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Organic compounds in indoor air—their relevance for perceived indoor air quality?☆

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Abstract

It is generally believed that indoor air pollution, one way or another may cause indoor air complaints. However, any association between volatile organic compounds (VOCs) concentrations and increase of indoor climate complaints, like the sick-building syndrome symptoms, is not straightforward. The reported symptom rates of, in particular, eye and upper airway irritation cannot generally be explained by our present knowledge of common chemically non-reactive VOCs measured indoors. Recently, experimental evidence has shown those chemical reactions between ozone (either with or without nitrogen dioxide) and unsaturated organic compounds (e.g. from citrus and pine oils) produce strong eye and airway irritating species. These have not yet been well characterised by conventional sampling and analytical techniques. The chemical reactions can occur indoors, and there is indirect evidence that they are associated with eye and airway irritation. However, many other volatile and non-volatile organic compounds have not generally been measured which could equally well have potent biological effects and cause an increase of complaint rates, and posses a health/comfort risk. As a consequence, it is recommended to use a broader analytical window of organic compounds than the classic VOC window as defined by the World Health Organisation. It may include hitherto not yet sampled or identified intermediary species (e.g., radicals, hydroperoxides and ionic compounds like detergents) as well as species deposited onto particles. Additionally, sampling strategies including emission testing of building products should carefully be linked to the measurement of organic compounds that are expected, based on the best available toxicological knowledge, to have biological effects at indoor concentrations. © 2001 Elsevier Science Ltd. All rights reserved.

Keywords: Airway irritation; Indoor air quality; OCIA; Odour annoyance; TVOC; Volatile organic compounds (VOCs)

1. Introduction

Already, Ramazzini, the father of occupational medicine, described inter alia the occupational environment of scholars and their illnesses (Ramazzini, 1713). He explained that small rooms became filled with smoke from oil lamps and gases emitted from humans and that these pollutants penetrated the brain skull. This resulted in depression and annoyance. Astronauts, more than 250 years later, also have suffered and still suffer from severe symptoms in the broad category of the sick-building syndrome (SBS) type, like headache and burning eyes. This is suspected to be caused by poor air quality of the station (Seife, 1999). After the focus on formaldehyde as a major indoor pollutant, there has been considerable interest in volatile organic compounds (VOCs) as potential causes of eye and airway irritation, in addition to other health effects. Although, recently, the provocative question, "Are we measuring the relevant indoor pollutants?" was raised (Wolkoff et al., 1997), it is generally assumed that indoor air pollution,

☆There is a call for an expansion of the VOC definition by WHO in 1989, because many organic compounds volatile as well as non-volatile may equally be well considered causative agents associated with indoor climate complaints.

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one way or another, causes an increase of indoor air complaints. This review will, in particular, focus on eye and airway irritation and odour annoyance (here referred to as sensory effects), because they are often reported in non-industrial buildings.

Nevertheless, health effects of indoor air also comprise systemic effects (Nielsen et al., 1997a). However, building occupants only perceive sensory effects, for example odour annoyance, eye and airway irritation, and headache (CNS effect), whereas other systemic effects will not be encountered. The carcinogenic compound benzene may illustrate this. The 90% percentile of its indoor air level is $20\,\mu g/m^3$ (WHO, 1989) and the lowest sensory threshold, the odour threshold, is $33\,mg/m^3$ (Jensen and Wolkoff, 1996). This supports that perceived indoor air quality largely should be evaluated from the sensory effects of the substances in indoor air.

VOCs as a group has been defined as organic compounds with boiling points from about 50°C to about 260°C (WHO, 1989). This interval was chosen for reasons of sampling and analytical capabilities rather than from the point of health effects (Wolkoff et al., 1997). WHO has also defined more volatile (VVOCs) and less volatile organic compounds (SVOCs) not always included in indoor air measurements and evaluations.

