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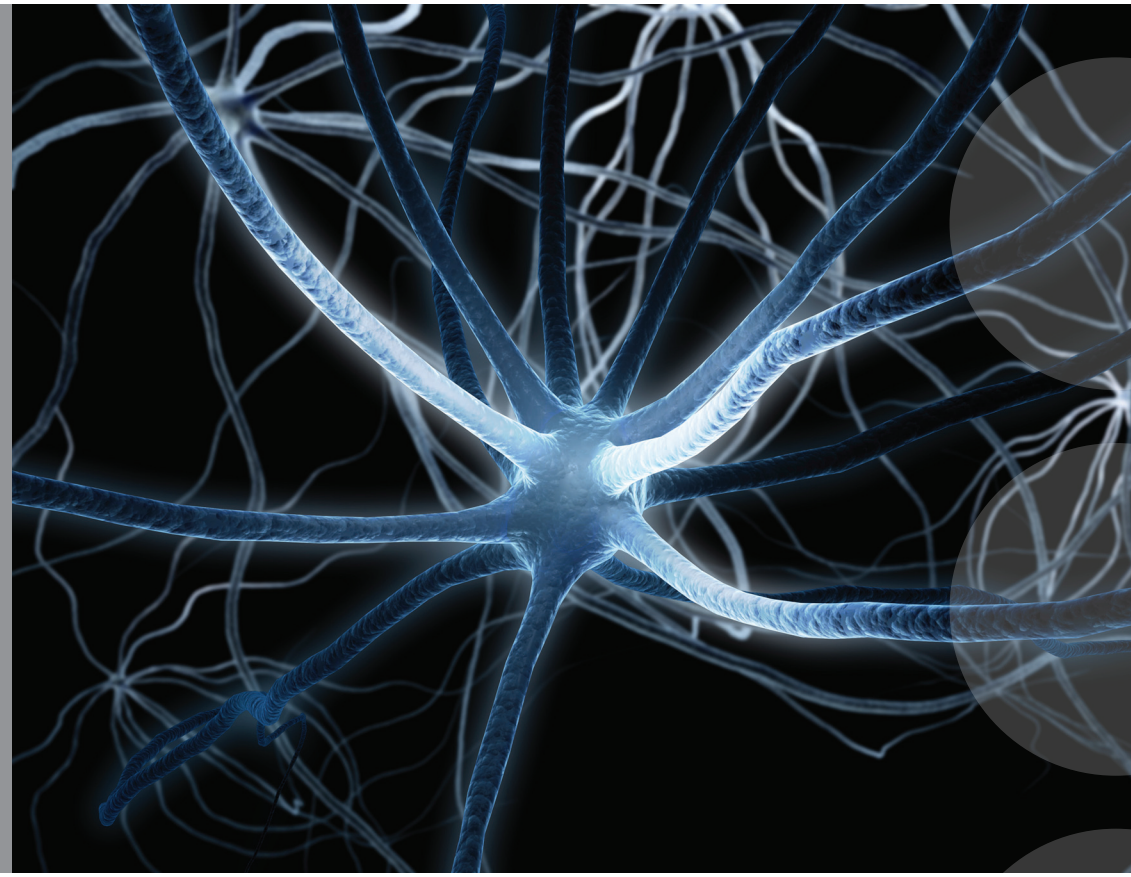
Spitzenverband

Occupational Disease Report 2/2007e



Occupational Disease Report 2/2007e

Occupational Disease No. 1317

Polyneuropathy or encephalopathy caused by organic solvents, in isolation or in mixtures

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Occupational Disease Report 2/2007e

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Polyneuropathy or encephalopathy caused by organic solvents, in isolation or in mixtures

– General and work-related information
– Recommendations for medical asssessment

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Abstract

The second edition of the Occupational Diseases Report 1317 enables quality-assured processing in cases with a suspicion of work-induced damage to the nervous system by organic solvents on the basis of technical and medical expert knowledge.

In the first part, there is technical information with specific information on solvents and mixtures whose neuro-toxicity has been proved according to the current level of knowledge. The Report contains overviews on the incidence of the substances in various industries as well as substance dossiers with chemical and physical data, limit values and absorption paths. In individual cases, this information should support the necessary investigations on the nature and extent of possible damaging effects and allow an overall technical evaluation for work.
The second focus of the Report is on the recommendations for assessment drawn up by experts from various disciplines with extensive experience in observation, treating and assessing the relevant diseases. In the Annex there is additional information in the form of evaluating summaries of literature data on the neuro-toxic effect threshold of individual substances and mixtures.

The Occupational Diseases Report thus offers accident insurers and medical assessors a well-founded basis for assessment for processing OD No. 1317.

Kurzfassung

Der in der zweiten Auflage vorliegende BK-Report 1317 ermöglicht eine qualitätsgesicherte Bearbeitung in Fällen mit Verdacht auf beruflich verursachte Schädigung des Nervensystems durch organische Lösungsmittel auf der Grundlage technischen und medizinischen Expertenwissens.

Im ersten Teil finden sich arbeitstechnische Hinweise mit speziellen Informationen zu Lösungsmitteln und Gemischen, deren Neurotoxizität nach aktuellem Erkenntnisstand gesichert ist. Der Report enthält Übersichten über das Vorkommen der Stoffe in verschiedenen Branchen sowie Stoffdossiers mit chemischen und physikalischen Daten, Grenzwerten und Aufnahmewegen. Diese Informationen sollen die im Einzelfall erforderlichen Ermittlungen zu Art und Umfang möglicher schädigender Einwirkungen unterstützen und eine arbeitstechnische Gesamtwertung ermöglichen.

Den zweiten Schwerpunkt des Reports bilden die Empfehlungen zur Begutachtung, die von Sachverständigen unterschiedlicher Disziplinen erarbeitet wurden, die über umfangreiche Erfahrungen aus der Beobachtung, Behandlung und Beurteilung entsprechender Krankheiten verfügen. Im Anhang finden sich zusätzliche Informationen in Form bewertender Zusammenfassungen von Literaturdaten zur neurotoxischen Wirkungsschwelle einzelner Stoffe und Gemische.

Der BK-Report bietet damit den Unfallversicherungsträgern und den ärztlichen Gutachtern eine fundierte Beurteilungsgrundlage für die Bearbeitung der BK-Nr. 1317.

Résumé

Le rapport BK 1317 (maladie professionnelle 1317), présent dans la deuxième édition, permet, en cas de suspicion de lésion du système nerveux d'origine professionnelle causée par des solvants organiques, un examen de qualité sur la base d'expertises techniques et médicales.

On trouve, dans la première partie, des indications fonctionnelles avec des informations spécifiques concernant les solvants et mélanges dont la neurotoxicité est confirmée selon l'état actuel des connaissances. Ce rapport comprend des récapitulatifs sur la présence de ces substances dans diverses branches ainsi que des dossiers sur les substances comprenant des données chimiques et physiques, des valeurs limites et les voies de pénétration. Ces informations doivent faciliter les recherches, nécessaires dans des cas précis, concernant le type et l'ampleur d'effets nocifs possibles et permettre une appréciation technique globale. Les recommandations pour les expertises, établies par des experts de différentes disciplines, représentent le deuxième point central de ce rapport. Ces experts disposent d'un grand nombre d'expériences tirées d'observations, de traitements et évaluations des maladies en cause. On trouve, en annexe, des informations supplémentaires sous forme de résumés d'évaluation de données littéraires concernant les seuils d'effet des différents mélanges et substances.

Ce rapport BK offre ainsi aux organismes d'assurance accidents et aux experts médicaux une base approfondie d'évaluations pour le traitement de la maladie professionnelle n° 1317.

Resumen

El informe sobre la enfermedad profesional Nº 1317, disponible en su segunda edición, permite una tramitación de calidad asegurada en casos con sospecha de afectación del sistema nervioso, de causalidad laboral, por acción de disolventes orgánicos, basándose en conocimientos de expertos técnicos y médicos.

En la primera parte se encuentran referencias técnico-laborales con informaciones especiales sobre disolventes y mezclas cuya neurotoxicidad está comprobada según el estado actual de los conocimientos científicos. El informe contiene cuadros sinópticos sobre la presencia de las sustancias en diversos ramos, así como dossiers de sustancias con datos químicos y físicos, valores límite y vías de ingreso. El objetivo de estas informaciones es apoyar las investigaciones necesarias en cada caso con respecto al tipo y alcance de posibles acciones nocivas y permitir una evaluación técnico-laboral global.El segundo punto principal del informe lo constituyen las recomendaciones para el examen pericial, elaboradas por peritos de distintas disciplinas con amplias experiencias adquiridas en la observación, el tratamiento y la evaluación de las enfermedades correspondientes. En el anexo se encuentran informaciones adicionales en forma de recopilaciones evaluadoras de datos bibliográficos sobre el umbral de acción neurotóxica de diversas sustancias y mezclas.

El informe sobre la enfermedad profe-sional ofrece, con esto, a los organismos de seguros de accidentes y a los peritos médicos una base de evaluación fundada para la tramitación de la enfermedad profesional Nº 1317.

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Foreword

The problems typically associated with the identification of occupational diseases which arise during investigation of the form and scale of harmful exposure and during evaluation in the context of the medical assessment also apply to formally recognized occupational disease No. 1317.

It is generally accepted that where documentation of exposure is inadequate or completely lacking for workplaces which no longer exist and which cannot be reconstructed, reference may be made to information from registers and data from comparable workplaces. The intended purpose of the Occupational Disease Report is for the form and scale of occupational exposure to be demonstrated as well as possible during the dealing with the cases concerned.

In the present 2nd edition of the Occupational Disease Report, the work-related information and data have been updated and revised, as have the recommendations for assessment overall. As a result, the legal provisions can be applied in a uniform manner on a scientifically validated basis.

The data now available for investigation of the exposure, including data from recent years, are considerably more comprehensive than those contained in the first edition. In particular, changes and additions to the limit values for the various solvents have also been taken into account.

The recommendations for assessment have also been brought into line with the latest medical findings. The literature survey in the annex of the Occupational Disease Report concerning the neurotoxic effects of solvents in isolation and in mixtures has been supplemented with more recent literature, and its evaluation updated. The code of practice for formally recognized occupational disease No. 1317 (reproduced in the annex) which was revised and announced by the BMGS (Bundesministerium für Gesundheit und Soziale Sicherung) in 2005 was also taken into consideration.

The recommendations for assessment also include the proposals for evaluation of the reduction in earning capacity caused by the occupational disease. The principles for evaluation presented in the previous edition of this Occupational Disease Report, according to which the reduction in impairment is determined, were reviewed based upon discussions in the symposium held by the Federation of Institutions for Statutory Accident Insurance and Prevention (HVBG, now DGUV) on 10 January 2001 in Hennef with the involvement of experts from the relevant medical disciplines and an expert from the Institute for Employment Research of the German Federal Labour Agency.

The DGAUM (German Society of Occupational and Environmental Medicine), the DGN (German Society of Neurology) and the GNP (Society of Neuropsychology) approved the recommendations for assessment.

I. General information

Formally recognized occupational disease No. 1317 – polyneuropathy or encephalopathy caused by organic solvents, in isolation or in mixtures – was included in the list of occupational diseases by the German regulation governing occupational diseases (BKV) adopted on 31 October 1997 (Federal Law Gazette [BGBl.] I p. 2623). Prior to that time, the diseases concerned had in some cases been dealt with reference to the substance under other formally recognized occupational disease numbers. Formally recognized occupational disease No. 1317 is more comprehensive in terms of the substances, and particularly includes mixtures of solvents. The relevant clinical pictures are described in greater detail in occupational disease No. 1317 than is the case for the majority of other occupational diseases caused by exposure to chemicals.

Differentiation from other formally recognized occupational disease numbers

Where different numbers in the list of formally recognized occupational diseases are in competition with each other, No. 1317 which is more specific with regard to the clinical picture takes precedence. A case of encephalopathy for example which is caused by benzene is processed under No. 1317 rather than No. 1303.

