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Substances with intense odours: general principles, evaluation and designation

MAK Value Documentation – Translation of the German version from 2023

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Abstract

The German Senate Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area (MAK Commission) evaluated data from literature and databases to identify workplace chemicals with objectionable odour and developed a concept to label relevant substances. Odours from substances at the workplace are often strong, unpleasant and perceptible even at concentrations below the valid MAK values (maximum concentration at the workplace). "Odour-associated symptoms" such as nausea and headaches may develop as a result of a special processing of neurophysiological signals, a specific neuroanatomical connectivity and the evolutionary significance of olfaction. These effects cannot be taken into consideration for the derivation of a MAK value because they occur only in isolated cases. Substances at the workplace that are associated with these kinds of effects are designated in the List of MAK and BAT Values with a corresponding footnote. This article presents the scientific background and the specific procedure used for applying the footnote. By stimulating specialized odour

receptors, odours are perceptible even at very low concentrations. After crossing only a few synaptic junctions, the odour information reaches regions of the brain such as the limbic system, the vegetative nuclei of the hypothalamus and the reticular formation. Odours, particularly unpleasant ones, are often perceived as a sign of danger based on individual experiences and evolutionary developments. However, individual responses differ considerably and this variation cannot be explained adequately by physiological mechanisms. Therefore, in order to have the potential of inducing "odour-associated symptoms", the workplace substances in question must have a low odour threshold and an unpleasant odour quality. The methods used to identify these odour characteristics are quite heterogeneous and have not been standardized. Different sources were used to determine the odour characteristics of the 43 workplace substances from the List of MAK and BAT Values that potentially met these criteria. After the data were checked for plausibility, 23 of the substances were designated with the footnote following a systematic evaluation.

1 Background

A footnote stating that "even if the MAK value is observed, 'odour-associated' symptoms cannot be ruled out in individual cases" was introduced with the 2021 List of MAK and BAT Values (DFG 2021) to draw attention to the possibility that "odour-associated" symptoms such as nausea or headaches may occur. As these effects are induced only in isolated cases, they are not taken into consideration for the derivation of a MAK value. Descriptions of individual cases in which these effects occurred can be found in the scientific literature (Shusterman 1992, 2001). However, no data are available to explain the underlying physiological mechanisms that lead to their development. For this reason, a general overview of the special physiological properties of the sense of smell is provided below to further an understanding of why these symptoms may occur. This is followed by a description of the methods and criteria used to apply the footnote.

2 Physiological and neuroanatomical basis

The main reason why the odours of certain substances at the workplace are able to trigger symptoms is the extreme sensitivity of the sense of smell. Another is that the sense of smell is closely connected to brain regions such as the limbic system or the vegetative nuclei of the hypothalamus and the reticular formation (Hatt 2019). These brain regions are involved in the development of emotions such as revulsion and regulate various vegetative functions. However, these are not direct, reflex-like reactions to an odour stimulus, but learned reactions that develop over a lifetime (Ayabe-Kanamura et al. 1998) and are, in part, subconsciously activated. Which activation patterns are initiated in the brain by an odour depends on the individual (Mantel et al. 2019), which is also the reason why the development of "odour-associated" symptoms varies so greatly from person to person (Stevenson 2010).

Many substances found at the workplace are able to activate olfactory receptors in concentrations that lie far below the MAK value. These substances have correspondingly low odour thresholds (van Thriel et al. 2006). The perceptions that thereby are induced already below the MAK value are categorized by humans along the "pleasant–unpleasant" axis, i. e. the hedonic effect of the odour.

After inhalation, the odorant molecules are transported to the olfactory epithelium that is located in the upper nasal cavity and activate the olfactory receptors there. The upper nasal cavity contains about 350 different olfactory receptors and odours are coded based on complex interactions between the odorant molecules and these receptors. However, these interactions are not governed by what is known as the lock–key principle. Olfactory receptors exhibit both high specificity for certain molecular properties as well as a tolerance for others. Therefore, a single olfactory receptor can be activated by different odorants and a single odorant can activate several different receptors. Activation releases electrical signals, initiating a neural activation pattern that undergoes further processing in higher-order brain centres (Hatt 2019). Various factors influence the binding of the odorant molecules to the receptors and thus how an odour is perceived. Odorant molecules reach the olfactory epithelium either through the nose or the throat. An odorant may vary in its solubility, for example, in the mucus of the nose and in that of the throat. Furthermore, the odorant

molecules may be converted by enzymes or transport proteins in the mucus, thereby changing their physicochemical properties (Genva et al. 2019; Schilling 2017).