VOCs are ubiquitous indoors. Some indoor VOCs are also present outdoors together with specific outdoor inorganic compounds (e.g., ozone). Major sources that contribute to the indoor pollution are human activities, building product emissions, and infiltration of the outdoor air. For new or renovated buildings, the primary emission of VOCs (e.g., solvents) from building products generally dominates for a period of up to some months. Ageing of building products, by chemical (e.g., ozone, maintenance, moisture) or physical (e.g., heat, weariness, UV-light) decomposition may result in secondary emissions (from building products), which contribute to the pollution indoors, in some cases continuously (Wolkoff, 1999). Their specific emission rates, however, are generally significantly lower than those of primary emissions. The use of the International Indoor Climate Labelling scheme to some extent limits the primary (and partially the secondary) emission of VOCs from building products (Wolkoff and Nielsen, 1996), and thus results in lower VOC concentrations with probably fewer indoor air complaints (Tuomainen et al., 2001).

It is difficult to explain the prevalence of eye and airway irritation, and for that matter other commonly reported symptoms (e.g., headache) based on available VOC measurements in non-industrial buildings (Wolkoff et al., 1997). For that particular reason, there is a tendency to look for other pollutants so far not considered or not yet identified. Alternatively, combinations of exposure loads should be considered. What is easily measured is not necessarily relevant for indoor air complaints. Real life may not be that simple and it becomes even more complicated when the psychology of complaints is to be included in the understanding of indoor air complaints.

The purpose of this work is to give an overview of the ongoing transition of the use of total volatile organic compounds (TVOC) to the compound-by-compound approach of VOC evaluation with regard to their impact on perceived air quality, i.e. odour annoyance and eye and airway irritation, indoor complaints often reported in epidemiological studies (cf., Brightman and Moss, 2000). To do this, a series of important interrelated questions will be discussed. These are:

(i) VOC concentrations—Where are we?
(ii) Is TVOC in general sufficient for the evaluation of building complaints or should additional approaches (pollutants) be developed and preferred? For example, is a more extended evaluation, based on the individual potency of VOCs, a better approach?
(iii) Are there alternative organic compounds that should be considered as biologically relevant[1] with regard to their health/comfort impact (cf., Seifert, 1995), because they are likely to increase the prevalence of reported symptoms?
(iv) What hypotheses to propose and to pursue.

2. VOC concentrations—where are we?

The number of observed and identified VOCs is directly related to the performance of the laboratory (i.e., the combination of sampling and analytical methods, in addition to the instrumental performance). This implies that generally only a certain chromatographic window of VOCs is measured that depends primarily on the sampling techniques and analytical conditions used. For example, it has been recommended that the sum of VOCs by use of Tenax TA as sampling medium and a chromatographic window that corresponds to hexane to hexadecane to be used (ECA, 1997). In addition, 64 known VOCs within the VOC definition by WHO (1989) shall be quantified and defined as TVOC.

The concentration of single VOCs was reviewed to be generally below $50\,\mu g/m^3$, with most below $5\,\mu g/m^3$ (Brown, 1999a). Similarly, both European and N.

[1] Biologically relevant for the indoor environment = a chemical compound or marker where a cause–effect relationship has been identified to play a role at typical indoor concentrations for the majority of the population. However, for sensitive people other dose dependencies may prevail.

American studies show that the mean concentration of the majority of single VOCs is generally below 10 μg/m^3 (Bornehag and Stridh, 2000; Brown and Crump, 1996; Bernhard et al., 1995; Girman et al., 1999; Shields et al., 1996). Table 1 shows some of the major and most often reported indoor VOCs. Some of the differences may depend on the use of sampling media and the conditions of the environment (e.g., high ozone concentrations). Generally, organic substances with halogens appear to be present in measurements carried out in N. America and Japan and are less common in Northern Europe. Most of the reported concentrations are stationary measurements. It appears that the VOC spectrum may have changed during the last decade with the addition of a series of new VOCs, partly because of a change in sampling techniques and partly due to the introduction of new building products and solvents used therein (Reitzig et al., 1998; Salthammer et al., 1998; Schleibinger et al., 2001). Breathing zone concentrations could be a factor of two to four higher, compared to the stationary measurements (e.g., Rodes et al., 1991). In addition, certain unsaturated VOCs (e.g., terpenes) could be underestimated in ozone-enriched environments, partly due to reactions at the sorption medium (Calogirou et al., 1996) and partly due to atmospheric reactions (Weschler, 2000). Despite of this, it has generally been assumed, partly on the basis of human exposure studies carried out at concentrations that are orders of magnitude higher (loc.cit. Wolkoff, 1995) that there exists a cause–effect relationship between typical indoor VOCs concentrations and health effects (e.g. airway irritation). This implicit, but undocumented, assumption has influenced the activities regarding air sampling, health evaluation, and the development of emission testing.