Formally recognized occupational disease No. 1317 is limited to the clinical pictures of polyneuropathy and encephalopathy. Other possible target organs, such as the liver or kidneys, should not therefore be handled under occupational disease No. 1317. In the case of disorders external to the nervous system, the limitations of other list numbers must be considered with regard to the defined substances and substance groups. Other neurological clinical pictures such as Parkinson's syndrome or multiple sclerosis are likewise not covered by BK 1317. No connection has yet been demonstrated scientifically between these conditions and exposure to solvents.

Contents of the Occupational Disease Report

The present Occupational Disease Report describes the technical information on solvents which is relevant to the procedure for formal recognition of a case of occupational disease. In particular, it contains a compilation of solvent exposure data in certain sectors and at certain workplaces to which reference may usefully be made during investigation into specific cases when the full facts are no longer available at the workplace of the insured individual concerned. Above all, the technical information is intended to assist the prevention service in recording and evaluating the exposure situation comprehensively and thoroughly. If data are available for the insured individual's actual

workplace, preference should be given to these data during evaluation rather than to the data from the register of areas of work.

The Report also contains a guide to assessment which has been produced in conjunction with medical experts. Observance of the recommendations for assessment ensures that all insured individuals are treated equally based upon the current state of medical knowledge.

The purpose of the Occupational Disease Report is that of ensuring that the decisions reached are based upon sound facts. The technical information is intended for the creation of a substantiated work history.

The recommendations for assessment are intended for creation of a basis for correct medical classification. Information on causality in an insurance context has also been included in Chapter III, “Recommendations for medical assessment”.

Generic, comprehensive procedural instructions in the form of flow charts etc. have not been produced since proper dealing with a case of occupational disease is not essentially dependent upon the specific occupational disease in question, and general procedures are adequately described in other guides (e.g. the Occupational Disease Manual and the Occupational Disease Report on fibre years).

II. Work-related information

1 Neurotoxic solvents

The 15 hazardous substances mentioned on the following pages have been taken from the scientific rationale for BK No. 1317 – polyneuropathy or encephalopathy caused by organic solvents, in isolation or in mixtures – (BMA, 1996), and are presented in the present Report with regard to their technical application. The table below lists the principal information concerning the 15 neurotoxic solvents (Official Journal of the European Communities, directive 67/548/EEC with adaptation directives).

The Occupational Disease Report refers at certain points to the Hazardous Substances Ordinance (GefStoffV – Gefahrstoffverordnung) and to the TRGS body of technical rules pursuant to it. As a result of the amendment to the Hazardous Substances Ordinance which came into force on 1 January 2005, a need exists for changes to the body of technical rules. However, it continues to remain valid in principle until its amendment provided it does not contradict the new Hazardous Substances Ordinance. All atmospheric limit values based upon the state of the art have ceased to be valid, however. The extent to which workplace limit values can be deduced for these substances with reference to occupational medicine and toxicology is under review. Substances with carcinogenic and mutagenic properties are primarily affected. The relevant information on the German occupational exposure limits has therefore been omitted from this new edition. This change does not affect the neurotoxic threshold values employed in the present Report for evaluation of the exposure levels (refer in this context to Parts III.6.2 and III.6.3). The authors of the Report continue to recommend the use of these values for retrospective evaluation of exposure in the context of occupational disease No. 1317; where applicable, they are adapted to new scientific findings.

Table 1:
Neurotoxic solvents – CAS number, classification, German occupational exposure limit, boiling point, vapour pressure, material safety data sheet, occupational disease code

❶	❷	❸			
Solvent	**CAS No. ZVG No.**	①	②	③	④ **Classification Remarks**
Aliphatic hydrocarbons					
n-Heptane	142-82-5 13820				F; R11 Xn; R65 Xi; R38 R67 N; R50-53
n-Hexane	110-54-3 510789			R_F3	F; R11 Repr.Cat3; R62 Xn; R65-48/20 Xi; R38 R67 N; R51-53 Y
Ketones					
2-Butanone (MEK,methyl ethyl ketone)	78-93-3 13330				F; R11 Xi; R36 R66 R67 H Y
2-Hexanone (n-butyl methyl ketone)	591-78-6 31940			R_F3	R10 Repr.Cat3; R62 T; R48/23 R67 H
Alcohols					
Ethanol (ethyl alcohol)	64-17-5 10420				F; R11 Y
Methanol (methyl alcohol)	67-56-1 11240				F; R11 T; R23/24/25- 39/23/24/25 Y

❹ German occupational exposure limit 5/2006	❺ Boiling point in °C	❻ Vapour pressure at 20 °C in hPa	❼ MSDS Mass percent	❽ Occupational disease code
Aliphatic hydrocarbons				
2,100 mg/m³	98.43	48	1.0	1317
180 mg/m³	68.74	160	1.0	1317
Ketones				
600 mg/m³	79.57	105	1.0	1317
21 mg/m³	127.2	3.5	0.1	1317
Alcohols				
960 mg/m³	78.33	59	5.0	1317
270 mg/m³	64.51	128.6	0.1	1306 1317

Table 1:
(Continuation)

❶	❷	❸			
Solvent	**CAS No. ZVG No.**	①	②	③	④ **Classification Remarks**
Glycol ether					
2-Methoxyethanol (ethanediol monomethyl ether)	109-86-4 10630			R_E2 R_F2	R 10 Repr.Cat2; R 60-61 Xn; R20/21/22 Z
Aromatic hydrocarbons					
Benzene	71-43-2 10060	K1	M2		F; R11 Carc.Cat1; R45 Muta.Cat2; R46 T; R48/23/24/25 Xn; R65 Xi; R36/38
Styrene (vinyl benzene, phenylethylene)	100-42-5 10110				R10 Xn; R20 Xi; R36/38 Y
Toluene (methylbenzene)	108-88-3 10070			R_E3	F; R11 Repr.Cat3; R63 Xn; R48/20-65 Xi; R38 R67
Xylene (o-, m-, p-Dimethylbenzene)	1330-20-7 10080 o: 95-47-6 o: 18470 m: 108-38-3 m: 18480 p: 106-42-3 p: 18490				R10 Xn; R20/21 Xi; R38 H
Chlorinated aliphatic hydrocarbons					
Dichloromethane (methylene chloride)	75-09-2 12630	K3			Carc.Cat.3, R40
Tetrachloroethylene (perchloroethylene, PER)	127-18-4 13680	K3		R_E3	Carc.Cat.3, R40 N; R51-53 H

❹ German occupational exposure limit 5/2006	❺ Boiling point in °C	❻ Vapour pressure at 20 °C in hPa	❼ MSDS Mass percent	❽ Occupational disease code
		Glycol ether		
16 mg/m³	124.6	8.1	0.5	1317
		Aromatic hydrocarbons		
3.25 mg/m³ *EU workplace limit value	80.10	99.7	0.1	1303 1317
86 mg/m³	145.14	6.24	1.0	1303 1317
190 mg/m³	110.63	27.8	1.0	1303 1317
440 mg/m³	o: 144.41 m: 139.1 p: 138.35	o: 6.7 m: 8 p: 8.2	1.0	1303 1317
		Chlorinated aliphatic hydrocarbons		
260 mg/m³	40.67	460.9	1.0	1302 1317
	121.2	18.9	1.0	1302 1317

Table 1:
(Continuation)

❶	❷	❸			
Solvent	**CAS No. ZVG No.**	①	②	③	④ **Classification Remarks**
Chlorinated aliphatic hydrocarbons (Continuation)					
1,1,1-Trichloroethane	71-55-6 26940				Xn; R20 N; R59 H Y
Trichloroethylene (TRI, ethylene trichloride)	79-01-6 10720	K2	M3		Carc.Cat.2, R45 Muta.Cat.3, R68 R67 Xi; R36/38 R52-53

❹	❺	❻	❼	❽
German occupational exposure limit 5/2006	Boiling point in °C	Vapour pressure at 20 °C in hPa	MSDS Mass percent	Occupational disease code
Chlorinated aliphatic hydrocarbons (Continuation)				
1,100 mg/m³	73.7	133.0	1.0	1302 1317
	86.7	77.1	0.1	1302 1317

Legend to Table 1:

Column ❶	Name of the solvent and its common synonyms
Column ❷	The CAS number (CAS No.) is a standard international code number for unambiguous identification of chemical compounds. This number is assigned uniquely to each chemical substance by the **C**hemical **A**bstracts **S**ervice of the American Chemical Society. The ZVG number (ZVG No.) is the centrally assigned number of the GESTIS information system on hazardous substances of the German institutions for statutory accident insurance and prevention.
Column ❸	Classification
Sub-column ①:	Carcinogenic potential (excerpt)
K1	Substances known to be carcinogenic to man. There is sufficient evidence to establish a causal association between human exposure to a substance and the development of cancer.
K2	Substances which should be regarded as if they are carcinogenic to man. There is sufficient evidence to provide a strong presumption that human exposure to a substance may result in the development of cancer, generally on the basis of • appropriate long-term animal studies • other relevant information
K3	Substances which cause concern for man owing to possible carcinogenic effects but in respect of which the available information is not adequate for making a satisfactory assessment. There is some evidence from appropriate animal studies, but this is insufficient to place the substance in category 2.
Sub-column ②:	Mutagenic potential (excerpt)
M2	Substances which should be regarded as if they are mutagenic to man. There is sufficient evidence to provide a strong presumption that human exposure to the substance may result in the development of heritable genetic damage, generally on the basis of: • appropriate animal studies • other relevant information.
M3	Substances which give rise to concern owing to a possible mutagenic effect in humans. Some indicators exist from suitable mutagenicity tests, but are not sufficient for the substance to be classified in Category 2.
Sub-column ③:	Reprotoxic potential (excerpt)
R_F2	Substances which should be considered a threat to human fertility.
R_F3	Substances which give rise to concern owing to a possible impairment of the reproductive capacity of humans.
R_E2	Substances which should be regarded as teratogenic in humans.
Sub-column ④:	Hazard symbol, R phrases, TRGS 900 remarks This column contains the risk phrases (R phrases) and hazard symbols of the classification. The classification has repercussions not only for labelling, but also for other statutory and administrative regulations. The H code (denoting a percutaneously absorptive substance) was taken from the TRGS 900.

Hazard symbols: (excerpt)

F (highly flammable) Xi (irritant) N (harmful to the environment)
Xn (harmful to health) T (toxic)

Y „Y“ denotes substances for which no risk of a teratogenic effect need be feared provided the atmospheric limit value and the biological limit value are observed.

Z „Z“ denotes substances for which a risk of a teratogenic effect cannot be excluded even when the workplace limit value and the biological limit value are observed.

Detailed information and definitions of the hazard symbols and R phrases can be found in the relevant literature (such as the Hazardous Substances Ordinance [GefStoffV]).

Column ❹

Current atmospheric German occupational exposure limit, as at: May 2006
* This binding EU workplace limit value is not a workplace limit value in the context of the GefStoffV 3 (6) (in which case no acute or chronic harmful effects upon health may generally be anticipated provided it is observed); for this reason, it is also not listed in the TRGS 900.
The limit values stated in this column refer to the concentration (weight per unit volume) of a hazardous substance in the workplace atmosphere.

Column ❺

Boiling point: [°C] under normal conditions

Column ❻

Vapour pressure: [mbar] or [hPa]. The reference temperature is 20 °C; deviations from the reference temperature are indicated in brackets.

Column ❼

Content in percent by weight above which a solvent must be stated in a material safety data sheet, according to its classification (in accordance with TRGS 220).

Column ❽

Occupational disease code for known inducers of occupational diseases. Taken from the list of formally recognized occupational diseases in accordance with the Second Amending Regulation for Amendment of the Occupational Disease Ordinance (BKV), 18 December 1992.

Excerpt:

1302: Diseases caused by halogenated hydrocarbons
1303: Diseases caused by benzene, its homologues, or styrene
1306: Diseases caused by methyl alcohol (methanol)
1317: Polyneuropathy or encephalopathy caused by organic solvents, in isolation or in mixtures

Restrictions upon use in accordance with the 2nd Ordinance for the Implementation of the Federal Immission Control Act (BImSchV) or prohibitions upon use under the Hazardous Substances Ordinance

2 Investigation of exposure

2.1 The relevance of the work history in the procedure for the handling of cases of formally recognized occupational disease

For recognition as a case of occupational disease No. 1317, a case of polyneuropathy or encephalopathy requires evidence of exposure to neurotoxic solvents or to a mixture containing neurotoxic components. This classification is based upon the investigations into occupational exposure conducted by the prevention services of the institutions for statutory accident insurance and prevention. In addition to surveys of the occupational activity, the agents employed, plant procedures and the workplace situation, these particularly involve definition as precisely as possible of the duration and level of exposure.

