

Analysis of allergens in metalworking fluids

MAJ-LEN HENRIKS-ECKERMAN¹, KATRI SUURONEN² AND RIITTA JOLANKI³

¹Chemical Agents, Turku, ²Occupational Medicine and ³Control of Hypersensitivity Diseases, Finnish Institute of Occupational Health (FIOH), 00250 Helsinki, Finland

Background: Metalworking fluids (MWFs) are well-known causes of occupational contact dermatitis in machinists.

Objective: To gain information about skin sensitizers in MWFs and to compare it with the information in safety data sheets (SDSs).

Methods: A total of 17 samples of MWF concentrates were analysed for skin sensitizers known or suspected to be used in MWF. Alkanolamines, formaldehyde, isothiazolinones, methyl-2-bromo-2-nitropropane (MDBGN), and iodopropynyl butylcarbamate (IPBC) were separated by liquid chromatography. Resin acids of colophonium (colophony) were separated by gas chromatography. The substances were identified with mass spectrometric detection and ultraviolet detection.

Results: Of the MWFs, 15 contained 6–39% of alkanolamines, mostly monoethanolamine and triethanolamine. Formaldehyde was detected in all MWFs: the concentrations of total formaldehyde ranged between 0.002% and 1.3%. Benzisothiazolinone and octylisothiazolinone were detected in one fluid each. IPBC was detected in nine MWFs, and the highest concentration was 0.09%. Methylisothiazolinone and MDBGN were not detected in any of the fluids. Resin acids of colophonium were detected in seven MWFs in concentrations ranging from 0.41% to 3.8%. On the whole, the allergens analysed were poorly declared in the SDSs.

Conclusions: The content of total formaldehyde was not declared in any SDS. IPBC, a relatively new allergen, seems to be common in MWFs. Isothiazolinones may be relevant allergens of machinists, and they should be analysed in MWFs in case other sources are not identified. The occupational relevance of positive patch test results to MWF ingredients in machinists is difficult to determine if information in the SDSs is relied upon.

Key words: alkanolamines; analysis; antimicrobial agents; biocides; colophonium; contact allergens; formaldehyde; iodopropynyl butylcarbamate; isothiazolinones; metalworking fluids; resin acids; safety data sheet. © Blackwell Munksgaard, 2008.

Accepted for publication 15 June 2008

Water-miscible metalworking fluids (MWFs) are complex mixtures consisting of a lubricating component (mineral or vegetable oil or synthetic lubricant) and various auxiliary substances such as emulsifiers, corrosion inhibitors, antioxidants, and antimicrobial agents. The MWF concentrates are mixed with water and used for cooling and lubricating as well as for removing metal chip-
pings formed in the machining process.

MWFs are well-known causes of occupational contact dermatitis in machinists (1), and they have also been reported to cause asthma (1–3). The adverse health effects are partly due to the irritancy of the fluids, but several MWF ingredients

are also known to be skin sensitizers. In recent studies, the most common causes of occupational allergic contact dermatitis (ACD) in machinists have been alkanolamines, formaldehyde, formaldehyde releasers, and colophonium (colophony) (1, 4), but other ingredients of MWF may also cause contact allergy (1, 4–9).

In the safety data sheets (SDSs), information on sensitizing substances has found to be deficient (10). The aim of this study was to obtain information about the occurrence of skin-sensitizing additives in MWFs by analysing commonly used MWF concentrates. The accordance of the analytical results with the information given in the SDSs is discussed.