Desorption studies of floor dust has shown that several organic compounds are adsorbed unto particles (cf., Wilkins et al., 1993). Additionally, office floor dust has been found to contain compounds with surface-active properties, like fatty acid salts (Clausen et al., 1998) and linear alkyl benzene sulphonates (Vejrup et al., 1999). It is probable that resuspended particles, one way or another, may reach the breathing zone and the eyes and possibly contribute to a biological effect (examples are given in Wolkoff et al., 1998). Health effects of combinations of gases and particles have also been reported. Some examples are ozone and carbon black (Jakab and Hemenway, 1994), ozone and particles (Krzyzanowski et al., 1992), and ozone and allergenes (Peden et al., 1995; Molfino et al., 1991). It has been found that nitrogen dioxide may increase the effect of dust mites (Tunnicliffe et al., 1996). Considering these findings, in addition to the formation of potent irritants in ozone/terpene reactions (vide infra), many other compounds, including those adsorbed unto particles, may explain indoor air complaints as the non-reactive VOCs, see Fig. 1. Thus, there appears to be both a chemical and biological justification to expand the present VOC window.

3. Is evaluation of TVOC sufficient?

A technical definition of TVOC (i.e., a sum of VOC concentrations (in μg/m^3) within the VOC chromatographic window) has been proposed by a European working group (ECA, 1997). However, it is also clearly stated by ECA that no cause–effect relationship exists between TVOC concentrations and health effects, in particular, airway irritation (cf., Andersson et al., 1997; Berglund and Johansson, 1996; Wolkoff, 1995).

It is important to realise that the TVOC concept as defined by ECA only represents a narrow chromatographic window of organic compounds that are volatile (see Fig. 1). Recently, it has been demonstrated that there are analytical problems of the determination of TVOC (e.g., Massold et al., 2000; Oppl et al., 2000). There are many other aspects to be considered in addition to the criticism already available. For example, the following compounds are not measured by conventional sampling techniques: (i) Reactive organic compounds like aldehydes, hydroperoxides, etc (cf. Weschler and Shields, 1997) and intermediary (irritants) reaction products in mixtures of ozone/nitrogen dioxide and unsaturated VOCs like terpenes (Wolkoff et al., 2000), in addition, some unsaturated VOCs may be underestimated due to reactions with ozone in the air (Weschler, 2000) or on the sampling media (Calogirou et al., 1996); (ii) Odorous compounds are present often at concentrations too low to be analysed. Finally, it is also possible that some biologically relevant compounds have not yet been discovered.

The key issue about the TVOC concept is to avoid the fallacy that TVOC has any biological relevance. The TVOC concept, however, has some useful applications, e.g. as a source finding method (e.g., by use of direct reading instrument), in quality control of building product emission or in intervention studies, in all cases, provided their profiles of VOCs are similar. For example, it may be applied in search of extreme concentration levels (or strong sources, like leakage from a gasoline tank, cf. Table 2.5.1 in Wolkoff, 1995).

4. Biologically based evaluations of VOCs

Parallel with the development of analytical methods for analysis of VOCs there has been a development of methods for the biological evaluation of their exposure effects in indoor environments.

Table 1
Ubiquitous VOCs in indoor air measured in European and North American field studies in order of ca. 20 most abundant in descending order