In the first instance, the following information is obtained from the insured individual:

- Employer, relevant periods of employment
- Description of the workplace, presumed exposure
- Changes at the workplace
- Form and progress of the disease
- Doctors treating the condition
- Company physician
- Health insurance fund
- Miscellaneous (pre-existing conditions, interest in diagnosis)

Information from other parties or persons (doctors/health insurance institutions) on existing and past conditions suffered by the person affected should be sought only once sufficient indicators of harmful exposure exist (German Social Code VII, 199 [3]). Sufficient indicators do not necessarily constitute a validated finding. Should insured individuals be able to provide plausible information on exposure or the exposure be confirmed in principle by the employer, sufficient indicators exist to necessitate the launching of investigations into the clinical picture.

Should it already be clear, owing to information from doctors, that the clinical picture is not consistent with a toxic encephalopathy or polyneuropathy, detailed investigations into solvent exposure are unnecessary. This does not apply of course, should the medical grounds for this diagnosis be (only) factually tenuous and should it be possible to clarify them (if at all) only in the course of an assessment.

Other occupational diseases are of no particular relevance during recording of the prior medical history. The pre-existing conditions which are relevant to the evaluation of occupational disease No. 1317 can be found in Chapter III of this Occupational Disease Report (Recommendations for medical assessment, 1.1.4 and 1.2.3).

Previous employment arrangements may vary in their relevance. Since the onset of polyneuropathy or encephalopathy must coincide in some way with exposure, periods of employment in the distant past need not necessarily be as relevant as is the case for other occupational diseases (such as occupational diseases Nos. 4104, 4105). Investigations may therefore focus primarily upon activity performed during the 10 to 15 years prior to reporting of the condition. Attention must however be paid during evaluation to the relevance of the duration of exposure (cf. Chapter III, Annex 6.2/6.3).

Where investigation is conducted on-site by the prevention service, the insured individual is entitled to attend (German Social Code VII 103 [2]). The insured individual must therefore be informed in advance of the date of the investigations in the plant. The attendance of the insured individual supports clarification of the facts, in that questions may be asked in as much detail as possible concerning the working method and exposure. Information provided afterwards to the insured individual on the results of the investigation may also contribute to agreement being reached on the actual circumstances.

The work-related comment is intended to provide the accident insurance's administration and the medical assessor with the most complete information possible on the circumstances of exposure, such that these parties need not ask further questions.
In particular, detailed information is required on:

- Tasks and areas of work of the insured individual
- Form of contact with solvents
- Types of solvents used (substances, mixtures, composition)
- Concentration in the breathing air (measured values; secondary: estimation based upon the MEGA database or Occupational Disease Report; if applicable, historical progress)
- Nature and scale of direct skin contact (duration, intensity, affected regions of the skin, etc.)
- Duration and intensity of exposure (daily, weekly, period of time)
- The findings of the occupational physician (biomonitoring, preventive health monitoring in accordance with the principles of the institutions for statutory accident insurance and prevention, Nos. G 10, 14, 17, 29, etc.)
- Other circumstances (e.g. ventilation, personal protective equipment, exposure peaks)
- Overall evaluation
  Here, the issue of exposure to neurotoxic solvents should be considered discriminatingly (see Sections II.1 and II.4). In the case of mixtures, reasons must be stated for whether and on the basis of what find-

ings components with neurotoxic action were involved.

For the statement of concentration values, priority must be given to measurements at the employed individual's specific workplace. The use of the average concentration values stated in Section II.4 is permissible only if no measurement results are available from the insured individual's area of work, retrospective measurement is not possible, and measured data cannot be obtained from comparable plants.

Since different measurements generally yield different atmospheric concentrations at the workplace, average values must be employed. 50th percentile values and 90th percentile values are stated in the substance dossiers. The 50th percentile value (median) is the concentration which is higher than 50% of all measured values and lower than the remaining 50%. In individual cases, exposure may be estimated within the range between the 50th and 90th percentile values, according to the measurement density. In order for underestimation of the actual exposure to be largely excluded, the convention should be followed of the 90th percentile value being employed for the assessment in substantiated cases (e.g. wide scatter) rather than the median. This means that independent of the distribution, 90% of all available values are below the stated concentration value, the remaining 10% above it. Corresponding conventions were followed for occupational disease No. 4104 with regard to the asbestos fibre concentration (Occupational Disease Report 1/97) and during investigation of the workplace benzo[a]pyrene concentration in relation to cases of lung cancer caused by polycyclic aromatic hydrocarbons (Occupational Disease Report 2/99).

In contrast to the formally recognized occupational diseases referred to above, the regulation governing occupational disease No. 1317 does not define a dose which must be attained or exceeded as a criterion for recognition. Whether the exposure as identified by an accident insurance institution may by virtue of its intensity and duration have been capable of causing polyneuropathy or encephalopathy in a given case is therefore an issue which must be determined primarily from a medical (generally occupational medical) perspective. The prevention service of the institution for statutory accident insurance and prevention has the task of investigating and quantifying the exposure as completely as possible. In the context of the overall evaluation, it must also evaluate the occupational health situation and compare the conditions with the limit values applicable to the hazardous substances concerned. The limit values are however not significant for all substances with regard to a neurotoxic effect. In the light of the above, the information on neurotoxic threshold values stated in the present Occupational Disease Report (Sections III.6.2 and III.6.3) must also be considered in the overall evaluation. The tasks of the prevention service do not extend to reaching conclusions concerning causality.

2.2 Investigation procedure

In the first step, a detailed work history is produced for the affected employee. This chapter presents a possible model for the procedure and for the recording of the necessary information and data. The relevant exposure is to be investigated based upon the detailed work history. Figure 1 shows the decision-making procedure by which data are obtained and the specific exposure identified.

For performance of a work history for occupational disease No. 1317, a concept was drawn up by the institution for statutory accident insurance and prevention in the mechanical engineering and metalworking industry for recording of the plant data (Page 1) and solvent exposure (Page 2), primarily for static workplaces. Should the periods of exposure to neurotoxic solvents not be contiguous, Page 2 must be produced for each period. In order for the data obtained to be evaluated, they should be indexed in accordance with the BGIA[1] coding lists. A software application containing these lists codes is available from the BGIA and can be used for computerized input and evaluation. For mobile areas of work, other surveys of work histories may also be performed.

[1] since 1st January 2010: Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung (IFA)

Work history for occupational disease No. 1317 **Page 1** **Polyneuropathy or encephalopathy caused by organic solvents, in isolation or in mixtures**	
Number:	.....
Last name, first name:	(Free text) .....
Date of birth	..... Sex: .....
Requesting body:	(Free text) .....
Our ref.:	..... File ref.: .....
Company:	(Free text) ....
Membership No.:	.....
Main form of business:	(According to the BGIA coding list of sectors).....
Employed from:	..... to .....
Occupation:	(According to the BGIA coding list) .....
Date of investigation:	.....
Persons involved in the investigation:	Insured person: ..... Employer/employer‘s representative:..... Safety professional: ..... Employee representative council member: ..... Company physician:..... Staff of the institution for statutory accident insurance and prevention:..... Other persons:.....
Remarks:	(Free text) .....

Work history for occupational disease No. 1317 **Page 2**
Polyneuropathy or encephalopathy caused by organic solvents, in isolation or in mixtures

Number:	.....
Last name, first name:	(Free text).....
Area of work/task:	From: ..... to: .....
Plant sub-type:	(According to the BGIA coding list of sectors)
Area of work:	(According to the BGIA coding list of working areas)
Task:	(Free text).....
Performed from:	..... to: .....
Period of time:	..... per ....., ... per .....
Room/area:	(As per the BGIA coding list)
Type of premises:	(Free text).....
Natural ventilation:	(As per the BGIA coding list)
Engineered ventilation:	(As per the BGIA coding list)
Air conduction:	(As per the BGIA coding list)
Measures against emissions:	(As per the BGIA coding list)
Collection (exhaust):	(As per the BGIA coding list)
Principle of operation:	(As per the BGIA coding list)
Installation type:	(Free text).....
PPE:	(Free text).....
Temperature:	(Free text).....
Arduousness of the work:	(Free text).....
Solvents:	(Product name, in free text).....
Acute effects:	☐ No ☐ Yes (details): .....
BAT biological tolerance values available:	☐ No ☐ Yes (details): .....
Remarks:	(Free text).....
	.....
	.....

Concentration of neurotoxic solvents in the area of work

Item	Solvent	Concentration	Determined based upon	Remarks
	Selection from the list of neurotoxic solvents		• Measurement result to TRGS 402 • BGIA Report • Estimation	

Investigation of exposure

The diagram in Figure 1 shows a proposed procedure for investigation of exposure to neurotic solvents.

During determination of the exposure for the relevant tasks/areas of work from measurements, documented measurement results and the exposure data in Section II.4 (substance dossier), the period (as part of the working day) to which the identified exposure value applies must first be specified. This period may be a shift and therefore an average shift value, possibly averaged over periods of varying exposure or even of no exposure, or it may be a task-based value with a task-specific reference period.

Since valuable indicators of exposure may be obtained from the results of relevant occupational medical examinations conducted by company or otherwise authorized physicians or from the results of studies of the biological material (biomonitoring), such information must always be requested. Details of BAT (biological tolerance) values can be found in the substance dossiers in Section II.4.

Example: investigation of solvent exposure at a GRP product manufacturer

Between 1987 and 1997, an employee worked as a GRP (**g**lassfibre **r**einforced **p**lastic) production operative, and regularly carried out the following tasks:

- Manipulation and placing in storage of prepreg mats
- Operation of the press
- Mechanical finishing of the cured GRP mouldings (removal of burrs, cutting)
- Handling and storage of the final products

During these tasks, the employee was exposed to styrene during "operation of the press"; he performed this task on average for approximately three hours each day. The styrene dossier (Section II.4.10) lists task-related values for "hot pressing" (Table 19) which may be regarded as approximate values specifically for the exposure over an entire shift during performance of the task of "operation of the press", with the usual interruptions.

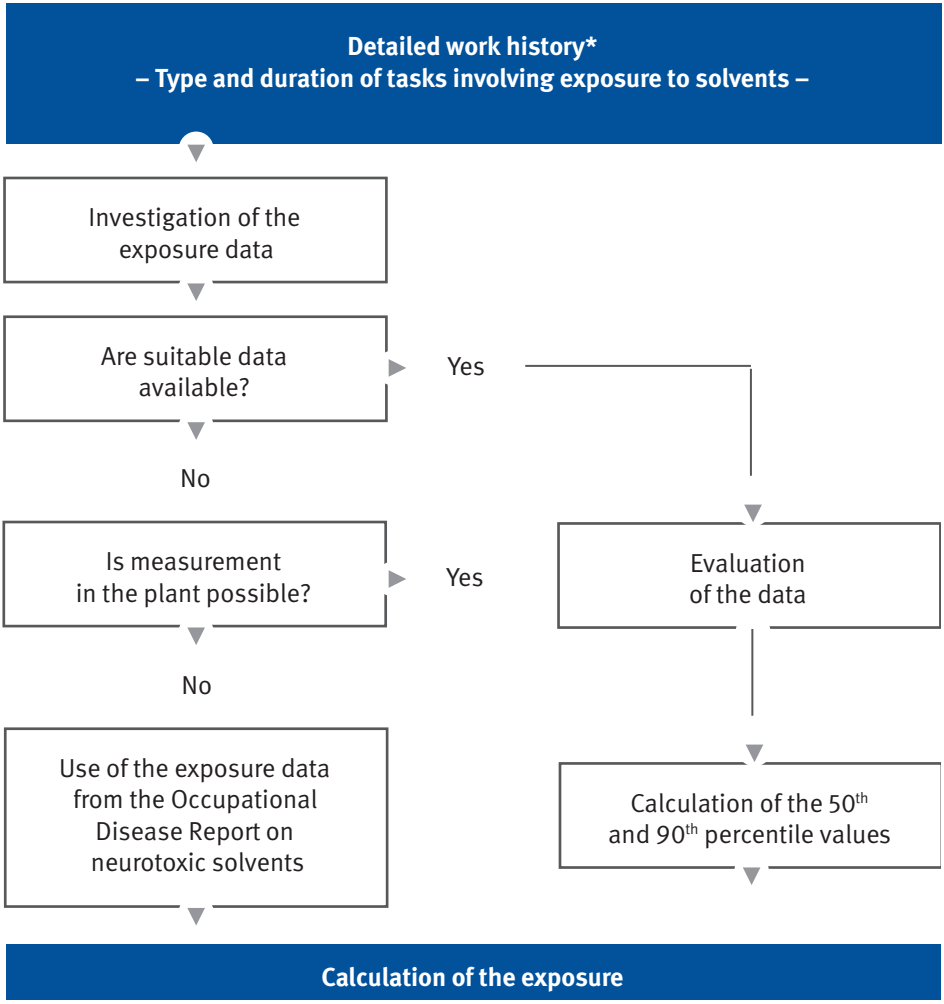
The employee was therefore exposed:

- Over a period of ten years
- For an average of three hours per day
- To up to 141 mg/m³ of styrene (Table 19)
- Extrapolated to an eight-hour working day: $3/8 \cdot 141\ mg/m^3 = 52.9\ mg/m^3$

Example: investigation of the solvent exposure of a fitter who performed painting work

Between 1993 and 1997, an employee worked as a fitter, during which he regularly performed (spray-)painting work.