Materials and Methods

A total of 17 samples of MWF concentrates were acquired from nine machine shops in Southern Finland. The samples were acquired in parallel with occupational hygiene measurements performed to assess airborne and skin exposure to the components of MWFs (11, 12). SDSs were provided for 16 of the studied concentrates. According to them, 10 were mineral oil based, 2 were vegetable oil based, and 4 were synthetic MWFs. The MWFs were analysed for the following substances: (i) alkanolamines, (ii) total formaldehyde (free and easily released), (iii) other antimicrobials, (iv) resin acids of colophonium, and (v) other skin-sensitizing additives identifiable by mass spectrometric (MS) analysis after gas chromatographic (GC) separation. In addition, the efficiency of the formaldehyde determination method was verified by analysing the total amount of released formaldehyde from four commercially available and undiluted formaldehyde releasing biocides: Acticide EF (*N,N*-methylenebismorpholine, CAS 5625-90-1, Thor, Speyer, Germany), Bioban CS 1135 (a mixture of 3,4-dimethyloxazolidine and 3,4,4-trimethyloxazolidine, CAS 81099-36-7, Dow Chemical Company, Horgen, Switzerland), Biocide OX/Grotan OX [*N,N'*-methylenebis(5-methyloxazolidine), CAS 66204-44-2, Schülke & Mayr, Norderstedt, Germany], and Grotan BK [hexahydro-1,3,5-tris(2-hydroxyethyl)-s-triazine, CAS 4719-04-4, Schülke & Mayr]. The theoretical amount of released formaldehyde was calculated by dividing the sum of molar masses of released formaldehyde molecules with the molar mass of the biocide and multiplying with the reported percentage purity.

Chemicals

For quantification, the following chemicals with at least 98% purity were used: monoethanolamine (MEA, CAS 141-43-5, Fluka, Buchs, Switzerland), diethanolamine (DEA, CAS 111-42-2, Fluka), triethanolamine (TEA, CAS 102-71-6, Fluka), methyl-diethanolamine (MDEA, CAS 105-59-9, Aldrich, St Louis, MO, USA), morpholine (CAS 110-91-8, Alfa Aesar, Heysam, England), benzyl alcohol (CAS 100-51-6, Merck, Darmstadt, Germany), dodecane (CAS 112-40-3, Aldrich, Steinheim, Germany), and 2-(2-ethoxyethoxy)ethanol (CAS 111-90-0, Merck) and as internal standards: *N,N*-diisopropyl aminoethanol (CAS 96-80-0, Fluka), heptadecanoic acid (CAS 506-12-7, Fluka), and heneicosanoic acid (CAS 2363-71-5, Fluka).

Chemicals with purity lower than 98% were amino-2-propanol (AP, CAS 78-96-6, purity

93%, Fluka), 2-amino-2-ethyl-1,3-propanediol (AEPD, CAS 115-70-8, purity 97%, Acros organics, Geel, Belgium), TEA borate (CAS 15277-97-1, purity 97%, Aldrich, Gillingham, England), formaldehyde (CAS 50-00-0, minimum 37% in water, Merck), MDBGN (1,2-dibromo-2,4-cyanobutane, MDBGN, CAS 35691-65-7, Schülke & Mayr), dehydroabiatic acid (CAS 1740-19-8, >95% purity, Promochem), isopimaric acid (CAS 5835-26-7, >95% purity, Promochem, Borås, Sweden), and 7-oxodehydroabiatic acid (CAS 18684-55-4) > 95% purity, Promochem).

The following antimicrobial agent standards were bought from Chemotechnique Diagnostics (Malmö, Sweden): Kathon CG (mixture of 2-methyl-4-isothiazolin-3-one (MI, CAS 2682-20-4) 0.375% and 5-chloro-2-methyl-4-isothiazolin-3-one (MCI, CAS 26172-55-4) 1.125%), 1,2-benzisothiazolin-3-one (BIT, CAS 2634-33-5, purity 94%), 2-*N*-octyl-4-isothiazolin-3-one (OIT, CAS 26530-20-1, purity 45%), iodopropynyl butylcarbamate (IPBC, CAS 55406-53-6), Bioban P 1487 (a mixture of 4-(2-nitrobutyl)morpholine (70%), and 4,4-(2-ethyl-2-nitrotrimethylene)dimorpholine, CAS 37304-88-4), Grotan BK (CAS 4719-04-4, hexahydro-1,3,5-tris(2-hydroxyethyl)-s-triazine, purity 76%).