Australian review[a]	European audit[b]	US review[c]	BASE study[d]	Swedish housing stock[e]	German study[f] Selected (new) VOCs
Benzene	Acetone	*o*-Xylene	Acetone	Toluene	Group 1:
Tetrachloroethylene	Isoprene	Benzene	Hexane	Decane	Phenoxyethanol
p-Dichlorobenzene	2-Methylpentane	Tetrachloroethylene	Toluene	Dodecane	Butyldiglycol acetate
Ethylbenzene	Hexane	*m*-, *p*-Xylenes	1,1,1-Trichloroethane	Nonanal	Longifolene
m-, *p*-Xylenes	2-Methylhexane/benzene	Ethylbenzene	Methyl chloride	Undecane	Dimethyl phthalate
1,1,1-Trichloroethane	Heptane	Trichloroethylene	Benzene	Limonene	
o-Xylene	Toluene	Toluene	Ethanol	C_{11}-Alkane	Group 2:
Decane	*m*-, *p*-Xylenes	1,1,1-Trichloroethane	2-Propanol	C_{12}-Alkane	α-Pinene
Toluene	*o*-Xylene	Dichlorobenzenes	Dichlorofluoromethane	Xylenes	Camphene
1,2,4-Trimethylbenzene	Decane	Styrene	*m*-, *p*-Xylenes	C_{10}-Alkane	*β*-Pinene
Hexane	Trimethylbenzene	Undecane	2-Butanone	Trimethylbenzenes	3-Carene
Nonane	Limonene	Dodecane	Trichlorofluoromethane	Butoxyethoxyethanol	Group 3:
Limonene		Octane	*o*-Xylene	Butoxypropanol	Styrene
			Undecane	C_7-Alkane	*o*-Xylene
			Tetrachloroethylene		C_{12}-Alkanes
			Methylene chloride		
			1,2,4-Trimethylbenzene		Group 4:
			Decane		1,2,3-Trimethylbenzene
					1,2,4-Trimethylbenzene
					Methylcyclohexane

[a] Brown, 1999a.
[b] Bernhard et al., 1995.
[c] Holcomb and Seabrook, 1995.
[d] Girman et al., 1999; includes 61–100% frequency.
[e] Bornehag and Stridh, 2000.
[f] Reitzig et al., 1998.

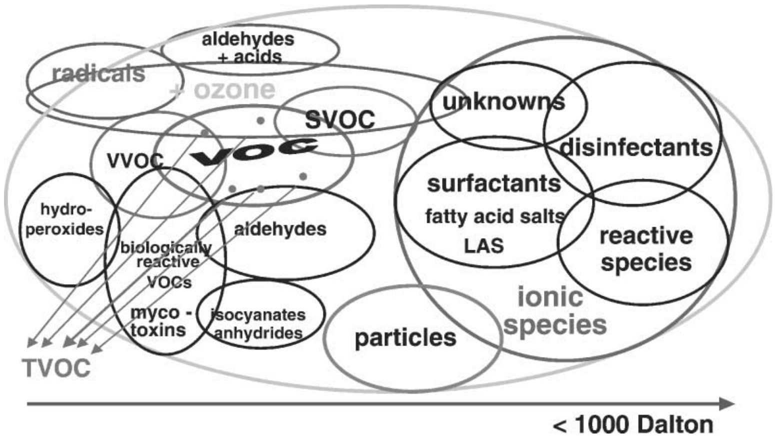

Fig. 1. A schematic and tentative presentation of the OCIA universe. OCIAs include organic compounds as well as organic compounds on particles, in addition to intermediary species (e.g., organic radicals), and ionic species. Compounds of microbiological origin (e.g., glucans, endotoxins) are not part of OCIA. The molecular weights of OCIAs are tentatively less than 1000 Da.

4.1. The impact of odorous VOCs

Among indoor air researchers, it is generally assumed that a low (chemical) emission building product is better than a high emission product for the indoor environment. If sensory perception (e.g., as odour intensity) is a valid criterion of comparison, the assumption should be considered with some caution, because a building product with low VOC specific emission rates may only be satisfactory if the sensory impact is low too, i.e. the emitted compounds have low odour indices (i.e., VOC_x concentration/odour threshold of VOC_x). Studies in the literature indicate that materials with high odour indices also result in unacceptable ratings in human panel evaluations (cf. Wolkoff et al., 1991).

Many indoor VOCs emitted from building products have odour thresholds sufficiently low to cause an impact on the perceived air quality, in some cases even malodorous events, in some cases for long periods, e.g. after renovation (Hodgson et al., 2000; Reitzig et al., 1998; Wolkoff and Nielsen, 1996). One aspect of building product emission testing and the evaluation thereof is the link between VOC emissions (concentrations) and perceived air quality. An understanding of this interrelation is essential to predict the possible impact of emitted VOCs. So far, it has been difficult to find correlation between emitted VOCs from building products and odour intensity (and acceptability) (Jensen et al., 1995; Knudsen et al., 1999). Adaptation to odours undoubtedly occurs (Gunnarsen and Fanger, 1992; Prah et al., 1998) and odours may also exhibit a masking effect on airway irritation (Cain and Murphy, 1980; Wolkoff et al., 1991).