Figure 1:
Procedure for investigation of exposure to neurotoxic solvents



* Should no data be available from the insured individual's plant, data for comparable areas of work can be determined for the period since 1981 if necessary by the institutions for statutory accident insurance and prevention or on their behalf by searches in the BGIA exposure database MEGA. Only if measured values are not available or not suitable is it permissible for the exposure data in the Occupational Disease Report to be employed for the tasks actually performed. In addition to these data, data for comparable areas of work from BG/BGIA recommendations may be referred to for the evaluation.

During this task, he was exposed to butanone, ethanol, n-heptane, methanol, 2-methoxyethanol and toluene. He performed this task for an average of approximately four hours each day. The relevant substance dossiers (Sections II.4.2, II.4.4, II.4.5, II.4.8, II.4.9, II.4.12) list task-based values for spray-painting which may be regarded as approximate values specifically for the exposure over an entire shift during performance of the task of "spray-painting", with the usual interruptions.

The employee was therefore exposed to the following substances for an average of four hours per day over a period of five years:

- Butanone: up to 22 mg/m³, extrapolated per shift: 4/8 · 24 mg/m³ = 12 mg/m³
- Ethanol: up to 18 mg/m³, extrapolated per shift: 4/8 · 18 mg/m³ = 9 mg/m³
- n-Heptane: up to 10 mg/m³, extrapolated per shift: 4/8 · 10 mg/m³ = 5 mg/m³
- Methanol: up to 14 mg/m³, extrapolated per shift: 4/8 · 14 mg/m³ = 7 mg/m³
- 2-Methoxyethanol: no exposure (< analytical limit of detection)
- Toluene: up to 19 mg/m³, extrapolated per shift: 4/8 · 19 mg/m³ = 9.5 mg/m³

Example: investigation of the solvent exposure of a floor-layer

The affected individual was employed as a floor-layer from 1965 to the end of 1997. In the last ten years of this period, his work also involved contact with polychloroprene adhesives. Among the contents of these adhesives are methyl acetate, acetone, toluene, methanol and butanone. The values encountered here are regularly several times the atmospheric limit values for discrete substances and particularly the sum limit value to TRGS 403. In addition, depending upon the substrate and the flooring to be laid, other adhesives were also employed which gave rise to lower solvent exposure levels.

The adhesives used by the affected person also contained smaller quantities of n-hexane. The concentrations of n-hexane in the breathing air were however low, less than one-tenth of the atmospheric limit value. Products containing toluene were frequently employed up to the early 1990s; the market share of these products then fell considerably, owing to the discussion of the teratogenic effect of toluene. Flooring adhesives containing toluene have hardly been used since the mid-1990s.

Like all self-employed floor-layers, the affected individual generally worked for longer than eight hours per day, and frequently for more than five days per week.

In consideration of the neurotoxic threshold values, the exposure of the affected person to neurotoxic substances from 1987 to around 1992 during the use of polychloroprene adhesives was relatively high. This particularly holds true when the very low neurotoxic mixture threshold values for mixtures such as butanone and toluene are considered. In this case, it can be assumed that the sum limit value for the neurotoxic substances are exceeded over ten-fold.

For the toluene-free adhesives, the sum limit value for the neurotoxic substances can be assumed to be observed.

Altogether, it can be stated that from around 1987 to 1992, considerable exposure to neurotoxic substances occurred which in the case of some specific adhesives substantially exceeded the sum limit value for the neurotoxic substances. Depending upon the adhesive employed, the work may have lasted for several weeks.

Following a transitional period, during which the use of adhesives containing toluene progressively decreased, toluene-free adhesives have been used almost exclusively since no later than 1995. It may therefore be assumed that, with exceptions of brief duration, the affected person ceased to be exposed to neurotoxic solvents above the neurotoxic threshold values as of 1995 at the latest.

3 Selection of areas of work/tasks with possible exposure to neurotoxic solvents

3.1 Overview: industrial sector/area of work/task and possible relevant neurotoxic solvents

With regard to the listing below, it is important to note that the product-specific formulations have changed over time, in some cases considerably, owing to prohibitions on use (* restrictions upon use in accordance with the 2nd Ordinance on the German Federal Immission Control Act [2nd BImSchV]) and product changeovers. In addition, special formulations are used in some sectors, depending upon the application. The procedures listed are those stated in the relevant "substance dossiers" in Section II.4 under "Use/areas of application". The hazardous substances are listed alphabetically. Further information can be found under the relevant "substance dossiers" in Sections II.4.1 to II.4.15.

Chemical industry (manufacture of base materials and formulations)

- Manufacture of lacquers and paints: benzene (up to around 1980), butanone, ethanol, n-heptane, n-hexane, tetrachloroethylene*, toluene (printing ink), 1,1,1-trichloroethane*, xylene

- Manufacture of adhesives: benzene (in the German Democratic Republic), butanone, ethanol, n-heptane, n-hexane, 2-hexanone, methanol,

2-methoxyethanol, toluene, tetrachloroethylene*, 1,1,1-trichloroethane*, trichloroethylene*, xylene

- Manufacture of pharmaceutical and cosmetic products:
  dichloromethane, ethanol, n-heptane, methanol, xylene
- Manufacture of preservatives and disinfectants:
  ethanol
- Extraction of vegetable oils in the food industry:
  n-hexane
- Manufacture of plastics and rubber:
  butanone, n-hexane, 2-methoxyethanol, styrene, trichloroethylene*, xylene
- Manufacture of natural and synthetic resins:
  butanone, n-hexane, 2-hexanone, methanol, 2-methoxyethanol, tetrachloroethylene*, toluene, 1,1,1-trichloroethane*, xylene
- Manufacture of cleaning agents and thinners:
  butanone, dichloromethane, n-heptane, n-hexane, tetrachloroethylene*, toluene, 1,1,1-trichloroethane*, trichloroethylene*, xylene
- Manufacture of stripping products:
  dichloromethane, methanol
- Manufacture of foaming agents:
  dichloromethane*, tetrachloroethylene*, 1,1,1-trichloroethane*
- Extraction of fats, oils, waxes, etc.:
  butanone, dichloromethane, n-hexane, tetrachlorethylene*, trichloroethylene*, toluene
- Synthesis of base materials:
  benzene, ethanol, methanol, toluene, xylene
- Manufacture of formulations for crop spray and pest control products:
  dichloromethane, toluene, xylene
- Bonding and repair of rubber conveyor belts:
  trichloroethylene*
- Coking plants and secondary recovery plants:
  benzene, xylene
- Refineries and fuelling areas:
  benzene (petrol/gasoline), butanone (dewaxing of mineral oils), xylene
- Production of motor fuels:
  benzene (petrol/gasoline), ethanol, methanol, toluene, xylene
- Loading and unloading of tanker vehicles and tanker vessels, filling stations:
  benzene (petrol/gasoline) (all other neurotoxic solvents, where transported)

- Laboratories: depending upon work performed, all neurotoxic solvents

Metals manufacture and use, electrical engineering, precision engineering, timber industry, upholstered furniture industry

- Use (spraying, brushing) of paints and lacquers:
  benzene (up to around 1980), butanone, ethanol, n-heptane, n-hexane, 2-hexanone, methanol, 2-methoxyethanol, tetrachloroethylene, toluene (printing ink), 1,1,1-trichloroethane*, xylene

- Use of natural and synthetic resins:
  butanone, n-hexane, 2-hexanone, methanol, 2-methoxyethanol, tetrachloroethylene, toluene, 1,1,1-trichloroethane*, xylene

- Use (lamination, puttying) of reaction resins:
  styrene, toluene

- Use (spraying, brushing, puttying) of adhesives:
  benzene (in the German Democratic Republic), butanone, ethanol, n-heptane, n-hexane, methanol, 2-methoxyethanol, toluene, 1,1,1-trichloroethane*, xylene

- Lubrication units in the metals industry:
  tetrachloroethylene*

- Use of surface cleaning agents (manual and by machine):
  butanone, dichloromethane, n-hexane, tetrachloroethylene*, toluene, 1,1,1-trichloroethane*, trichloroethylene*, xylene

- Use of stripping agents (cold paint stripping):
  dichloromethane, methanol

- Use of foaming agents etc.:
  dichloromethane*, tetrachloroethylene*, 1,1,1-trichloroethane*

- Cleaning and maintenance of tanks and tank fittings:
  benzene (petrol/gasoline)

- Foundries (unintended production):
  benzene, ethanol (manufacture of cold-box cores, application of mould-coating materials)

- Monitoring/maintenance, repair, test benches (automotive manufacture, automotive repair shops):
  benzene (petrol/gasoline)

Leather, textiles and garments trade

- Dry-cleaning:
  tetrachloroethylene*

- Garments industry:
  1,1,1-trichloroethane*

- Manufacture of artificial leather:
  butanone

- Use (spraying, brushing, puttying) of adhesives:
  benzene (in the German Democratic Republic), butanone, ethanol, n-heptane, n-hexane, methanol, 2-methoxyethanol, toluene, 1,1,1-trichloroethane*, xylene

- Shoe manufacture:
  dichloromethane* (used up to around 1990 as a separator during the manufacture of polyurethane shoe soles)

Printing industry

- Rotogravure (solvent and cleaning agents):
  toluene
- Offset printing (cleaning agents):
  n-heptane, n-hexane, 1,1,1-trichloroethane*, trichloroethylene*
- Screen printing
  (solvent and cleaning agents):
  n-heptane, toluene, xylene
- Rotogravure package printing
  (solvent and cleaning agents):
  ethanol
- Flexography (solvent and cleaning agents):
  ethanol

Paper industry

- Manufacture of transparent paper:
  butanone
- Impregnation:
  butanone, ethanol, n-heptane, methanol
- Silicon and protective coatings:
  1,1,1-trichloroethane*

Construction industry

- Use of paints and lacquers (for example for corrosion protection):
  butanone, ethanol, n-heptane, n-hexane, 2-hexanone, methanol, 2-methoxyethanol, toluene, 1,1,1-trichloroethane*, xylene
- Use (lamination, puttying) of reaction resins (acidproof installation):
  styrene, toluene
- Use of adhesives during floor-laying work:
  butanone, ethanol, n-heptane, n-hexane, methanol, toluene, xylene
- Use of wood putty and parquet sealants:
  butanone, ethanol, toluene, xylene
- Use of insecticides and wood treatment formulations:
  xylene
- Building cleaning work (including the use of wood/stone care products, anodized aluminium cleaners):
  butanone, dichloromethane, ethanol, n-hexane, toluene, xylene
- Use of stripping agents:
  dichloromethane, methanol
- Asphalt laboratories:
  trichloroethylene*
- Stone working:
  trichloroethylene*

3.2 Description of tasks/areas of work

Tasks and areas of work are described more closely below with regard to contact with and possible exposure to neurotoxic solvents.