The physicochemical properties of odorant molecules regulate their ability to bind to and activate olfactory receptors. Even minimal changes in their molecular structure may markedly change how an odour is perceived (Ohloff 1990). The quality and intensity of an odour, for example, depends on the position of its functional groups, the symmetry of the odorant molecule and its stereochemistry.

Another factor that may play a decisive role is the length of the carbon chain: the longer the chain, the easier it is to distinguish between two smells (Boesveldt et al. 2010; Laska and Teubner 1999) and the lower the detection threshold (Cometto-Muñiz and Cain 1990).

The functional groups of an odorant molecule correlate with certain odour qualities. Aldehydes, for example, are described as having a citrus smell, esters are frequently called fruity, whereas amines are considered rather fishy and thiols as rotten or foul-smelling (Genva et al. 2019). However, there are also odorant molecules that have the same functional groups but different odour qualities. As an example, certain lactones have very similar molecular structures, but their odours are perceived very differently with descriptors used such as "minty", "buttery" and "like terpene or camphor". The same odour, for example a "musk-like smell", can also be produced by organic substances that differ greatly in their structure (Genva et al. 2019). Furthermore, enantiomers may differ markedly in their smell in spite of their identical physical and chemical properties. These chiral molecules are oriented to one another in three-dimensional space as mirror images. Two typical examples are limonene and carvone. (R)-Limonene has an orange smell while its mirror image, (S)-limonene, smells like lemon. (S)-Carvone smells like caraway and (R)-carvone like spearmint (Friedman and Miller 1971). Enantiomers may likewise have different odour thresholds (Legrum 2015, p. 35–61).

Recent study findings (Poivet et al. 2016, 2018) have demonstrated that the principles used to describe and classify molecules in organic chemistry are often not suitable for predicting the effects of odours. The findings show, for example, that a specific ring size or specific composition with nitrogen, oxygen or hydrogen atoms is not decisive for the activation of the olfactory receptors by certain odorant molecules with benzene or heteroaromatic rings, but rather the polarity of the molecular surface (Poivet et al. 2016).

The odorant concentration may likewise have an effect on the odour quality because the number of activated olfactory receptors increases with the concentration. The odorants skatole and indole have an extremely nauseating faecal smell; however, at low concentrations, their odour is reminiscent of exotic flowers and overripe fruit. These substances are responsible for the fragrance of jasmine and lilac flowers. Another example is ionone, which smells like violets in low concentrations and has a woody smell in high concentrations (Albrecht and Wiesmann 2006). In many cases, dilution leads to a more pleasant smell. Phenylacetic acid, for example, smells like rotting horse urine in concentrated form, but like honeycomb in strong dilution (Legrum 2015, p. 35–61).

Over the last few years, artificial intelligence (AI) has been used to establish associations between the molecular structure of odorants and the effects of their odour. The AI models are able to attribute odour qualities to molecules with certain structures and predict their odour intensity and hedonic tone (Keller et al. 2017; Keller and Vosshall 2016). However, the reliability of these models cannot yet be evaluated conclusively.