Heterogeneous reactions between components in naturally occurring or polymeric building products with one or more unsaturated C–C bond structure and oxidants (e.g., oxygen, ozone and nitrogen dioxide) can form low molecular weight aldehydes and fatty acids, i.e., secondary emissions (Wolkoff, 1999). Some of these are characterised by low odour thresholds and therefore they may influence the perceived air quality (Knudsen et al., 1999, 2000). Thus, emission testing of some building products under enriched environments of ozone and nitrogen dioxide may be required.

The evaluation of odour effects of measured VOCs by means of their odour index is clearly relevant. However, the analytical limitations mentioned under TVOC also apply in this context. Substances as aldehydes, carboxylic acids, and amines may have low odour thresholds, but may not be detected analytically. This argues for a broader analytical window than that of the VOC definition by WHO (1989), and in some cases for extended analyses within the classic VOC window. It is important to realise that inorganic compounds like ammonia and ozone also should be considered biologically relevant, in particular ozone because of its chemical reactions with unsaturated organic compounds (Weschler, 2000).

4.2. Airway irritation

A direct cause effect relationship between exposure to typical chemically non-reactive indoor VOCs and adverse impact on health, in particular the sensory effects, has been implicitly assumed for about two decades. In particular, eye and airway irritation and other symptoms have been considered. The scientific evidence thereof for typical indoor concentrations of non-reactive VOCs, however, has not been supportive (cf. Andersson et al., 1997; Hempel-Jørgensen et al., 1998; Holcomb and Seabrook, 1995; Mølhave et al., 2000; Nielsen et al., 1995; Wolkoff et al., 1997). Further, studies of quantitative structure-activity relationships and the principle of addition have not been able to predict indoor air complaints of a (non-reactive) VOC mixture evaluated from the potency of each VOC present at typical indoor levels (Alarie et al., 1996).

On the contrary, formaldehyde and acrolein are considered reactive VOCs and they are well known airway irritants (cf., Rothweiler and Schlatter, 1993; Wolkoff et al., 1997; see also Nielsen et al., 1997b). These compounds have low estimates of airway irritation in humans (Jensen and Wolkoff, 1996). Similarly, reactions of unsaturated VOCs (e.g., terpenes) with oxidants (e.g., ozone and nitrogen oxides) can form reactive species that are strong airway irritants (Kane and Alarie, 1978; Wolkoff et al., 2000). For example, radicals are chemically reactive, and as reactive species they are expected to have a strong potential for eye and airway irritation. These intermediary species may rearrange to stable products like fatty acids and aldehydes. They may be responsible for the deterioration of the perceived air quality (i.e., odour annoyance), possibly in association with adsorption onto particles and inhalation thereof.

The sum of microbiological VOCs (MVOCs) has also been used as a marker like TVOC, but it is unlikely that their concentrations, as typically measured, could result in airway irritation (Pasanen et al., 1998; Wilkins et al., 1998). However, several MVOCs have low odour thresholds and thus may result in odour annoyance.

Although, the overwhelming majority of evidence supports the conclusion that chemically non-reactive VOCs cannot in general explain eye and airway irritation indoors (vide supra), the time aspect still remains open and requires further studies. For example, repetitive exposure and/or long-term exposure to an irritant stimulus could modulate either the psychological and/or the physiological response to a given VOC (Hummel et al., 2000). Thus, an increase of effects over time has been found for formaldehyde (e.g., 0.25 ppm) (Cain et al., 1986) and environmental tobacco smoke concentrations (Cain et al., 1987; Walker et al., 1997). On the contrary, the irritation threshold for nicotine is the same among smokers and non-smokers, which indicates that repeated exposure to nicotine does not result in a lower threshold thereof (Thuerauf et al., 2000). Repetitive exposures to acetic acid in the home environments of subjects have been studied for three weeks with acetone as a control odorant (Hummel et al., 2000). It was shown that the response to acetic acid decreased during the exposure period, while the response to acetone showed little change over the course of the long-term exposure. Time studies at high VOC concentrations have shown some increase over time, usually during the first 30 min of exposure (Cain and Murphy, 1980; Hempel-Jørgensen et al., 1998; Hudnell et al., 1993). On the contrary, the exposure to similar VOCs has also resulted in apparent adaptation to airway irritation observed among women subjects (Prah et al., 1998). A significant increase of neutrophils, indicator of inflammatory response, was found in nasal lavage of healthy men exposed to a mixture of VOCs (total, ca. 25 mg/m^3) and this effect was observed even after 24 h (Koren et al., 1992). The usually high VOC concentrations, however, hampers an interpretation of the effect of time at indoor relevant concentrations.