A comprehensive presentation for all areas stated under Section 3.1 is beyond the scope of the present report. The technical departments of the individual institutions for statutory accident insurance and prevention possess expertise for the relevant areas.

The selection which serves as an example does not imply that all the areas concerned are particularly subject to exposure. Nor can it be concluded that areas of work which are not described in greater detail can be classified as safe with regard to a relevant exposure.

3.2.1 Chemical industry

Manufacture of paints and lacquers (coatings)

Conventional paints and lacquers containing solvents generally consist of binders, pigments, dyes, fillers, additives and solvents. The solvent component generally lies between 30 and 85% by weight. The manufacturing process for paints and lacquers generally comprises six main steps:

- Preparation:
  weighing out and mixing of the components
- Dispersion
- Completion of mixing, correction of the final product
- Quality control
- Screening and filling
- Cleaning of the vessels used for preparation

The solid or liquid constituents are weighed or measured volumetrically, inserted in a certain sequence into mixing vessels equipped with agitators, and agitated until a homogeneous mixture free of streaks is produced. This mixture is then processed in dispersion units in order to achieve fine distribution and thorough wetting of the pigments and fillers by the binders. Further binder and additive components may then be added in accordance with the recipe, and the colour tones adjusted according to the specifications. Following checking against further specifications, the paints and lacquers are passed through screens and filled into transport vessels.

Both mixing vessels and any transport vessels which may have been returned are cleaned with solvents in a machine or manually.

During the manufacture of high-viscosity coatings, such as fillers, printing and art dyes, etc., kneaders or roller mills are primarily employed for mixing and dispersion.

A large number of chemical compounds are employed, generally in the form of mixtures.

The mineral oil fractions employed contain aliphatic and aromatic hydrocarbons as a function of their distillation range, including n-hexane, n-heptane, benzene (below 0.01%), toluene and xylene.

Typical solvent mixtures may also contain alcohols (including ethanol) and ketones (including 2-butanone). Benzene has not been used as a raw material for paints and lacquers since the mid-1950s; its component as an impurity in hydrocarbon mixtures must not exceed 0.1%. Chlorinated hydrocarbons are no longer significant in paint and lacquer production. In the past, trichloroethylene was employed in large quantities for immersion-coating lacquers.

Insulating varnishes for the coating of copper wire for the electrical industry contain up to 4.5% n-hexane. Up to 1992, wood varnishes had a maximum permissible n-hexane content of 1.5%. Since 1992, n-hexane-free solvents have been employed for the manufacture of varnishes.

Manufacture of adhesives

Contact adhesives

Polychloroprene chips are dissolved in toluene or xylene in high-speed, hermetically sealed dissolvers at speeds of around 600 rpm and under high shear forces. Since 1989, however, xylene has replaced toluene in the majority of recipes. Owing to the high forces which must be generated in order for correspondingly high shear forces to be exerted upon the polychloroprene chips, and the associated high speeds of the dissolvers, process constraints require the manufacturing process to be performed in a fully sealed system. In order for solvent losses during production to be reduced to a minimum, vapours which are produced (generally xylene) are liquefied and returned to the mixture by a condenser and backflow.

Only on some older installations are polychloroprene chips still charged manually into the dissolver through a manhole. Residual vapours (in most cases xylene) from the previous formulation may result here in brief solvent exposure.

The solvent itself is fed by a pump system into the self-enclosed dissolver. Only in very rare cases does this pumping process not feature a gas-shuttle system, in which case the displacement vapours are instead discharged via the roof. Here, however, a conflict exists with the German Federal Immission Control Act (BImSchG); even these older installations may not therefore discharge vapours containing xylene directly into the atmosphere.

Into the 1980s, charging installations were still in use which in some cases did not feature explosion protection. In order to prevent explosive atmospheres from forming, these installations have been encapsulated and equipped with forced ventilation and exhaust (primary explosion protection). As a result, the exposure of workers to xylene or toluene in the charging area was also limited.

Only in areas in which charging machines with explosion protection were employed and forced ventilation and exhaust was not employed were elevated emissions of toluene or xylene vapours detectable.

PVC solvent adhesive

PVC powder is dissolved in tetrahydrofuran (THF) and n-hexane. Amorphous silicic acid is also added, for adjustment of the viscosity.

Since the PVC powder can easily become electrostatically charged during charging of the vessel, and bunch discharge sparks must be anticipated in the dissolver, inertization by means of nitrogen is particularly important with this method in order for the risk of explosions to be avoided. It follows that the process must be performed in a fully enclosed system in order for the production staff not to be exposed to solvents.

Exposure of employees is possible only during charging of the adhesive. Exposure in this case is primarily to THF emissions.

Water-based adhesives

Glues containing casein or dextrin or other water-based adhesives, which are used for example for labelling, may have a solvent content of up to 5%. The solvent in this case is generally ethanol, and in rare cases also isopropanol. The solvent is added once the initial water-based charge has been produced. Since ethanol and isopropanol are water-soluble organic solvents, exposure of the workers employed in this area may be classified as very low.

Other adhesives

Adhesives for special areas of application contain trichloroethylene or tetrachloroethylene. Depending upon the application, fast-drying adhesives may contain up to 1% n-hexane, contact adhesives up to 2% n-hexane. Foam adhesives contain dichloromethane.

Manufacture of cleaning agents and thinners

Cleaning agents

Cleaning agents consist primarily of tensides, organic solvents and water. Their composition varies widely according to the area of application. The raw materials are piped into agitators or charged manually. The agitators are frequently open. Depending upon the type and quantity of the solvents employed, the agitators may be fitted with covers and fume exhaust facilities. Following the mixing process, the cleaning agents are drawn off manually or automatically. The manufacturing process is very similar to that for paints and lacquers.

The solvent content may vary from a few percent to almost 100%. Alcohols such as isopropanol and ethanol or aliphatic hydrocarbons are frequently employed. In the past, halogenated hydrocarbons such as trichloroethylene and tetrachloroethylene were generally employed for the degreasing of metals.

Employees in manufacturing are particularly exposed during metering in of the raw materials and during discharge. The level of exposure depends heavily upon the vapour pressure and the quantity of the solvents employed. Since fume exhaust equipment was frequently not employed in the past and many tasks were performed manually, it may be assumed that exposure levels were higher (up to the mid-1980s) than under present conditions.

Thinners

Thinners are substances or mixtures of substances which are employed for the dilution of concentrated substances and for the adjustment of viscosity. They are generally liquids which vaporize easily and are added to lacquers, paints, inks and synthetic resins during manufacture or use. In most cases, they are manufactured in closed installations. Thinners consisting of mixtures of substances are occasionally manufactured in dissolvers, particularly in the lacquerindustry.

All solvents typically employed in the lacquer industry may be encountered. Turpentine oil, turpentine oil substitute or terpenes are employed for oil-based paints and for varnishes. Aromatic hydrocarbons such as toluene and xylene, and aliphatic hydrocarbons such as alcohols, esters or ketones, are employed for the dilution of synthetic resin lacquers.

Since solvents are produced in closed installations in large plants in the chemical industry, virtually no exposure of employees need generally be anticipated there. During mixing processes in the lacquer industry, exposure to solvents may particularly occur during manual tasks.

Manufacture of stripping products

For the stripping of binders which rely upon a physical drying process, such as vinyl chloride copolymers, nitrocellulose or polyacrylates, and of chemically dried or crosslinked coatings, such as oil varnishes, dried alkyd resins, crosslinked polyester coatings and crosslinked epoxy and isocyanate coatings, solvents are employed which are capable of dissolving the binders or causing them to swell strongly. In combination with light esters or ketones, dichloromethane is particularly suitable for this purpose.

The dichloromethane component in dichloromethane-based paint-strippers and façade cleaning agents used in Germany is approximately 80%. Further components added are 2 to 5% thickening agent (cellulose or cellulose derivatives), 15% alcohols such as methanol or isopropanol, which act as cosolvents, and emulsifiers, wetting agents, etc.

Extraction of fats, oils, waxes, etc.

Solvents are used to extract soluble constituents from solids. Examples of technical extraction processes include oil-seed extraction, bone extraction, the recovery of natural substances from drugs, and the extraction of sugar from sugar-beet. The solid is first mixed with the solvent in an extractor. The solvent must be able to penetrate the solid.

The resulting extraction solution is separated from the leached solid, for example by centrifuging or filtration. The extract is then distilled from the solvent.

Where liquid mixtures can be separated by distillation either only with great effort or not at all, liquid-liquid extraction is generally performed. Applications include the separation of vitamins and flavours from water-based solutions and the separation of aromatics from mineral-oil fractions. Here too, the liquid mixture and the solvent must be mixed intensively. This causes substance exchange from the liquid mixture to the solvent. The mixed liquids are then left to stand, causing the mixture to be extracted and the solvent to separate. Finally, the two phases are separated, and the solvent removed by distillation.

The requirements for the extraction agent (solvent) differ, depending upon the extraction task. A universal solvent does not exist. Substances used include hydrocarbons such as n-hexane, alcohols such as methanol and ethanol, chlorinated hydrocarbons such as tetrachloroethylene, trichloroethylene, dichloromethane, and acetone, ether or toluene. Extraction is generally performed in closed installations, either continuously or in batches. Exposure to solvents may occur during sampling or the removal of filter residues. Exposure must also be anticipated when transfer or discharge processes are performed manually.

Animal fat is recovered in flaying houses. Tetrachloroethylene in particular was used there in the past for separation of the animal fat. In the 1980s, mechanical processes gradually replaced the use of tetrachloroethylene for fat separation. The transition to mechanical processes was completed by the end of the 1980s.

The use of toluene to extract lignite produces a raw wax which can be treated further with dichloromethane to produce pure montan wax.

Synthesis of base materials

Base materials such as benzene, ethanol, methanol, styrene, toluene and xylene are synthesized exclusively in encapsulated installations. Exposure is possible only in exceptional cases, for example during sampling, repair, maintenance or discharge, or in the event of a malfunction. These substances in turn are generally base materials for the manufacture of paints, plastics, pharmaceuticals, and crop spray and pest control products.

Butanone, dichloromethane, n-heptane, n-hexane, 2-hexanone, 2-methoxyethanol, tetrachloroethylene, 1,1,1-trichloroethane and trichloroethylene are primarily employed as the solvents.

Bonding and repair of rubber conveyor belts

Trichloroethylene is an essential component of adhesives used to bond the ends of rubber conveyor belts and for their repair.

Manufacture of formulations for crop spray and pest control products

Crop spray and pest control products are generally distributed commercially in the form of solutions. Common solvents include dichloromethane, toluene and xylene. Exposure to these solvents generally occurs only during application of the crop spray and pest control products.

Refineries and fuelling areas

In refineries, crude oil is first distilled into volatile components (distillate) and distillation residue. Besides a number of other hydrocarbons, the distillate contains the aliphatic hydrocarbons n-hexane and n-heptane, and the aromatic hydrocarbons benzene, toluene, xylene and ethylbenzene. In the platforming process, the aromatic component of certain distillates is increased by the conversion of aliphatic hydrocarbons. This is performed in particular in order to obtain motor fuel components of higher quality, with the highest possible octane number.

The volatile preparations are generally stored in floating-roof tanks or fixed-roof tanks with gas shuttling, in order to keep the emissions as low as possible. The processing installations are generally fully enclosed, and the product can escape only during sampling or when the installations are opened for repair purposes. In addition, refineries are exclusively open-air installations. Hydrocarbons can therefore generally be detected in working areas only in extremely small quantities ($< 1\ mg/m^3$).