Decisive for the determination of an odour threshold are the parameters that control the transition of the odorant from the gas to the condensed phase (including the dipolarity/polarizability ratio of the dissolved substances). However, the odour thresholds predicted for certain groups of substances (for example, organic acids, mercaptans) were too low. As a result, the models were revised to include group-specific intensification factors (Abraham et al. 2012). Khan et al. (2007) were able to predict whether an odorant would be regarded as pleasant or unpleasant. Other approaches involving AI models focused on characterizing the receptor binding potential of odorant molecules (Gupta et al. 2021). However, even though a large number of studies have been carried out, it is not possible at present to accurately predict the smell of a substance based on its structure. This is because molecular structure is not the only factor involved in the perception of smell. Instead, smell is a holistic process that combines all available information regarding what the body is perceiving at any particular moment, stimuli from the environment as well as past experiences (Bierling

et al. 2021). In general, smelling is not about detecting individual odorant molecules, but mixtures of many different odorants. Two different processes actively play a role in the perception of mixtures of odours (Howard and Gottfried 2014). Configural processing involves the recognition of mixtures of odours as a "configural whole". This means that different odorants are combined to form a unique, perceivable whole. As an example, a mixture of ethyl isobutyrate (strawberry) and ethyl maltol (caramel) is perceived as smelling of pineapple (Coureaud et al. 2022). At the basic level of processing, a mixture of odours is derived from the sum of the various odorants. As the odours are combined, one odorant may weaken or intensify the ability to detect another odorant (Thomas-Danguin et al. 2014) even if the substance itself is odourless (Xu et al. 2020). Likewise, certain odours in a mixture cease to be perceived over time. Habituation to certain odorants in a mixture (selective adaptation) leads other odours not subject to adaptation to be perceived more prominently. Therefore, the longer humans are exposed to the smell of the same mixture, the more they will begin to perceive a different odour (Frank et al. 2017). In the past, it was assumed that these processing steps occur only in higher-order brain centres; however, there is growing evidence that these processes already take place at the olfactory receptors (Xu et al. 2020).

The findings relating to the relationships between odorant molecules and the effects of an odour are of only limited use for identifying the odour actually perceived by an individual. This still requires the human nose.

3 Methods for determining odour thresholds and qualities

Olfactometry (lat. *olfacere* "to smell") describes the use of psychophysical methods for studying the sense of smell. One of its objectives is the determination of odour thresholds. An odour detection threshold is defined as the substance concentration at which a non-specific odour can be perceived. Conversely, the odour recognition threshold is defined as the concentration required to identify an odour, or odour quality (for example, "banana-like") (Doty and Laing 2015). The detection threshold is much lower than the recognition threshold (Hatt 2019). At any given moment, many factors influence the ability to just barely perceive an odour. These include expectations, motivation, attention and concentration. It is therefore not possible to determine the exact odorant concentration at which a test person is still able to detect a smell. The odour detection threshold is thus conventionally defined as the concentration at which a test person reacts 50% of the time after repeated presentation of an odorant (Gescheider 1997).

As there are no normed or standardized methods for determining odour thresholds for chemicals at present, a description of the general procedure used is provided below.

An odour detection threshold is determined by first preparing a dilution series, that is, a series of different concentration steps. The concentration range is chosen in such a way that the lowest levels are never detected and the highest levels are always detected. According to Weber–Fechner's law (Gescheider 1997), a linear increase in the subjectively perceived odour intensity corresponds to the logarithm of the increase in the objectively measurable odorant concentration. This means that two adjacent concentrations should differ approximately by a factor of 2.

To determine an individual odour threshold, test persons sniff samples for each dilution step in the series, reporting whether they were able to perceive an odour after each presentation. This process is generally repeated multiple times by each test person to determine an individual odour threshold.

Different methods and apparatuses are used to prepare the dilution series and to present each odour sample to the test persons for sniffing. Publications with odour threshold values (for example, Devos et al. 1990; van Gemert 2011) often report very different findings for one and the same odorant with data varying by ± 1000% and more (Cain and Schmidt 2009). This variability is mainly due to methodological shortcomings. It is imperative to verify analytically that the desired concentration of odorant is actually present at the test person's nose. The variability in the odour thresholds determined for different test persons and by different studies can be reduced also by using standardized methods to select and train test persons (Ueno et al. 2009).

Two methods are currently available for the determination of reliable odour detection thresholds for individual substances. The first is the "Triangle Odour Bag Method" (Iwasaki 2003) used in Japan and the second is the olfactometer

"VDD-8" used in the United States (Schmidt and Cain 2010). A European norm DIN EN 13725 (DIN 2022) has been adopted that provides a description of olfactometric methods and establishes standards. However, this norm was developed for the determination and assessment of environmental odours and is only conditionally suitable for the determination of odour threshold values for individual substances.