There is no support for the hypothesis that typical building product emissions (tested in Denmark) can result in the increase of airway irritation after the initial decay of the primary emission (Knudsen et al., 1999; Nielsen et al., 1997b), except for cases of high formaldehyde emissions (e.g., Wolkoff et al., 1991).

5. The paradigm shifts I–II

5.1. Measurements—expansion of the VOC window

The difficulty to use VOCs as an explanatory model for eye and airway irritation (Wolkoff et al., 1997), and for that matter all other indoor air complaints, has prompted a Nordic working group to recommend a new concept OCIA (organic compounds in indoor air) (Bornehag and Cain, 2000; Bornehag et al., 2001). The new broader definition includes all biologically relevant organic compounds, non-proteins, non-glucans, etc, (i.e., organic compounds tentatively with molecular weights less than 500–1000 Da) in the indoor environment. The organic compounds are all airborne, i.e. organic gases and vapours including organic compounds as defined by WHO (1989), in addition organic species (e.g., radicals, and ionic species like acid salts and ionic surface-active compounds) and/or adsorbed onto particles. The OCIA concept should take care of compounds not previously covered by the WHO definition. The suggested OCIA definition reflects:

(i) Biological relevance at indoor concentrations.
(ii) A broader window with respect to molecular weight and vapour pressure i.e., retention times on GC columns.
(iii) Indoor air concentrations as normally encountered, i.e., in the lower μg/m^3 range.
(iv) Atmospheric reactions in indoor air.
(v) So far poorly characterised (intermediary) species, like radicals, and ionic species
(vi) Substances adsorbed on particles.

The OCIA concept is a challenge for both the analytical chemist and the toxicologist and it demands for careful analysis of the biological relevance of potential compounds to be measured. This implies that measurements should be related to a given or otherwise scientifically anticipated health/comfort effect like odour and airway irritation. In addition, international guidelines or hypotheses may be pursued. Table 2 lists some possible OCIAs of which certain effects are believed to be relevant and possibly with similar probabilities to cause adverse health effects (e.g., airway irritation and/or odour annoyance) than the traditional (chemically non-reactive) VOCs. It should be noted that the OCIA concept, for the time being, is limited not to incorporate compounds of microbiological origin, like glucans, endotoxins, etc. which all may be biologically relevant for the study of moisture damaged buildings.

5.2. The reactive chemistry—in search for new hypotheses of cause–effect relationships

The hypothesis that ozone and unsaturated VOCs (e.g., terpenes) form strong airway irritants has recently been supported by experimental evidence by use of an animal bioassay (Wolkoff et al., 2000). Although, it is well-known that these reactions form aldehydes, carboxylic acids, in addition to hydroperoxides and Criegee biradicals (Weschler and Shields, 1997), the observed biological response of measured compounds can only partially be explained by the identified compounds. Apparently, one or more unidentified potent sensory irritant(s) has been formed, which has not been analysed by the use of conventional sampling techniques. These reactions occur sufficiently fast at typical indoor conditions (Weschler, 2000) and they compete with the air exchange rate, particularly at low rates (Weschler and Shields, 2000). It should be acknowledged that low terpene concentrations, per se, simply might reflect chemical reactions that could contribute to airway irritation. Similar considerations could be made for the measurements in particular ozone and nitrogen dioxide.

So, it appears reasonable to assume that the reactive chemistry may produce strong airway irritants. For example, a mixture of 2-butene, but not butane, nitrogen oxides and UV light has an airway irritation potential like formaldehyde (Kane and Alarie, 1978); similarly, (Stephens et al., 1961) found that mixtures of 2-butene and butadiene and ozone produce eye irritants.