Production of motor fuels (petrol/gasoline)

Motor fuels are mixtures of suitable hydrocarbons together with various additives which deliver the engine-running properties desired by the customer. These properties are, in particular, the knocking behaviour, volatility and vapour pressure. In order for these properties to be obtained, defined quantities of various components are brought together in line blenders, and stored in low-emission final-product tanks. Such components include platformate, raffinate from aromatics manufacture (free of aromatics), pyrolysis gasoline (a by-product of the production of ethylene), propylene, straight-run gasoline in the form of MTBE (methyl tert-butyl ether, an anti-knock additive) and methanol. The hydrocarbons which occur in refineries are also constituents of motor fuels. The mixing processes take place within enclosed systems in open-air installations. As a result, the hydrocarbon concentration is below $1\ mg/m^3$.

Loading and unloading of tanker vehicles and tanker vessels, filling stations

In the refineries, motor fuels are loaded onto tanker vehicles and vessels for transport to the consumer. Two procedures are employed for reduction of the emissions:

- Top-loading of the vehicles with exhaust of the fumes which are displaced during filling

- Bottom-loading of the vehicles, with displacement of the filling vapours into an enclosed shuttle system

These low-emission filling methods have been introduced by the motor-fuel manufacturers in recent years.

3.2.2 Construction industry

Numerous tasks are encountered in the construction sector which are associated with exposure to solvents. In some of these tasks, relatively high solvent concentrations occur, not infrequently above the atmospheric limit values stated in the TRGS 900 (*Rühl and Kluger,* 1995; *Kersting et al.,* 1995).

A preliminary remark concerning n-hexane: this substance is not found in any construction chemical at concentrations exceeding 1%, if it is found at all.

Floor-laying work

The GISCODE divides primers and adhesives for flooring into four main groups: products containing dispersions, products with a high solvent component, epoxy resin products and polyurethane products.

Polyurethane and, in particular, epoxy resin products are employed for the most part in special cases, and do not therefore result in solvent exposure, at least not over a longer term. For the majority of dispersion products, too, the solvent concentrations are negligible in use. Dispersion primers and adhesives containing toluene which result in significant solvent exposure above the limit values disappeared from the market almost completely many years ago. Table 2 shows the GISCODE groups of the products with a high solvent component the use of which is associated with considerable exposure to solvent.

Table 2:
GISCODE for primers and adhesives for flooring use (extract)

Primers and adhesives for flooring use with a high solvent component	
S 1 Free of aromatics and methanol	S 4 Methanol-free
S 2 Free of toluene and methanol	S 5 Toluene-free and containing methanol
S 3 Aromatics-free	S 6 Containing toluene

Table 3 (see page 44) shows the assessment indices of the primers and adhesives for flooring use which are associated with a relevant solvent exposure in practice (BG/BGIA Recommendation governing primers and adhesives for flooring use).

S 4 and S 6 products for parquet and other wooden floors and S 5 products for other flooring are virtually irrelevant; in addition, no exposure data exist for these cases.

S 1 adhesives contain neither aromatic hydrocarbons, nor methanol. In 64 measurements taken during work by floor-layers, n-hexane was analysed 23 times (maximum assessment index 0.06) and butanone 8 times (maximum assessment index 0.11). In 62 measurements taken during parquet-

Table 3:
Assessment indices (sum of the measured value/German occupational exposure limit quotients) of the relevant primer and adhesive groups for flooring use (95th percentiles; in brackets: number of measured values)

Parquet and other wood flooring			Other floorings			
S 1	S 3	S 5	S 1	S 3	S 4	S 6
5.2 (62)	6.9 (108)	13.8 (10)	2.0 (64)	9.8 (13)	8.7 (106)	10.1 (75)

laying work, n-hexane was analysed 10 times (maximum assessment index 0.01) and butanone 6 times (maximum assessment index 0.12). Other neurotoxic substances were not analysed.

S 3 adhesives do not contain aromatic hydrocarbons. Methanol was analysed during all 13 measurements taken during flooring work: the maximum assessment index was 4.9. Methanol was analysed during 108 measurements taken during parquet laying work: the maximum assessment index was 9.1. Other neurotoxic substances were not analysed.

S 4 adhesives do not contain methanol; in some cases, however, they contain toluene, xylene, n-hexane and butanone, in one and the same product. These substances were analysed numerous times in 106 measurements taken during flooring work involving S 4 adhesive. The relatively low neurotoxic threshold values for the binary mixtures of these substances must be considered in this context. The S 4 adhesives thus exhibit a high neurotoxic potential. The flooring adhesives containing toluene have however largely disappeared from the market since the GISCODE were formulated at the beginning of the 1990s. The measurements evaluated here were all taken in the period from 1990 to 1993.

S 5 adhesives do not contain toluene; solvent exposure is dominated by the methanol component (assessment index of almost 14).

The situation for S 6 adhesives is similar to that for S 4 adhesives. High exposure to neurotoxic substances applies, particularly since butanone and toluene are in some cases both present in the same adhesive. In this case too, however, the flooring adhesives containing toluene have largely disappeared from the market since the GISCODES were formulated at the beginning of the 1990s.

Surface treatment of wood flooring

Parquet sealants and wood putties are divided by the GISCODE into water-thinnable products and those with a high solvent content. Use of the water-thinnable products is associated with low solvent exposure, if at all. The product groups with a high solvent content are listed in Table 4. The characterizations of the GISCODE groups show that these products are often free of aromatics.

During the sealing of wooden flooring with sealing varnish and wood putties with a high solvent component, very high solvent concentrations occur (Table 5, BG/BGIA Recommendation for the surface treatment of parquet and other wood floorings).

G 1 and G 2 products do not contain aromatic hydrocarbons. With the exception of ethanol, they contain no further neurotoxic substances in significant concentrations. The ethanol concentrations measured during sealing work involving these products lie below 190 mg/m³ for G 1 products, and below 950 mg/m³ for G 2 products.

G 3 products contain toluene, xylene and ethanol, among other substances.

SH 1 products contain butanone, toluene, xylene and ethanol, among other substances.

Measurements performed during contact with KH 1, KH 2 and DD 1 products reveal no relevant concentrations of neurotoxic substances.

Table 4:
GISCODE for wood flooring surface-treatment agents with a high solvent content

G 1	Primer sealants and wood putties, de-aromatized and free of low-boiling-point components
G 2	Primer sealants and wood putties, de-aromatized and containing low-boiling-point components
G 3	Primer sealants and wood putties, containing aromatics and low-boiling-point components
KH 1	Oil-based synthetic-resin sealants, de-aromatized
KH 2	Oil-based synthetic resin sealants, containing aromatics
DD 1	Polyurethane sealants, de-aromatized
DD 2	Polyurethane sealants, containing aromatics
SH 1	Acid-hardening sealants

Table 5:
Assessment indices for the sealing of parquet
(sum of the measured value/limit value quotients) of the relevant parquet sealants and wood putties (95th percentile values; in brackets: number of measured values)

Wood putties		Parquet sealants						
G 2	G 3	G 1	G2	G 3	KH 1	KH 2	DD 2	SH 1
15.4 (53)	18.9 (27)	4.0 (14)	5.0 (6)	15.5 (96)	1.0 (16)	8.7 (24)	3.7 (67)	14.4 (13)

DD 2 products contain toluene, xylene and ethanol, among other substances.

Decorating work

Provided no more than 2.5 l of undiluted alkyd resin lacquer (GISCODE M-LL-02) or primer product (GISCODE M-GP-03), in both cases low in aromatics, applied manually by brush or roller during the usual paint work on construction sites, the solvent exposure is in the order of an assessment index of less than 1 (BG/BGIA Recommendation for the use of construction lacquers).

The neurotoxic substance component in the alkyd resin lacquers used is relatively low (n-hexane < 0.1%; toluene < 0.3%; xylenes < 7.0%).

If these products are applied by spraying, or should paints and lacquers employing a physical drying process (such as chlorinated rubber paints) with a higher solvent content be used, the assessment indices may be substantially higher, depending upon the circumstances (room size, ventilation, quantities applied, etc.).

Stripping work

High exposure occurs during work involving stripping agents containing dichloromethane (description of exposure for the use of stripping agents containing dichloromethane in the construction chemicals manual, „Handbuch Bauchemikalien“, *Rühl and Kluger,* 2003).

Such stripping work is rarely performed over an entire shift and hardly ever for longer than a few days, however.

Corrosion-protection work

Alkyd, epoxy and polyurethane resin-based single and two-component products with a high solids content are generally employed for corrosion-protection work. In addition to longer-chain aliphates, these products also contain solvents in the form of aromatic hydrocarbons, glycol ethers, esters and alcohols. Neurotoxic substances are present in the form of toluene and xylene.

Measurements during corrosion-protection work yielded the results in Table 6.

Styrene in acidproof installation

Values significantly exceeding the atmospheric limit value for styrene occur during acidproof-installation work involving styrene resins (*Krommes et al.,* 1995; *Kersting et al.,* 1995).

High styrene exposure lasting several weeks may occur among acidproof installation fitters; within the acidproof installation companies, however, specialists do not exist for styrene resin coatings who perform such work throughout the year.

Styrene in polymer concrete production (see also Section II.3.2.3)

Polymer concrete consists of a mixture of mineral substances which are mixed with a

Table 6:
Measurements during corrosion-protection work

Task	Assessment index (toluene)	Assessment index (xylene)
Manual application outdoors	< 0.1	< 0.1
Manual application in enclosed rooms	< 0.1	0.3
Sprayed application outdoors	< 0.1	0.9
Sprayed application in enclosed rooms	0.19	2.1

polyester resin solution. Mixing is generally performed in an enclosed mixing machine; the mass is then transferred to moulds primarily by hand, where it then cures. Styrene exposure at these workplaces is in the order of an assessment index above 2.

Concrete remediation work, coating of industrial floors

Around 80% of the epoxy-resin products currently available for concrete remediation work and for the coating of industrial floors are solvent-free. Products of various composition (e.g. polyester resins, acrylates, polyurethane resins, epoxy resins, etc.) containing solvents may however also be used; among the solvents concerned are the neurotoxic solvents styrene, toluene and xylene. Data on the workplace concentrations arising during the use of these products cannot be stated since measurement results are not available in sufficient quantity.

Concrete release agents, forming oils

The majority of release agents employed in the construction sector contain high-boiling-point hydrocarbons and/or other film-forming constituents, but no solvents. Products employing water-based emulsions are also used in some cases. Exposure to neurotoxic solvents during the use of these two product groups can be excluded.

Where particularly high demands are placed upon the surface quality of the concrete and during prefabricated construction, release agents employing solvents may however be employed.

The use of any concrete release agent is generally only brief. The period of use typically extends from a few minutes to around an hour each day.

Building cleaning work

Solvents may be found in the majority of cleaning agents (BG Regulation for the use of cleaning and care agents). Solvent concentrations in the product as supplied vary

widely, up to a maximum of 30%. Since the products are generally strongly diluted for use, the solution in the form used has a substantially lower solvent component (glass cleaners ready for use have a solvent content of 1%, the concentrate as supplied 25%). Essential solvents here are alcohols such as ethanol, isopropanol, and glycol ethers such as ethylene glycol monoethyl ether and ethylene glycol monobutyl ether. The workplace concentrations are substantially below the limit values. In addition, building cleaning work is not generally performed for eight hours.

Wood- and stone-care products contain higher proportions of solvents. Essentially, they contain hydrocarbon mixtures of up to 80%. Workplace concentration data are not available. Since such work is carried out with the undiluted product over large areas, limit values may be exceeded.

Work involving products for the removal of graffiti is associated with a similar dichloromethane exposure to that for the stripping work described.

Industrial cleaning

The solvent exposure may differ widely in this case. The level of exposure at the workplace depends not only upon the cleaning agent used, but also upon the machines and surfaces to be cleaned and the solvents which may already be present there.

Door surfacing

The surfacing of room and cupboard doors with plastic film involves the use of adhesives containing toluene, among other substances.

Remediation work at filling stations

Work performed during the remediation of filling stations, i.e. the opening of the surfacing, uncovering of pipes and tanks, excavation of contaminated soil and loading of it for transport, may result in both aliphatic and aromatic hydrocarbons being released which have entered the soil together with the fuel as a result of accidents, leaks, or drip loss.