For derivatization, extraction, and chromatographic analysis, the following chemicals were used: methanol [high-performance liquid chromatography (HPLC) gradient grade; J.T. Baker, Deventer, Holland], acetonitrile (HPLC grade S; Rathburn, Walkerburn, Scotland), acetone (Lichrosolv; Merck, Darmstadt, Germany), formic acid (purity 98%, J.T. Baker), dinitrophenylhydrazine (DNPH, Aldrich, 97%), hydrochloric acid (fuming 37%, Merck), tert-butylmethylether (TBME; Uvasol, Merck), tetramethylammonium hydroxide (TMAH, 10% in methanol; Fluka), and phenolphthalein (1% in ethanol; J.T. Baker).

Instrumental

All liquid chromatographic (LC) analyses were performed with Waters Alliance 2690XE connected to Waters Platform LCZ MS detector and to Waters 2487 Dual Absorbance Detector. The GC analyses were performed with Agilent 6890N GC systems connected to an Agilent 5973N Mass Selective Detector (MSD). The compounds were separated on a Varian Factor Four capillary column VF-5ms (30 m × 0.25 mm inner diameter, df = 0.25) with the MSD in the electron ionization (EI) scan mode. The injection temperature was 250°C, which was high enough to completely methylate the acids but only partly methylate the hydroxy/keto groups in the oxidized resin acids.

LC analysis

Alkanolamines. The samples were desorbed in methanol, and the methanol extracts were analysed by LC with MS detection as described earlier (11).

Total formaldehyde. The specimens of the MWF concentrates were accurately weighed and emulsified in a known amount of water (50 mg/14 ml and 100 mg/10 ml, Millipore purified) to obtain concentrations of about 3 mg/ml and 10 mg/ml. After ultrasonic treatment for 15 min, 0.5 ml was removed to another test-tube containing 3 mg of recrystallized DNPH-hydrochloric acid and 90 µl of concentrated hydrochloric acid in 1.5 ml acetonitrile. The mixture was kept at 70°C for 1 hr to completely release formaldehyde from the biocides and to achieve a complete formation of the corresponding hydrazone. The formaldehyde hydrazone was analysed with LC and ultraviolet (UV) detection at 372 nm on a Chromsep C18 column (200 × 3 mm ID) with 0.5 ml/min, a mixture of acetonitrile (55%) and water (45%). Ten microlitres was injected. For quantification, a solid hydrazone derivative of formaldehyde with DNPH was prepared in the laboratory. The LC purity was determined to be over 98%, as no other peaks appeared in the chromatogram during the analytical conditions of the analysis. The repeatability of the method was determined to be within 5%. The detection limit for formaldehyde was 15 ng/ml. This method was developed from a method used to determine free formaldehyde in foundry resins (13).

Other antimicrobial agents. MCI, MI, BIT, OIT, IPBC, Bioban P 1487, and MDBGN were determined in methanol–water (1 + 3, v + v) solutions of accurately weighed specimens (about 10 mg/ml) of the MWF concentrates. The biocides were separated by LC on a Symmetry shield C18 column (150 × 2 mm ID, 3.5 µm particles) with methanol–water containing 2 mM of ammonium acetate as eluent. A gradient elution was used starting with 34% methanol for 5 min. After that, the methanol content was increased to 95% in 6 min and then kept at 95% for 7 min. The column temperature was 30°C, and the autosampler temperature was 10°C. The injection volume was 5 µl, and the flow rate was 0.2 ml/min. The biocides were quantified using the external standard method by monitoring protonated molecular ions in the single ion monitoring mode (cone voltage 20 V) in MS and by UV detection at 230 nm and 270 nm, but MDBGN was monitored by the positive ions 282 and 284 as no protonated molecular ions were seen in the scan. Isothiazolinones were calculated using the UV detection signals and IPBC using the MS monitoring. Two stand-

ard concentrations of each biocide were used to calculate the quantitative results: 5 µg/ml and 10 µg/ml. Results from peaks with a signal to noise level of at least 10 were accepted. The extraction efficiency was determined by the standard addition method of six parallel samples at the 0.02% level and was found to be $89 \pm 12\%$ for IPBC. The corresponding extraction efficiency for BIT was $100 \pm 25\%$ and for OIT $95 \pm 2\%$.

