl radical in a manipulated but realistic indoor environment, *Environ. Sci. Technol.*, **31**, 3719–3722.
Weschler, C.J. and Shields, H.C. (1997b) Potential reactions among indoor pollutants, *Atmos. Environ.*, **31**, 3487–3495.
Weschler, C.J. and Shields, H.C. (1999) Indoor ozone/terpene reactions as a

source of indoor particles, *Atmos. Environ.*, **33**, 2301–2312.
Weschler, C.J. and Shields, H.C. (2000) The influence of ventilation on reactions among indoor pollutants: modeling and experimental observations, *Indoor Air*, **10**, 92–100.
Whelton, A.J. and Dietrich, A.M. (2004) Relationship between intensity, concentration, and temperature for drinking water odorants, *Water Res.*, **38**, 1604–1614.
Wilkins, C.K., Clausen, P.A., Wolkoff, P., Larsen, S.T., Hammer, M., Larsen, K., Hansen, V. and Nielsen, G.D. (2001) Formation of strong airway irritants in mixtures of isoprene/ozone and isoprene/ozone/nitrogen dioxide, *Environ. Health. Perspect.*, **109**, 937–941.
Wilkins, C.K., Wolkoff, P., Clausen, P.A., Hammer, M. and Nielsen, G.D. (2003) Upper airway irritation of terpene/ozone oxidation products (TOPS). Dependence on reaction time, relative humidity and initial ozone concentration, *Toxicol. Lett.*, **143**, 109–114.
Willers, S., Andersson, S., Anderson, R., Grantén, J., Sverdrup, C. and Rossell, L. (1996) Sick building syndrome symptoms among the staff in schools and kindergartens: are the levels of volatile organic compounds and carbon dioxide responsible? *Indoor Built Environ.*, **5**, 232–235.
Winters, W., Devries, S., Van Diest, I., Nemery, B., Veulemans, H., Eelen, P., Van de Voestijne, K. and Van den Bergh, O. (2003) Media warnings about environmental pollution facilitate the acquisition of symptoms in response to chemical substances, *Psychosom. Med.*, **63**, 332–338.
Wolkoff, P. (1995) Volatile organic compounds – sources, measurements, emissions, and the impact on indoor air quality, *Indoor Air Suppl.*, **3**, 1–73.
Wolkoff, P. (1999) How to measure and evaluate volatile organic compound emissions from building products. A perspective, *Sci. Total Environ.*, **227**, 197–213.
Wolkoff, P. (2003) Trends in Europe to reduce the indoor pollution of VOCs, *Indoor Air*, **13**, 5–11.
Wolkoff, P. and Nielsen, G.D. (2001) Organic compounds in indoor air – their relevance for perceived indoor air quality, *Atmos. Environ.*, **35**, 4407–4417.
Wolkoff, P., Clausen, P.A., Nielsen, P.A. and Mølhave, L. (1991a) The Danish twin apartment study; part I: formaldehyde and long-term VOC measurements, *Indoor Air*, **1**, 478–490.
Wolkoff, P., Nielsen, G.D., Hansen, L.F., Albrechtsen, O., Johnsen, C.R., Heinig, J.H. and Franck, C. (1991b) A Study of human reactions to building materials in climatic chambers. Part II: VOC measurements, mouse bioassay, and decipol evaluation in the 1–2 mg/m^3 TVOC range, *Indoor Air*, **1**, 389–403.
Wolkoff, P., Clausen, P.A., Jensen, B., Nielsen, G.D. and Wilkins, C.K. (1997) Are we measuring the relevant indoor pollutants? *Indoor Air*, **7**, 92–106.
Wolkoff, P., Schneider, T., Kildesø, J., Degerth, R., Jaroszewski, M. and Schunk, H. (1998) Risk in cleaning: chemical and physical exposure, *Sci. Total Environ.*, **215**, 135–156.
Wolkoff, P., Clausen, P.A., Wilkins, C.K., Hougaard, K.S. and Nielsen, G.D. (1999) Formation of strong airway irritants in a model mixture of (+)-α-pinene/ozone, *Atmos. Environ.*, **33**, 693–698.
Wolkoff, P., Clausen, P.A., Wilkins, C.K. and Nielsen, G.D. (2000) Formation of strong airway irritants in terpene/ozone mixtures, *Indoor Air*, **10**, 82–91.
Wolkoff, P., Skov, P., Franck, C. and Pedersen, L.N. (2003) Eye irritation and environmental factors in the office environment. Hypotheses, causes, and a physiological model, *Scand. J. Work. Environ. Health.*, **29**, 411–430.
Wolkoff, P., Nøjgaard, J.K., Troiano, P. and Piccoli, B. (2005a) Eye complaints in the office environment: precorneal tear film integrity influenced by eye blinking efficiency, *Occup. Environ. Med.*, **62**, 4–12.
Wolkoff, P., Knudsen, H.N., Clausen, P.A., Wilkins, C.K. and Shibuya, H. (2005b) The impact of information on perceived air quality–"organic" versus "synthetic" building materials, 10th International Conference on Indoor Air Quality and Climate, Beijing, September 4–9, 2005, Vol. 2, 2059–2063.
Woodfield, M. and Hall, D. (1994) *Odour Measurement and Control – An Update*, Culham, Abingdon, AEA Technology, 1–19.
World Health Organization (1989) *Indoor Air Quality: Organic Pollutants*, EURO Reports and Studies No. 111. Copenhagen, World Health Organization.
World Health Organization. *Air Quality Guidelines for Europe*, Copenhagen: World Health Organization, Regional Office for Europe, 2000. Ed. 2, 1–273.
Yerkes, R.M. and Dodson, J.D. (1908) The relation of strength of stimulus to rapidity of habit formation, *J. Comp. Neurol. Psychol.*, **18**, 459–482.