Odour thresholds are derived using the method of limits and the method of constant stimuli.

When applying the method of limits, the odorant is presented in increasing or decreasing concentrations. In an ascending trial, the procedure begins with a concentration at which the odour is not perceptible. The concentration is gradually increased until the test person is able to detect the odour. In a descending trial, the procedure begins with a concentration at which the odour is clearly perceptible. This is reduced until the odour is no longer noticeable.

The test persons respond with "yes" if they believe that they have detected an odour. The trial is stopped at the concentration at which the responses change from "yes" to "no" (descending series) or from "no" to "yes" (ascending series). It is common practice to confirm the change at least one more time at the next step; in an ascending trial, for example, this would mean two consecutive "yes" responses. The use of this stop criterion means that it is not necessary to test all concentrations that were prepared for a dilution series. In general, an individual odour threshold is calculated as the geometric mean of the first detected odorant concentration and the last concentration that was not detected.

Errors resulting from habituation may pose a problem when using this method. Habituation is defined as the tendency of a test person to continue to report the perceived stimulus during decreasing trials (or to continue to report the absence of the stimulus during ascending trials). Another problem may be caused by expectation. If all tests begin with the same initial concentration and use the same number of concentration steps, test persons can count along and thereby predict which of the samples represents the dilution step to which they have to respond. Possible solutions to this problem are the use of different initial concentrations or interspersing "blank samples" containing odourless air instead of the next concentration step.

When applying the method of constant stimuli, all prepared concentrations are presented in random order to prevent errors of habituation and expectation. As each test person generally completes each dilution series more than once, the data collected for each dilution step can be used to determine how often the odour was detected. This is likewise possible for an entire test group. The probability of detecting an odour (the percentage of "yes" responses) is then plotted for each odorant concentration. The result is a psychometric function in the form of a logistic curve. The odour detection threshold is the odorant concentration at which the odour is detected in exactly 50% of the cases. It may be necessary to interpolate this value.

A problem inherent in this method is the time and effort it requires. As all dilution steps have to be tested in each case, this may lead to fatigue.

The yes/no procedure described above is used to identify what is known as the "absolute" threshold. Conversely, the "differential threshold" corresponds to the point at which a difference becomes just noticeable. The forced-choice method is generally used to determine this threshold. The test person must compare at least two samples, an odourless blank sample and an odour sample, and then decide which sample contains the odour. The number of correct and incorrect responses are counted. The two odour samples are presented either simultaneously (VDD-8 olfactometer, Schmidt and Cain 2010; Japanese triangle odour bag method, Iwasaki 2003) or successively (DIN 2022).

When the forced-choice method is applied in combination with the method of limits such as the Japanese triangle odour bag method, the trial ends the first time an incorrect response is given in the decreasing dilution series. As described above, the individual odour threshold is determined by calculating the geometric mean of the last detected concentration and the first concentration no longer detected.

When the forced-choice method is applied in combination with the method of constant stimuli, the odour detection threshold is determined by calculating the percentage of correct responses. As described above, these are presented as a logistic curve. If two samples are presented, there is a 50% probability of correctly choosing the sample with the odour. For this reason, the differential threshold is calculated using the odorant concentration that was correctly

detected in 75% of the cases. If three samples are presented, as is the case when applying the VDD-8 olfactometer, there is a 33.3% probability of correctly choosing the odour sample. In this case, the differential threshold is calculated using the standard method, namely as the odorant concentration that was correctly identified in exactly 50% of the cases.

Odour threshold values are considered to be of high quality if they were obtained using a standardized method, for example DIN EN 13725 (DIN 2022), or a method of comparably high quality. The studies published by the research groups of Abraham, Cain and Cometto-Muñiz and essentially also that of Nagata (2003) all fall into this category.