GC analysis

Resin acids. The specimens of the MWF concentrates were accurately weighed and dissolved with a mixture of TBME and methanol (90:10, v/v) to obtain concentrations of 5–10 mg/ml. The fatty acids, heptadecanoic acid and heneicosanoic acid, were added as internal standards (about 10 µg to 10 ml) before methylation. After addition of one to two drops of 1% phenolphthalein in ethanol as indicator, 0.1 M of the methylation reagent TMAH in methanol was added dropwise until a stable reddish colour was formed. To allow complete methylation of the acid groups, the samples were stored for at least 1 day after the TMAH addition, and subsequently analysed with GC. The standards for quantification were treated in the same way. The resin acids were identified by comparing their MS to MS in the Wiley and National Institute of Standards and Technology (NIST) library. A probability of 85% or more was considered as a positive identification. Pimaric-type resin acids were quantified using the response of isopimaric acid, and abietic-type resin acids were quantified using the response of dehydroabietic acid. Heptadecanoic acid was used as internal standard in the calculations.

Other MS-identified allergens. The specimens of the MWF concentrates were accurately weighed and diluted in acetone to achieve a concentration of max 1 mg/ml. The following external standards in acetone were used: triethanolamine borate (for oxazolidine compounds), benzyl alcohol (for aromatics), dodecane (for aliphatics), and ethoxyethoxyethanol (for aliphatic alcohols). In order to test whether oxazolidines could be formed during the GC–MS analysis, a mixture of DEA and formaldehyde was injected into the GC–MS with injector temperature of 250°C. The compounds were identified by comparing their MS to MS in the Wiley and NIST library. A probability of 85% or more was considered as a positive identification.

Results

The results of both GC and LC analysis and their accordance with the SDSs are presented in Table 1.

Table 1. Concentrations of skin-sensitizing compounds in 17 metalworking fluid concentrates and the accordance of the results with the information given in material SDS

Analysed compound	Concentrations (% w/w)		Accordance with SDS
	Range	Median	x/n
Alkanolamines and alkanolamine derivatives			
Monoethanolamine	1.4–11	7.2	4/12
Diethanolamine	20–39	21	1/3
Triethanolamine	5.9–26	11	1/7
Methyldiethanolamine	10		1/1
Triethanolamineborate	5.3–24	10	1/7
2-Amino-2-ethyl-1,3-propanediol ^a	0.06–0.39	0.09	0/3
Amino-2-propanol ^b	0.09–2.3	1.4	0/5
Morpholine ^c	1.7–4.6	3.6	3/4 ^d
Formaldehyde ^e			
Total formaldehyde (free and easily released)	0.002–1.3	0.59	0/17
Biocides other than formaldehyde releasers			
Benzisothiazolinone ^e	0.011		1/1
Octylisothiazolinone	0.036		0/1
Iodopropynyl butylcarbamate	0.0002–0.089	0.0021	1/9
Colophonium ^e			
Resin acids	0.41–3.8	1.7	0/7
Other mass spectrometric-identified allergens			
o-Phenylphenol	3		0/1

n, number of concentrates containing the analysed compound; SDS, safety data sheets; x, number of products, where the analysed additive was declared in the safety data sheet of the corresponding product.

^aAdded as such or indicates addition of Bioban CS 1246 (7-ethylbicyclooxazolidine).

^bAdded as such or indicates addition of *N,N*-methylenebis (5-methyloxazolidine).

^cIndicates addition of *N,N*-methylenebismorpholine.

^dDeclared as methylenebismorpholine.

^eClassified as skin sensitizer in the EU.