The relevance of the above findings is supported by some epidemiological studies. For example, it has been demonstrated that ΔTVOC (sum of lost VOCs, i.e. the change of the sum of VOC concentrations during transport from the air supply inlet to a sampling point in the room), was correlated with complaint rates in 86 Swedish offices (Sundell et al., 1993). It should be noted, however, that the mean geometric TVOC levels were below 100 $\mu g/m^3$. Additionally, increased formaldehyde concentrations were weakly associated with ΔTVOC. A similar observation has been found to explain SBS prevalence and low TVOC levels (Groes et al., 1996). Other studies have shown a positive correlation between the use of photocopiers that are known to emit ozone, nitrogen dioxide and VOCs (Brown, 1999b; Leovic et al., 1996), and the rate of reported airway and general symptoms. For example, in the Danish Town Hall study, increased eye and airway irritation was associated with work with visual display units, the use of photocopiers, and handling of carbonless copy paper (Skov et al., 1989). The use of photocopiers has also been associated with increased rating of airway irritation symptoms in other similar investigations (Bourbeau et al., 1997; Fisk et al., 1993; Jaakkola and Jaakkola, 1999; Sundell et al., 1994). One study has shown increased nasal resistance among office workers and wood workers at elevated ozone levels, compared to other risk groups (Höppe et al., 1995). In a field study in six office buildings, it was found that limonene levels correlated with eye symptoms (Subramanian et al., 2000), and similarly, it has been observed that limonene concentration was generally lower in "complaint" buildings than in "non-complaint" buildings (Saarela et al., 1999). These studies add further support that reactive chemistry is related to symptoms, like eye irritation. The observed associations could be rationalised in terms of reactions between limonene and ozone/

Table 2
Examples of organic compounds that are anticipated or postulated to influence the indoor air quality

Acid anhydrides (Becher et al., 1996).
Acrylates.
Amines (Becher et al., 1996), incl. quaternary ammonium compounds (Purohit et al., 2000).
Isocyanates (Becher et al., 1996).
Alkylated aromatics, e.g. alkyl benzenes, quinones, phenols, etc.
Biocides (Rofzkamp et al., 2001).
Sulphur VOCs, mercaptanes, sulphides, disulphides, etc. (low odour thresholds, Jensen and Wolkoff, 1996).
Unsaturated VOCs, e.g., terpenes, styrene, isoprene and their reactions with oxidants, e.g. ozone and nitrogen dioxide (Weschler and Shields, 1997; Wolkoff et al., 2000).
Semi- and non-volatile chemicals on particles, e.g. surface-active compounds like fatty acid salts and linear alkyl benzene sulphonates (Clausen et al., 1998; Vejrup et al., 1999).

nitrogen dioxide forming irritants (vide supra). In another study, eye irritation among workers in joinery shops and repair of cement kiln, respectively, turned out to be significant, and this could partly be associated with terpene/ozone reactions, although ozone was not measured (Eriksson et al., 1997; Sanderson et al., 1999). Eye symptoms were also found to be significant in a human exposure study carried out in a simulated office environment, in which subjects were engaged in typical office work including photocopying and laser printing (Wolkoff et al., 1992). In this study, a significant formaldehyde production was observed that might be related to reactions between ozone and toner powder VOCs (e.g., styrene) and human exhalation of isoprene (Fenske and Paulson, 1999).

6. Conclusion

For the general population, there is no evidence that supports a causative relationship between typical indoor (chemically) non-reactive VOC concentrations and eye/airway irritation in case of low formaldehyde concentrations. However, it cannot be ruled out that a subgroup of the population may be more sensitive to non-reactive VOC concentrations normally measured indoors. For this reason, it is generally recommended to use low emitting building products wherever possible, for example by the use of labelling schemes (Tuomainen et al., 2001; Wolkoff and Nielsen, 1996). In case of a complaint about such products, it is more likely driven by odour perception and not airway irritation, per se, because irritation estimates generally are above odour thresholds (Wolkoff, 1999). However, if indoor pollutants cause (short-term) irritation in the majority of building occupants, it appears fruitful to look for explanations other than VOCs. They only represent a narrow window of the chemical universe of pollutants indoors (cf. Fig. 1), and at normal indoor concentrations cannot explain indoor air complaints. In addition, future sampling strategies including emission testing of building products should carefully be linked to the measurement of organic compounds that are known to have biological relevance at indoor concentrations or at least associated with one or more plausible hypotheses.

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