Odour threshold values are considered to be of low quality if they were published without data for the experimental conditions that can be adequately validated. This applies particularly to the odour threshold values that were compiled in early reviews (Amoore and Hautala 1983; Devos et al. 1990; Hellman and Small 1974; Leonardos et al. 1969; Punter 1983; Ruth 1986).

The uncertainty in olfactometric determinations was calculated taking into account the requirements of DIN EN 13725 (Boeker and Haas 2007). A certain degree of measurement uncertainty is given due to the discrete dilution steps used by the olfactometric method of determination. The measurement uncertainty can be reduced markedly by increasing the number of test persons and reducing the range of odour thresholds of a single test person. If the requirements of DIN EN 13725 are observed, the measurement uncertainty is equal to about a factor of 2 or lies at ± 0.3 on a logarithmic scale.

If the compiled data include odour threshold values of varying quality, the procedure should be carried out using the lowest values. This is recommended by Cain and Schmidt (2009). This research group found that the odour threshold values obtained by applying more modern methods show less interindividual variation and are generally much lower than the odour threshold values valid up until this time for a particular substance.

The hedonic tone of an odour is determined by applying psychometric methods such as the hedonics scale or the method of polarity profiles (Sucker and Hangartner 2012). However, databases or reviews with systematically compiled information for the "pleasant–unpleasant" quality of odours are not available.

In spite of the individual differences mentioned above, current psychophysical and psychometric methods can be used to identify the properties of an odour such as odour threshold, odour intensity or hedonic tone (pleasant/unpleasant) with fairly high reliability. This information is suitable for describing the effects on the olfactory system induced by a particular substance at the workplace.

The information used as the basis for applying the footnote was compiled by systematically evaluating various sources that provide data relating to the olfactory properties of chemicals.

4 Description of the procedure

The following criteria for applying the footnote were established by the Commission and first published in the 2021 List of MAK and BAT Values (DFG 2021): (a) low, psychophysically determined odour threshold, (b) very unpleasant odour even in the range of the perception threshold or (c) case reports or observations which describe the increased occurrence of "odour-associated" symptoms.

a) Low, psychophysically determined odour threshold

While deriving MAK values for the two alkyl thiols 2-butanethiol and 2-methyl-2-propanethiol based on a study of ethanethiol that was carried out with test persons, it became apparent that by analogy the development of "odour-associated" symptoms at concentrations below the MAK value could not be ruled out. The Commission identified 41 other substances from the MAK list that are characterized by an intense, unpleasant odour and that have been assigned MAK values. The scientific literature includes several reviews that provided a compilation of odour thresholds for chemicals. These publications were used to compile odour thresholds for 7 alkanolamines, 17 alkyl amines, 5 aromatic amines, 6 alkyl thiols, 1 aromatic sulfur compound and 7 other substances at the workplace and to derive consolidated

odour thresholds. The data were taken from 5 reviews (AIHA 2013; Brauer 2002; van Gemert 2011; Nagata 2003; Ruth 1986). Other sources (including Sheftel 2000; U.S. Coast Guard and Department of Transportation 1990) were used for purposes of comparison. The consolidated odour threshold corresponds to the lowest odour detection threshold found (consistently) in several sources. The consolidated odour threshold is expressed in mg/m^3. A quotient was calculated from the MAK value and the consolidated odour threshold. If this quotient lies above 1, the odour of a substance at the workplace is expected to be perceptible at levels even below the MAK value. The larger the quotient, the greater the probability that (a) the odour is perceptible and (b) the odour increases in intensity. To apply the footnote, the quotient must be higher than 1. However, no other conclusions can be drawn based on the value of the quotient because there is great variability in the odour threshold values compiled in the reviews. As a result of this variability, the quotient is not suitable for more extensive and more differentiated uses. This procedure represents the worst-case scenario because it always uses the lowest odour threshold.