Two MWFs did not contain any detectable amounts of alkanolamines (DEA < 0.1% and the others < 0.02%). The rest of the products contained mostly MEA and TEA, and the total concentrations of alkanolamines were 6–39%.

Formaldehyde was detected in all products. Three concentrates contained ≤ 0.01% of total formaldehyde. The others contained 0.08–1.3% of total formaldehyde.

3-Oxazolidine-ethanol (CAS 20073-50-1) was detected by GC–MS in all DEA-containing MWFs (three products) in the concentration range 0.5–1.8%. Oxazolidine (CAS 504-76-7) was detected in most MWFs (seven products) that also contained formaldehyde and MEA at the same time. The concentration of oxazolidine was

about the same as the total formaldehyde concentration (0.5–0.9%). 3-Oxazolidine-ethanol was also found to be formed from the standard mixture of DEA and formaldehyde in the GC–MS analysis.

The efficiency of the method for determination of total formaldehyde is reported in Table 2. In all the tested biocides, the total amount of formaldehyde released was between 85% and 114% of the theoretical maximum amount.

BIT or OIT were detected in two MWFs. MCI, MI, MDBGN, or Bioban P 1487 were not detected in any samples. The detection limit for MI/MCI was < 0.0005% and for MDBGN and Bioban P 1487 0.001%. IPBC was detected in nine products. The highest concentration was 0.09%.

Table 2. Amounts of total formaldehyde (free and easily released) from four formaldehyde releasing biocides (n = 3)

Biocide	Released formaldehyde (% w/w)	
	Total amount	Theoretical maximum amount
Acticide EF ^a (<i>N,N</i> -methylenebismorpholine)	15.9	16.1
Bioban CS 1135 (contains 77% of the active components 3,4-dimethyloxazolidine and 3,4,4-trimethyloxazolidine)	26.0	22.8
Biocide OX/Grotan OX ^a (methylenebis(5-methyloxazolidine))	41.3	16.0–48.4 ^b
Grotan BK (contains 76% of the active component hexahydro-1,3,5-tris(2-hydroxyethyl)triazine)	29.1	31.2

^aPer cent of active components in the biocide not reported.

^bDepending on whether 1, 2, or 3 formaldehyde molecules are released from one.

Resin acids were detected in seven concentrates. The concentration ranged between 0.41% and 3.8%. No 7-oxodehydroabietic acid was detected (<0.005%).

Discussion

In the present study, ingredients of MWF capable of causing skin sensitization were analysed in 17 MWFs in the Finnish market, and a new method was developed for determining total formaldehyde content in MWFs. In addition, a method for determining preservatives other than formaldehyde releasers in a single analysis was also developed.

According to present EU legislation, sensitizers that appear in concentrations of at least 0.1% in chemical preparations need to be declared in the SDS with a danger phrase R43, 'May cause sensitization by skin contact' (14). Of the substances analysed in the present study, formaldehyde, BIT, MCI/CI, and colophonium are classified as skin sensitizers according to the Annex I of the European Commission Directive 67/548/EEC (European Community) (15). However, not all substances known to cause contact allergy are listed in the Annex I.

Contact sensitizers were found in all the MWFs, the most common ones being formaldehyde, MEA, and IPBC. MEA has been reported to be the most common contact allergen in machinists in Germany (4, 16). As a whole, alkanolamines seem to be poorly declared in the SDSs, although some of them are present in high concentrations. Additions of MEA, DEA, and TEA and their corresponding borates were listed in the SDSs as 'boron amine esters' or 'alkanolamine borates' in 11 of the SDSs without any specification of the alkanolamine. Thus, relevance of contact allergies of machinists to each alkanolamine may be difficult to show due to the defective information in SDS. Although not classified as sensitizers in the EU, MEA, MDEA, and DEA are classified as irritant or corrosive according to Annex I of the European Commission Directive 67/548/EEC (15), and they should thus be declared in the SDS if their concentration is $\geq 1\%$. TEA is not listed in the Annex, and therefore, it does not have to be declared.