In addition to the substances relevant to occupational disease No. 1317 (n-hexane, benzene, toluene and xylene), cyclohexane, ethylbenzene, aromatics-rich hydrocarbon mixtures, cumene and trimethylbenzenes are encountered. Owing to frequent alternation of tasks throughout the entire construction activity, direct correlation between an atmospheric limit value and a shift is not always possible. Where reference is made below to the atmospheric limit value, it is not therefore automatically assumed to apply to a shift. The measured values are considered in the following three areas of work: earth-moving work during filling station remediation, tank cleaning, and soil remediation installations.

- Earthmoving work during filling station remediation:

Table 7 provides an overview of the measured values.

- Tank cleaning:
  In some cases, the benzene concentrations exceeded 30 mg/m³; 5% of the measured values exceeded 45 mg/m³; maximum values of 73 mg/m³ were measured. All values for toluene lay below 190 mg/m³, for xylene below 440 mg/m³ and for n-hexane below 180 mg/m³.

- Reception and processing in biological soil-remediation installations of soil and filling-station material contaminated with mineral oil hydrocarbons:
  All values measured for benzene lay below 0.07 and 0.8 mg/m³ (soils contaminated with mineral oil hydrocarbons and filling-station material respectively); for n-hexane, all values were below 0.2 and 8.2, for toluene below 1.3 and 19.5, and for xylene below 1.6 and 42.6 mg/m³ respectively.

3.2.3 Minerals and earths industry

Asphalt and construction-material laboratories (trichloroethylene)

Samples of the manufactured mixed material are analysed in asphalt laboratories for their composition in accordance with the specification. For this purpose, the binder, bitumen, is extracted from the asphalt sample, i.e. it is leached out until the mineral substances and the binder have been completely separated. The solvent is then distilled back from the bitumen/solvent mixture. The cold and hot extraction methods are employed.

Cold extraction refers to dissolving out of the binder by means of cold or heated solvent. Extraction may be performed manually in an open process in a laboratory fume cupboard, or in a closed system with automatic extraction apparatus.

Table 7:
Earthmoving work during filling station remediation (measurements)

Substance	Mean value in mg/m³	Maximum value in mg/m³
Benzene	0.08	3.02
Toluene	0.49	14.96
Xylene	0.76	12.78

Hot extraction is the dissolving out of the binder by means of a solvent which is made to boil and condense cyclically in special extraction apparatus.

Before further analyses are performed, the minerals are dried in a drying oven.

Solvent exposure occurs primarily by open contact with trichloroethylene during filling/emptying of the extraction apparatus, during extraction when performed manually, and during charging/emptying of the drying oven. The level of exposure also varies according to whether work is performed within or outside a fume cupboard. If enclosed extraction apparatus is employed, it is generally used within an enclosed fume cupboard. Extraction in enclosed apparatus is increasingly becoming the norm, and represents the state of the art (*Kolmsee,* 1990).

Until well into the 1980s, asphalt was extracted manually in some cases in small field laboratories at the mixing installations, by means of heated trichloroethylene in an open mixing vat standing on a heater plate. An improper procedure leading to high solvent exposure cannot be ruled out under these conditions.

The former institution for statutory accident insurance and prevention in the civil engineering sector modelled the relevant exposure conditions and performed personal measurements, with the following results: During the use of preheated trichloroethylene in the open extraction of asphalt, up to 485 mg/m³ and 2,958 mg/m³ trichloroethylene were measured in the breathing air for two different room dimensions (11 · 5 · 3 m³ and 3.5 · 1.6 · 2.5 m³ respectively).

The manual method of extraction in an open mixing vat has been abolished almost entirely; it is now performed, if at all, only in a laboratory fume cupboard. The evaluation of 25 measurement results from 12 laboratories obtained in the period from 1997 to 2001 reveals a range of values from 7 to 424 mg/m³, with a 90th percentile value of 353.5 mg/m³.

During the use of trichloroethylene to clean machine parts soiled with bitumen, up to 775 mg/m³ was measured during cleaning by wiping, brushing and scrubbing of the floor in closed halls, and up to 5,380 mg/m³ during cleaning by spraying of trichloroethylene onto the floor in closed halls.

Polymer concrete production (styrene) (see also Section II.3.2.3)

Depending upon the application, polymer concrete consists of a mixture of mineral substances (gravel, sand, grit, possibly crushed marble, fibrous substances) which are mixed with a polyester resin solution. Mixing is generally performed in a closed mixing machine. The material is normally distributed manually into moulds, where it cures.

Solvent exposure occurs primarily during transfer of the polymer concrete mixture into the moulds, since adequate ventilation

methods are difficult to implement here. The mixing installation is generally equipped with a fume exhaust facility.

Stoneworking (styrene)

Styrene-based fillers and stone cements are employed in conjunction with hand tools to correct defects in workpieces. Adhesives containing styrene are employed for repairs to workpieces or for the lamination of workpieces in sheet form.

Solvent exposure occurs during flashing off of the workpieces following the work.

Stoneworking (trichloroethylene)

Stone polishes employed for surface finishing are applied manually or by machine to the surface to be worked, and distributed manually or by machine. The polishes and stone care products may consist of waxes dissolved in trichloroethylene.

3.2.4 Timber industry

Bonding work involving contact adhesives

Contact adhesives are employed for a range of purposes in the timber industry. They are used by manufacturers of upholstered furniture for example to bond coverings to wooden frames. These contact or polychloroprene adhesives are applied over very large areas. Where the wood is very absorbent, a primer coat of dilute adhesive is often required.

Depending upon the viscosity of the adhesives, they may be applied by means of brushes, spreaders, pneumatic spray guns or rollers.

Contact adhesives used in the timber industry continue to have a very high component of homologues of benzene and of esters. In addition, contact adhesives containing chlorinated hydrocarbons (generally dichloromethane) are still in use in some areas (such as mattress manufacture).

Application of lacquer by curtain coating, roller coating, immersion coating and flow coating

Curtain and roller coating are generally employed in the furniture industry. Immersion coating and flow coating are employed in the manufacture of construction elements (such as windows). During curtain and roller coating, the workpiece surface may be heated to a temperature of 40 to 80 °C prior to actual application of the lacquer. This prevents air inclusions from forming in the lacquer film. Preheating is achieved by the application of hot air or infrared radiation for approximately one minute.

Curtain coating machines can be used to apply lacquer to flat items without complex geometry, provided their surface can be covered by a single curtain of lacquer. Such machines are equipped with a coating head which extends over the entire width of the machine and has an adjustable-width slit on the underside. The lacquer is ejected through the slit in the coating head in the

form of a fine, continuous curtain, and falls onto the surface of the workpiece. The workpiece passes beneath the coating head on a conveyor belt. Lacquer which does not fall onto the workplace flows back via a trough into a reservoir. A pump transports the lacquer from this reservoir back into the coating head. Lacquers employed in curtain coating machines generally have a high solvent content; they contain high proportions of esters and homologues of benzene, and also smaller quantities of alcohols.

The **roller coating process** is employed for the application of both small and relatively large quantities of lacquer. This process is employed when the pore structure of a wood surface is to be retained. The quantity of lacquer applied can be varied infinitely and may lie between 5 and over 200 g/m² for a single pass. Where larger quantities are to be applied, two coating rollers arranged one after the other are used, or two separate roller coating machines with a brief drying interval between them. Two rubberized cylindrical rollers are situated above the workpiece. The distance between the rollers is infinitely variable. The lacquer is poured between the two rollers which differ in size, and is then distributed evenly over their entire surfaces. The smaller roller is the metering roller; it is used to adjust the quantity of lacquer applied. The larger roller is the spreader roller; this roller has the function of applying the lacquer to the workpieces as they pass beneath it. The spreader roller may be smooth, or its surface may feature small wells. As with the immersion coating method, lacquers with a high solvent component are generally still in use in the roller coating method. The proportion of low-solvent and solvent-free lacquer systems has however recently been on the increase.

In the **immersion coating process,** the workpiece is immersed into the coating agent manually or by means of suitable handling equipment and then removed again. The excess coating agent must run off the surface by gravity action. In this process, the speed at which the immersed workpiece is withdrawn again from the immersion tank, the run-off speed of the immersion coating lacquer from the workpiece and the rate at which the lacquer dries must be matched to each other. The workpieces must be free of pockets or depressions in which lacquer could collect. The immersion method is employed for the lacquering of smaller, smooth workpieces (such as wooden stamps) and workpieces for which the lacquer layer is not required to have a high-quality appearance. This method is the simplest and cheapest lacquering method. Owing to the requirement for drying to be as fast as possible, lacquers containing solvents (homologues of benzene, alcohols, esters) are employed almost universally.

The **flow coating process** is similar to immersion coating. In flow coating, lacquer is poured over the workpiece; the excess lacquer must run off of its own accord. As in the immersion process, workpieces must be free of pockets or depressions in which lacquer could collect. Lacquers for the flow coating process have a solvent content even higher than that of immersion

coating lacquers. The solvents employed have a major influence upon the lacquering process. Flow coating can be performed only in automatic installations. These installations adjust the lacquer viscosity and temperature and the transport speed precisely to each other.

In the timber industry, both lacquering and staining are performed by means of curtain and roller coating installations. The proportion of solvent stain to water-based stain in use is approximately 2:1. The roller and curtain coating installations are almost all equipped with fume exhaust facilities.

Spray stands

On manual spray stands, pneumatic and airless spray methods are generally employed.

Pneumatic spraying is the most common spraying method. It requires dry compressed air, since water droplets in the lacquer may cause blisters, craters or holes in the surface. The compressed air is fed to the spray gun through a hose. Depending upon the product being sprayed, the operating pressure lies between 1.5 and 7 bar. High-viscosity and cold lacquers require higher pressures than do their low-viscosity or warm counterparts. The compressed-air consumption depends primarily upon the nozzle diameter and the pneumatic pressure. With a nozzle diameter of 1 mm and a pneumatic pressure of 2 bar, for example, 9 m^3 of air is consumed in an hour. The most important components of the spray gun are the air valve, the fluid nozzle, the air nozzle and the fluid cup. The sprayed fluid is transported from a fluid cup or tank to the fluid nozzle. The term gravity-fed cup refers to a fluid cup located above the material nozzle; suction-fed describes a fluid cup located beneath the fluid nozzle. Where the lacquer consumption is high, the sprayed fluid is transported pneumatically or by means of a circulation pump from a lacquer reservoir, via a hose, to the fluid nozzle. The fluid nozzle has a diameter of between 0.8 and 2.5 mm. Different fluid nozzles can be fitted, according to the viscosity of the sprayed fluid.

High-pressure spraying has several advantages. The atomization of the lacquer can be adjusted on the spray unit, assuring a clean spray pattern. The process can be used for both high and low-viscosity coating fluids. Use of a suitably small fluid nozzle and a higher pneumatic pressure permits patining with lacquer or fogging with stain. During patining, colour variations are attained artificially by the application of stain or lacquer as appropriate.

A particular disadvantage of high-pressure spraying is the strong formation of lacquer fog. A properly functioning exhaust facility must therefore always be in place.

As its name implies, **airless spraying** involves spraying without compressed air. The sprayed fluid is supplied via a material hose and forced through a small nozzle aperture at a pressure of 125 to 250 bar, causing it to be atomized. A pure lacquer mist is produced. The essential components of an airless installation are the fluid pump, the

high-pressure fluid hose, and the spray gun. The fluid pump has the function of drawing the sprayed fluid from a lacquer reservoir and compressing it. The fluid pump is driven either electrically or pneumatically. The compressed sprayed fluid is transported through a high-pressure hose, several metres in length and resistant to chemical attack, to a spray gun manufactured from high-grade steel. Owing to the abrasive action of the coating material, the nozzle is manufactured from cemented carbide. The nozzle has a diameter of between 0.3 and 0.5 mm.

Heating of the sprayed material to approximately 90 °C prior to its compression enables the spray pressure and material loss to be reduced considerably, and the life of the spray nozzle to be extended. Since spraying is airless, blisters, fogging and craters are not formed in the surface coat. Lacquer consumption is lower than for pneumatic spraying. No air eddies are created, and spray air is not reflected back from the surface being sprayed. The airless method can be used to coat large areas substantially more quickly than is possible using a pneumatic spray gun. It cannot however be used for patining, fogging or staining.