b) Very unpleasant odour already in the range of the perception threshold

Comparable reviews or systematic compilations are not available for odour quality. The only source that provides systematic and well-founded documentation for "odour-associated" symptoms such as "nausea" is a loose-leaf collection entitled "Gefahrstoff-Sensorik" ("Sensory Analysis of Hazardous Substances") (Brauer 2002). A systematic description of odour quality can be made using the 146 descriptors (such as minty, peppermint; fruity, citrus) published by Andrew Dravnieks (Dravnieks 1982). Detailed information about odour-induced effects is available only for tetrahydrothiophene and trimethylamine. For this reason, the descriptions of odour quality as well as the designation of "odour-associated" symptoms were mainly taken from the GESTIS substance database (https://gestis.dguv.de/) and PubChem (https://pubchem.ncbi.nlm.nih.gov/). Exact information about the source and quality of these data is not available; in many cases the information is based on data from Brauer (2002). The footnote may be applied only if the data consistently and clearly confirm an unpleasant odour quality (see "odour quality" columns in Table 1).

c) Case reports or observations which describe the increased occurrence of "odour-associated" symptoms

When applying the footnote, other sources from the fields of occupational medicine and toxicology were consulted that included reports of symptoms induced exclusively by the odour of a substance at the workplace. These include findings and observations from studies carried out with test persons.

The footnote was not applied if valid studies carried out with test persons (MAK Commission 2019, available in German only) that systematically investigated the perception of odour and "odour-associated" symptoms at concentrations in the range of the MAK value concluded that these types of effects are unlikely to occur even in isolated cases (see column "Comments" in Table 1).

Tab. 1 Overview of 43 substances at the workplace and a systematic review of their olfactory properties.

Substance	CAS No.	Molar mass	MAK (DFG 2022)		former Cat. V	Odour quality			consol. OT (mg/m³)	MAK/ consol. OT	Foot-note	Comments
			(mg/m³)	(ml/m³)		GESTIS	PubChem	Brauer 2002				
alkanolamines												
2-aminobutanol	96-20-8	89.14	3.7	1	no	amine-like	–	–	–		no	
2-aminoethanol	141-43-5	61.08	0.51	0.2	no	ammonia-like	ammonia-like	light, ammonia-like, fishy	6.6[a)]	0.077	no	
2-(2-aminoethoxy)ethanol	929-06-6	105.1	0.87	0.2	no	mild, amine-like	light, fishy, amine-like	light (no other data)	–		no	
2-amino-2-methyl-1-propanol	124-68-5	89.14	3.7	1	no	amine-like	–	ammonia-like	–		no	
diethanolamine	111-42-2	105.1	1 I	–	no	weak, ammonia-like	light, fishy, ammonia-like	mild, ammonia-like	1.2[a)]	0.83	no	
2-diethylaminoethanol	100-37-8	117.2	24	2	no	amine-like	nauseating, ammonia-like	sharp, amine-like, ammonia-like	0.05[a)]	480	**yes**	
triethanolamine	102-71-6	149.2	1 I	–	no	amine-like	light, ammonia-like	light, very weak, ammonia-like	62[a)]	0.016	no	
alkyl amines												
isopropylamine	75-31-0	59.11	12	5	yes	amine-like	ammonia-like	strong, pungent, ammonia-like	0.06[a)]	200	**yes**	
N′-(3-aminopropyl)-N′-dodecylpropane-1,3-diamine	2372-82-9	299.5	0.05 I	–	no	amine-like	–	–	–		no	
isobutylamine	78-81-9	73.14	6.1	2	yes	amine-like	fishy	ammonia-like, amine-like	0.0045[b)]	1400	**yes**	
n-butylamine	109-73-9	73.14	6.1	2	yes	ammonia-like	ammonia-like	pungent, ammonia-like	0.24[a)]	25	**yes**	
sec-butylamine	13952-84-6	73.14	6.1	2	yes	ammonia-like	fishy, ammonia-like	–	0.5[c)]	12	**yes**	
tert-butylamine	75-64-9	73.14	6.1	2	yes	amine-like	strong, amine-like	–	0.5[c)]	12	**yes**	
cyclohexylamine	108-91-8	99.17	8.2	2	yes	amine-like	strong, fishy, amine-like	strong, fishy, amine-like	10[a)]	0.82	no	