The AP detected in five products in the LC analysis of alkanolamines indicates addition of a *N,N*-methylenebis(5-methyloxazolidine) containing biocide, although it may also be used as, e.g., corrosion inhibitor as such (16). In two of the SDSs, *N,N*-methylenebis(5-methyloxazolidine) was declared as 'oxazolidine'. Morpholine that was detected in four products in concentrations of 1.7–4.6% indicates addition of an *N,N*-methylene-

nebismorpholine containing biocide. In three of the four products' SDSs, this biocide was declared in concentrations of up to 5%. It was recently reported that *N,N'*-methylenebismorpholine may be a potent contact allergen in machinists and that more research is needed to evaluate its clinical relevance (16). At Finnish Institute of Occupational Health, *N,N*-methylenebismorpholine has been routinely tested with machinists since 2005, and occasional positive patch test reactions in patients with formaldehyde allergy have occurred, suggesting that formaldehyde is the underlying cause of the reactions (17). Small amounts of AEPD were found in three products. AEPD may be used as such as, e.g., emulsifier (16), or it could have been released from Bioban CS 1246 (7-ethylbicyclooxazolidine). Bioban CS 1246 was declared in none of the SDS.

Two oxazolidine derivatives not used in common MWF antimicrobials were identified in the present GC–MS analysis: 3-oxazolidine-ethanol is theoretically formed from formaldehyde and DEA, and oxazolidine is theoretically formed from MEA and formaldehyde. We tested if oxazolidines could have been formed during analysis by injecting a mixture of DEA and formaldehyde into the GC–MS, and indeed, a peak identified as 3-oxazolidine-ethanol was detected. Whether oxazolidine compounds can be formed during machining processes and released into the air probably depends on the processing temperature.

Formaldehyde was found in all the MWFs, which emphasizes the importance of formaldehyde as an occupational allergen in machinists. In 14 products of 17, the total concentration of formaldehyde was more than 0.008% (80 p.p.m.), which is probably enough to cause dermatitis in some sensitized individuals (18). The measured total formaldehyde concentration gives information about the potential for sensitizing, as it is a sum of free formaldehyde in the fluid and formaldehyde that may be released from the antimicrobial agent. Free formaldehyde was not determined in this study because we were not able to analyse the fresh samples immediately after the work places visits.

Formaldehyde releasers in MWFs were not quantified in the present study as such because their analysis is demanding due to their instability when in contact with heat or neutral or acidic water. However, some oxazolidine and morpholine compounds can be identified by LC analysis as formaldehyde and alkanolamine derivatives specific for the respective antimicrobial. This was the case with AEPD, AP, and morpholine. In rare cases, when allergy to formaldehyde releasers without concomitant formaldehyde allergy

is found, it could be useful to analyse specific antimicrobials.

The total amounts of formaldehyde released from the studied commercial preservatives (Table 2) were close to the theoretical amounts, when the reported purity of the commercial biocide was taken into account (85–114%). Consequently, our method for determining total formaldehyde content has an efficiency of at least 85%, especially as the percentages of active components in the biocides Acticide EF and Biocide OX were not known and could be expected to be below 100%. The repeatability of the method was also excellent, within 5%.

In the present study, we found that antimicrobials other than those releasing formaldehyde are also noteworthy. IPBC was common in the MWFs analysed (Table 1); although so far, only a few cases of contact allergy to it have been reported in machinists (3, 8). The highest concentration, 0.09%, was found in the only product with a declaration of the IPBC content. Based on the present results, isothiazolinones may be relevant allergens of machinists, and they should be analysed in MWFs in case other sources are not identified. It is recommendable to analyse isothiazolinones from the used MWFs, as they may originate either from the concentrate or from the separate antimicrobials added to the fluids in use. The developed method for isothiazolinones with both UV and MS detection will provide more reliable qualitative results than UV detection only (19).

In the present study, the sum of resin acids was used to indicate colophonium in the products. Colophonium itself could not be quantified as the proportion of resin acids is not constant in it. However, colophonium, resin acids, or tall oil addition was mentioned in any of the SDSs. According to the GC analysis, all MWFs with resin acids also contained fatty acids, but not every product containing fatty acids contained detectable amounts of resin acids. Colophonium in MWFs originates mainly from distilled tall oil, which contains typically 10–30% colophonium. Colophonium is a frequent cause of ACD in machinists (20), and it is classified as a skin sensitizer in the EU (15). Thus, it should be declared in concentration at or above 0.1%, even if the amount of oxidized resin acids considered as the allergens in colophonium is low (21). The low level of oxidized resin acids in MWFs (20) is supported by our results, as we detected no 7-oxodehydroabietic acid, one of the main colophonium allergens, in any of the present products.

As a whole, not all MWF ingredients known to cause ACD are classified as skin sensitizers in the EU, and their declaration thus is not required.

In addition, according to present EU legislation, only sensitizers that appear in concentrations of at least 0.1% need to be declared (14). Many of the alkanolamines, formaldehyde releasers, and other harmful ingredients may either have several chemical names or may be present in a very low concentration, thus making the interpretation of the chemical information in SDSs demanding. Other reasons for the shortcomings in SDSs might be lack of knowledge or carelessness of the producer or distributor regarding the ingredients of their preparations. To overcome some of the problems listed, market surveillance is needed.

Patch testing of a patient's own MWFs at 10%, 3.2%, and 1% in petrolatum (22) detects contact allergy to the fluid ingredients fairly well. Exceptionally, patients may have a false negative test reaction to their own MWF due to the fact that the concentration of the ingredient in the MWF test preparation is too small. It is recommended to analyse the MWF, especially if the patient has an allergic reaction to a possible MWF ingredient. Specific information obtained from the manufacturer and that stated in SDS may be incomplete.

To summarize the results of this study, all MWFs contain some skin-sensitizing substances, but the specific substances and their concentrations vary. The relevance of positive patch test results in connection with MWF ingredients may be difficult to determine due to deficiencies in SDSs, especially if the patch test result to MWF itself is negative. The content of total formaldehyde was not declared in any of the SDSs. IPBC, a relatively new allergen, seems to be a common additive in present MWFs. Isothiazolinones may be relevant allergens for machinists, and they should be analysed in MWFs in case other sources are not identified.

References

1. Suuronen K, Aalto-Korte K, Piipari R, Tuomi T, Jolanki R. Occupational dermatitis and allergic respiratory diseases in Finnish metal working machinists. *Occup Med* 2007; 57: 277–283.
2. Zacharisen M C, Kadambi A R, Schlueter D P, Kurup V P, Shack J B, Fox J L et al. The spectrum of respiratory disease associated with exposure to metal working fluids. *J Occup Environ Med* 1998; 40: 640–647.
3. Piipari R, Tuppurainen M, Tuomi T, Mantyla L, Henriks-Eckerman M L, Keskinen H et al. Diethanolamine-induced occupational asthma, a case report. *Clin Exp Allergy* 1998; 28: 358–362.
4. Geier J, Lessmann H, Dickel H, Frosch P J, Koch P, Becker D et al. Patch test results with the metalworking fluid series of the German Contact Dermatitis Research Group (DKG). *Contact Dermatitis* 2004; 51: 118–130.
5. Aalto-Korte K, Makela E A, Huttunen M, Suuronen K, Jolanki R. Occupational contact allergy to glyoxal. *Contact Dermatitis* 2005; 52: 276–281.