Tab. 1 *(continued)*

Substance	CAS No.	Molar mass	MAK (DFG 2022)		former Cat. V	Odour quality			consol. OT (mg/m³)	MAK/ consol. OT	Foot-note	Comments
			(mg/m³)	(ml/m³)		GESTIS	PubChem	Brauer 2002				
diethylamine	109-89-7	73.14	6.1	2	yes	amine-like	fishy, ammonia-like	intense, musty, fishy, ammonia-like, amine-like	0.01[a)]	610	**yes**	
dimethylamine	124-40-3	45.08	3.7	2	yes	fishy, ammonia-like	fishy, ammonia-like	strong, fishy, ammonia-like, depending on the concentration: fishy or ammonia-like	0.0014[a)]	2600	**yes**	
N,N-dimethylethylamine	598-56-1	73.14	6.1	2	yes	ammonia-like	strong, ammonia-like, fishy	intense, strong, ammonia-like	1.4[b)]	4.4	**yes**	
N,N-dimethylisopropylamine	996-35-0	87.16	3.6	1	no	amine-like	–	ammonia-like	–		no	
ethylamine	75-04-7	45.08	9.4	5	yes	ammonia-like	sharp, fishy, ammonia-like	intense, sharp, ammonia-like	0.05[a)]	190	**yes**	
methenamine 3-chloroallylchloride	4080-31-3	251.2	2 I	–	no	pungent	pungent	–	–		no	
methylamine	74-89-5	31.06	6.4	5	yes	ammonia-like	pungent, fishy	pungent, intense, sharp, fishy, at high concentrations (130–650 mg/m³): ammonia-like	0.0012[a)]	5300	**yes**	
morpholine	110-91-8	87.12	36	5	yes	ammonia-like	fishy	fishy, amine-like	0.036[a)]	1000	**yes**	
triethylamine	121-44-8	101.2	4.2	1	yes	fishy, ammonia-like	strong, ammonia-like to fishy	intense, strong, unpleasant, fishy, amine-like, ammonia-like	0.022[a)]	190	**yes**	
trimethylamine	75-50-3	59.11	4.9	2	yes	amine-like	fishy at low concentrations, ammonia-like at higher concentrations	pungent, fishy at 2 mg/m³, ammonia-like at 240–1200 mg/m³	0.000049[a)]	100000	**yes**	

Tab. 1 *(continued)*

Substance	CAS No.	Molar mass	MAK (DFG 2022)		former Cat. V	Odour quality			consol. OT (mg/m³)	MAK/ consol. OT	Foot-note	Comments
			(mg/m³)	(ml/m³)		GESTIS	PubChem	Brauer 2002				
aromatic amines												
aniline	62-53-3	93.13	8	2	no	amine-like	musty, fishy	pungent, oily, aromatic, sweetish, amine-like	0.0002[e)]	40 000	no	no symptoms at 2 ml/m³ (Käfferlein et al. 2014)
N-(1,3-dimethylbutyl)-*N*′-phenyl-*p*-phenylenediamine	793-24-8	268.4	2 I	–	no	–	–	aromatic	–		no	
diphenylamine	122-39-4	169.2	5 I	–	no	floral	pleasant, floral	floral	0.15[a)]	33	no	pleasant odour
N-isopropyl-*N*′-phenyl-*p*-phenylenediamine	101-72-4	226.3	2 I	–	no	–	aromatic	–	–		no	
p-phenylenediamine	106-50-3	108.1	0.1 I	–	no	–	–	–	–		no	
alkyl thiols												
1-butanethiol	109-79-5	90.19	3.7	1	no	unpleasant, rotten onions, skunk-like	strong, skunk-like	intense, strong, skunk-like, disgusting	0.00001[a)]	370 000	**yes**	
2-butanethiol	513-53-1	90.19	7.5	2	no	foul-smelling	strong, unpleasant, skunk-like	strong, skunk-like, putrid	0.000002[b)]	3 800 000	**yes**	
ethanethiol	75-08-1	62.14	1.3	0.5	yes	penetrating, biting	overpowering, garlic-like, skunk-like	overpowering, persistent, disgusting, leek-like (mephitic), earthy, sulfidic	0.000022[a)]	59 000	**yes**	
methanethiol	74-93-1	48.11	1	0.5	yes	unpleasant	sharp, unpleasant, garlic-like, rotten cabbage	pungent, disgusting, sulfidic, at low concentrations like cooked cabbage, putrid	1E–12[a)]	1E12	**yes**	
2-methyl-2-propanethiol	75-66-1	90.19	3.7	1	no	unpleasant	strong, unpleasant, skunk-like	strong, skunk-like, putrid	0.000006[b)]	620 000	**yes**	warning agent for gas