6. Gruvberger B, Isaksson M, Frick M, Ponten A, Bruze M. Occupational dermatoses in a metalworking plant. *Contact Dermatitis* 2003; 48: 80–86.
7. le Coz C J. Allergic contact dermatitis from sodium pyri-thione in metalworking fluid. *Contact Dermatitis* 2001; 45: 58–59.
8. Majoie I M, van Ginkel C J. The biocide iodopropynyl butylcarbamate (IPBC) as an allergen in cutting oils. *Contact Dermatitis* 2000; 43: 238–240.
9. Kanerva L, Tupasela O, Jolanki R. Occupational allergic contact dermatitis from ethylhexylzinc dithiophosphate and fatty acid polydiethanolamide in cutting fluids. *Contact Dermatitis* 2001; 44: 193–194.
10. Henriks-Eckerman M -L, Suuronen K, Jolanki R, Alanko K. Methacrylates in dental restorative materials. *Contact Dermatitis* 2004; 50: 233–237.
11. Henriks-Eckerman M-L, Suuronen K, Jolanki R, Riala R, Tuomi T. Determination of occupational exposure to alkanolamines in metal-working fluids. *Ann Occup Hyg* 2007; 2007: 153–160.
12. Suuronen K, Henriks-Eckerman M L, Riala R, Tuomi T. Respiratory exposure to components of water-miscible metal-working fluids. *Ann Occup Hyg* 2008; doi:10.1093/annhyg/men048
13. Olivia-Teles M T, Paiga P, Delerue-Matos C M, Alvim-Ferraz M C M. Determination of free formaldehyde in foundry resins as its 2,4-dinitrophenylhydrazone by liquid chromatography. *Anal Chim Acta* 2002; 467: 97–103.
14. Directive 1999/45 EC of the European Parliament and of the Council of 31 May 1999 concerning the approximation of the laws, regulations and administrative provisions of the Member States relating to the classification, packaging and labelling of preparations. *Off J Eur Union L*, 200: 1999: 1–68.
15. Council Directive 67/548/EEC, Annex 1: Index of dangerous substances for which harmonized classification and labelling have been agreed at community level, 29th Adaptation to technical progress. *Off J Eur Union L* 2004; 152: 30/04/2004 (available from http://ecb.jrc.it/DOCUMENTS/Classification-Labelling/DIRECTIVE_67-548-EEC/ANNEX_I_OF_DIRECTIVE_67-548-EEC/Annex_I_of_Directive_67548EEC.doc).
16. Geier J, Lessmann H, Becker D, Bruze M, Frosch P J, Fuchs T et al. Patch testing with components of water-based metal-working fluids: results of a multicentre study with a second series. *Contact Dermatitis* 2006; 55: 322–329.
17. Aalto-Korte K, Suuronen K, Kuuliala O, Alanko K. Occupational contact allergy to formaldehyde and formaldehyde-releasers. *Contact Dermatitis* 2008; 59: 280–289.
18. Jordan W P Jr, Sherman W T, King S E. Threshold responses in formaldehyde-sensitive subjects. *J Am Acad Dermatol* 1979; 1: 44–48.
19. Frauen M, Steinhart H, Rapp C, Hintze U. Rapid quantification of iodopropynyl butylcarbamate as the preservative in cosmetic formulations using high-performance liquid chromatography-electrospray mass spectrometry. *J Pharm Biomed Anal* 2001; 25: 965–997.
20. Geier J, Lessmann H, Schnuch A, Uter W. Contact sensitizations in metalworkers with occupational dermatitis exposed to water-based metalworking fluids: results of the research project “FaSt”. *Int Arch Occup Environ Health* 2004; 77: 543–551.
21. Karlberg A T, Gäfvert E. Isolated colophony allergens as screening substances for contact allergy. *Contact Dermatitis* 1996; 35: 201–207.
22. Jolanki R, Estander T, Alanko K, Kanerva L. Patch testing with a patient’s own material handled at work. In: *Handbook of Occupational Dermatology*, Kanerva L, Elsner P, Wahlberg J E, Maibach H I, eds: Heidelberg, Germany, Springer, 2000: 998–999.

Address:
Maj-Len Henriks-Eckerman
Finnish Institute of Occupational Health (FIOH)
Chemical Agents
Lemminkäisenkatu 14-18 B
FI-20520 Turku
Finland
Tel: +358 30 4741
Fax: +358 30 4747 556
e-mail: maj-len.henriks-eckerman@ttl.fi