Tab. 1 *(continued)*

Substance	CAS No.	Molar mass	MAK (DFG 2022)		former Cat. V	Odour quality			consol. OT (mg/m³)	MAK/ consol. OT	Foot-note	Comments
			(mg/m³)	(ml/m³)		GESTIS	PubChem	Brauer 2002				
thioglycolates (salts of thioglycolic acid)	68-11-1 (thioglycolic acid)	–	2 I	–	no	thioglycolic acid: unpleasant	thioglycolic acid: strong, unpleasant, characteristic of mercaptans	thioglycolic acid: strong, very unpleasant	–		no	
aromatic sulfur compounds												
tetrahydrothiophene	110-01-0	88.17	183	50	no	pungent	stench	intense, disgusting, stench, unpleasant	0.0001[b)]	1 800 000	**yes**	warning agent for gas, odorant
others												
n-butyl acrylate	141-32-2	128.2	11	2	no	pungent	sharp, fragrant, biting, fruity	–	0.0015[a)]	7300	**yes**	
ethyl acrylate	140-88-5	100.1	8.3	2	no	unpleasant, pungent	biting, penetrating, sour, pungent, like hot plastic	persistent, biting, pungent, sweet, earthy, ester, plastic	0.000027[a)]	310 000	**yes**	
methyl acrylate	96-33-3	86.09	7.1	2	no	pungent	biting	sharp, sweet, fruity, biting, plastic	0.01[a)]	710	**yes**	
methacrylic acid methyl ester	80-62-6	100.1	210	50	no	characteristic	biting, fruity, sulfur-like, sweet, sharp, unpleasant	pungent, sulfidic, biting, fruity, plastic, sharp, habituation seems to occur	0.0582[a)]	3600	**yes**	
methyl styrene (all isomers)	25013-15-4	118.2	98	20	yes	unpleasant	characteristic	annoying, very annoying, intense	240[d), e)]	0.41	no	according to documentation (Hartwig and MAK Commission 2019) first noticeable as unpleasant at 250 mg/m³ and above

Tab. 1 *(continued)*

Substance	CAS No.	Molar mass	MAK (DFG 2022)		former Cat. V	Odour quality			consol. OT (mg/m³)	MAK/ consol. OT	Foot-note	Comments
			(mg/m³)	(ml/m³)		GESTIS	PubChem	Brauer 2002				
hydrogen sulfide	7783-06-4	34.08	7.1	5	yes	rotten eggs	strong, unpleasant, rotten eggs	extremely unpleasant, rotten eggs at low concentrations, sweetish at higher concentrations	0.0001[a)]	71000	no	according to documentation (Hartwig 2010, available in German only) no unreasonable nuisance from odour at the MAK value
hydrogen selenide	7783-07-5	80.99	0.02	0.006	no	decayed horseradish	decayed horseradish	annoying, repulsive, decayed horseradish	0.0016[d), e)]	13	**yes**	

[a)] AIHA 2013
[b)] van Gemert 2011
[c)] Nagata 2003
[d)] Ruth 1986
[e)] Brauer 2002
GESTIS: http://www.dguv.de/ifa/stoffdatenbank/; Cat V: Peak Limitation Category V (substances with intense odours) of the List of MAK and BAT Values up to 2001; consol.: consolidated; OT: odour threshold; PubChem: https://pubchem.ncbi.nlm.nih.gov/

Notes

Competing interests

The established rules and measures of the Commission to avoid conflicts of interest (www.dfg.de/mak/conflicts_interest) ensure that the content and conclusions of the publication are strictly science-based.

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