Trade businesses performing frequent coating work are equipped with a separate spray area with dry or sprinkler spray walls. The air is supplied via filter mats fitted into the ceiling. The exhaust air is drawn off either above the spray stands or, in larger coating areas, through floor grates fitted with special filter mats.

For larger items of furniture, spray stands with ventilation and exhaust facilities are often integrated adjacent to the coating lines. At these spray stands, edges for example are then sprayed or minor defects corrected. Virtually all forms of lacquers, stains and thinners are employed on the spray stands. The focus however lies upon the use of nitro and Desmodur®/ Desmophen® (PUR) lacquers.

Cleaning in this context refers to removal of the non-greasy or grease-free dirt components or the elimination of all forms of dirt. Degreasing refers to the removal of greasy and oily impurities such as lubricating oils, corrosion-protection oils, etc.

Examples of cleaning work in the timber industry include:

- The cleaning of carcasses manufactured from plastic-faced particle board prior to packaging
- The cleaning of spray guns or roller coating installations in the surface-finishing department
- The cleaning of laminating tools in polyester processing
- The removal of adhesive residues, for example during the use of contact or pressure-sensitive adhesives
- The cleaning of the mixing head during the use of two-pack polyurethane casting resins or rigid foams

The following factors are decisive for selection of a suitable cleaning agent:

- The (surface) material of the items to be cleaned
- The type and composition of the dirt
- The quality requirements for cleaning
- Work and environmental aspects

The following organic solvents and solvent mixtures are employed for cleaning:

Organic solvents

In industrial use, pure discrete components such as alcohols (e.g. isopropanol), esters (e.g. ethyl acetate or butyl acetate) or ketones (e.g. acetone) are occasionally employed. The use of chlorinated hydrocarbons such as trichloroethylene, tetrachloroethylene or dichloromethane has now virtually ceased in the timber industry. A clear exception is the cleaning of the mixing head during the use of two-pack polyurethane casting resins (foams), for which dichloromethane is generally employed.

Solvent mixtures

The following groups are most frequently employed in this context:

- Cellulose thinners
  These are generally solvents and thinners for nitrocellulose lacquers. They contain aliphatic (including hexane, heptane, octane) and aromatic (including toluene, xylene, ethylbenzene) hydrocarbons, ketones (including butanone, hexanone, acetone), esters (including ethyl acetate, butyl acetate) and glycol ethers (including ethylene glycol monoethyl ether, butoxyethanol).
- Solvent cleansers
  Solvent cleansers are products based upon de-aromatized hydrocarbon mixtures. Solvent cleansing mixtures are also distributed as special boiling-point spirits, white spirit or dry-cleaning spirit.

3.2.5 The use of reaction resins containing styrene for the manufacture of plastic components

During the use of reaction resins containing styrene (UP resins: unsaturated polyester resins; VE resins: vinyl ester resins) in the manufacture of plastics (GRP), styrene is employed as a solvent and as a reactant. The following applications and uses are found in the metals and chemical industries:

- Open use of large areas of resin; the use of glassfibre mats and UP resin to produce GRP mouldings such as shrouds, commercial vehicle and motor caravan roofs, boats' hulls, swimming pools, galvanizing tanks (acidproof construction), and GRP vessels of all kinds. Manual laminating methods and machine methods are employed, as are spray processes.
- Open use of large areas of resin for the manufacture of rotationally symmetrical

hollow bodies (such as GRP pipes). Winding and lamination are performed on a special winding bench. The reinforcing body (textile tape, thread) is wound onto the mould core with simultaneous addition of a polyester resin mixture. The workpiece produced in this way is then stored temporarily together with the mould to allow it to cure. The cured blank is demoulded and then machined. During the open working of large areas of resin, exposure to solvents exists during application of the reinforcing body with the addition of the polyester resin mixture, and in the entire working areas of the employees, since the finished workpieces are either stored in these areas temporarily, or pass through them during transport to the intermediate store, during which they give off vapours.

- Casting methods (including making-up and the cleaning of mixing vessels), casting of rods (for the production of decorative fittings by the subsequent turning of GRP rods) and the casting of GRP models
- Vehicle bodywork production: levelling out, smoothing and polishing during repairs to passenger and goods vehicles, in boat construction (the use of UP resins with hardener, e.g. benzoyl peroxide)
- The use of polystyrene on injection moulding, extrusion and deep-drawing installations, for example for the manufacture of refuse bins
- Hot-cutting of polystyrene sheets and mouldings
- Use of synthetic resin-based paints and UP resin-based dispersions

4 Substance dossiers

The dossiers for specific hazardous substances list information concerning the following areas:

- Identification criteria (synonyms, CAS number)
- Selected physical and chemical data (boiling point, vapour pressure)
- Chronology of the limit values
- Uptake routes
- Use/areas of application (past and present areas of application, substitutes, products, working methods)
- Exposure (evaluation results of the MEGA database)

Preliminary remarks for description of the uptake routes:

The information contained in the literature on the uptake rates for one and the same substance via the various uptake routes differs, in some cases widely. This applies in particular to dermal absorption, for the measurement of which very different methods are employed by the individual research groups (animal/human skin, in vivo/in vitro, etc.) (ECETOC, 1993). Considerable variation is also known to exist between individuals in

the human population. Finally, the different skin regions of a single person may vary by two powers of ten in their dermal absorption of a given substance (*Emmett,* 1992). The figures presented in the section below can therefore serve only as a general guide.

Certain solvents (carriers) facilitate the penetration of the skin by accompanying substances. It must be noted that all organic solvents degrease the skin and that they therefore not only prepare the way for skin diseases, but may also influence the uptake rates of hazardous substances.

For a proper understanding of the results of evaluation from the MEGA database, certain points must be considered:

The hazardous-substance-specific concentrations of neurotoxic solvents listed in the tables are based upon measurement data obtained in the context of the BGMG[1] – Measurement system for exposure assessment and archived in the MEGA documentation (BGIA, 1999). They correspond to the current state of knowledge, and are extended and updated in consideration of more recent findings.

Relevant areas of work and working methods have been selected and evaluated statistically from a total of over 150,000 data records from more than 18,000 plants. The data material has been differentiated in accordance with the structure of the index of plant types/areas of work (BGIA, 2003). In the present evaluation, exposure measurements in the workplace atmosphere were considered only if they satisfied the following conditions:

- Measurement was performed by means of the sampling system (sampling method and sample carrier) valid within the BGMG at the time of measurement.
- Analysis was performed by means of the analysis system valid within the BGMG at the time of analysis.
- Only measured values with a duration of exposure exceeding one hour were considered. Measurement values yielding reduced exposure owing to the process were not extrapolated to the length of the shift.

Where different levels of exposure were evident, the evaluation specific to the area of work differentiated between the data periods (1985 to 1991, 1992 to 1997 and 1998 to 2002).

Bodies of data were formed and analysed statistically only when more than nine measured values in each case were available from at least five plants and two institutions for statutory accident insurance and prevention, in order to exclude re-anonymization.

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[1] since 1st January 2010: MGU – Messsystem Gefährdungsermittlung der Unfallversicherungsträger

The 50th percentile and 90th percentile values were employed for the concentrations stated in the tables, irrespective of the distribution type of the body of measured values under consideration. These values mean that 50% and 90% respectively of all available concentration values were below the threshold indicated, the remaining 50%/10% above it (*Jambu*, 1992).

4.1 Benzene

Identification criteria
(BGIA, 2006)

Synonyms:
Benzol, carbon oil, coal naphtha, cyclohexatriene, phenyl hydride

CAS No.: 71-43-2

Selected physical and chemical data
(BGIA, 2006)

Boiling point: 80.1 °C (1,013 hPa)

Vapour pressure:
99.7 hPa (20 °C)
157.8 hPa (30 °C)
358.2 hPa (50 °C)

Chronology of the German occupational exposure limit
(BGIA, 2006; BIA, 11/1994; DFG, 1958 to 2003)

Up to the early 1970s, benzene was added to lacquers and thinners as a solvent in order to improve application. Since benzene was however an important initial product for chemical synthesis and was therefore in short supply on the market, it was frequently substituted for by aromatics obtained from higher-boiling-point fractions of tar distillation, i.e. solvent naphtha types. Owing to their use, these substances were referred to as "industrial grade benzene" or "heavy benzene", despite not actually containing benzene.

Industrial grade benzene 1:
70% xylene, 25% cumene, 5% toluene

Industrial grade benzene 2:
60% cumene, 35% xylene,
5% naphthalene oil

German occupational exposure limits:

1958 to 1970
Maximum workplace concentration value (MAK value) 80 mg/m³ (25 ml/m³)

1970
MAK value 32 mg/m³ (10 ml/m³)

From 1971 onwards
Suspension of the MAK value owing to demonstration of carcinogenic action; restriction upon use owing to introduction of a 1% classification limit

From 1976
Ban on the use of benzene, benzene content in solvents and thinners limited to 1%

1976
Introduction of the TRK technical exposure limit of 10 ml/m³ (TRK = Technische Richtkonzentration)

1977
TRK value 26 mg/m³ (8 ml/m³)

1985
TRK value 16 mg/m³ (5 ml/m³)

From 1992 onwards
Benzene content in solvents limited to 0.1%

Table 8:
EKA values for Benzene (as of 2002); EKA = Expositionsäquivalente für krebserzeugende Arbeitsstoffe, exposure equivalents for carcinogenic substances)

Benzene concentration in the atmosphere		Benzene measured in whole blood	S-Phenyl-mercapturic acid measured in urine	trans-trans-Muconic acid measured in urine
in ml/m³	in mg/m³	in µg/l	in mg/g creatinine	in mg/l
0.3	1.0	0.9	0.010	–
0.6	2.0	2.4	0.025	1.6
0.9	3.0	4.4	0.040	–
1.0	3.3	5	0.045	2
2	6.5	14	0.090	3
4	13	38	0.180	5
6	19.5	-	0.270	7

From 1993
TRK limit value splitting:
TRK value: 8.0 mg/m³ (2.5 ml/m³)
– In coking plants, in fuelling areas in the mineral oil industry, during the repair and maintenance of components carrying petrol/gasoline or benzene

TRK value: 3.2 mg/m³ (1.0 ml/m³)
– Elsewhere

1997
Decision by the European Commission to introduce a harmonized lower workplace limit value of 3.2 mg/m³ (1.0 ml/m³) following a transitional period of three years

2003
TRK value: 3.25 mg/m³ (1 ml/m³)

2005
EU workplace limit value of
3.25 mg/m³ (1 ml/m³)

As a carcinogenic agent, benzene has still not been assigned a BAT value (BAT = Biologische Arbeitsstofftoleranz, biological tolerance), since no biological value could be stated which could be regarded as safe. In the light of this, relationships have been formulated since 1984 between the benzene concentration in the workplace atmosphere and the substance/metabolite concentration in the biological material (EKA, exposure equivalents for carcinogenic substances). From these values, the internal exposure can be determined which would result from exclusively respiratory uptake of the substance.

Uptake routes

The primary uptake route for benzene is via the respiratory tract. When inhaled, benzene absorption following attainment of the blood/air equilibrium is 40 to 50%

(BUA, 1988; *Greim and Lehnert,* 1994).

If the skin is wetted with benzene or benzene solutions which are free to evaporate, less than 1% of the applied benzene enters the body (*Franz,* 1984; *Maibach and Anjo,* 1981; *Susten et al.,* 1985; *Greim,* 1988). Under occlusive conditions (immersion in liquid benzene for a longer period), the rate of penetration through human skin lies between 0.2 and 1.8 mg · cm^{-2} · h^{-1} (*Hanke et al.,* 1961; *Blank and McAuliffe,* 1985). For petrol/gasoline solutions with a benzene component of 5%, an uptake rate of 0.06 mg · cm^{-2} · h^{-1} is stated (*Blank and McAuliffe,* 1985).

Dermal absorption of benzene from the gas phase is negligible compared to the respiratory uptake (*Hanke et al.,* 1961; *Blank and McAuliffe,* 1985; *Tsuruta,* 1989).

Applications/areas of use
(BGIA, 2006; BIA, 11/1994; DFG, 1958 to 2003; *Pflaumbaum et al.,* 1993; MWV, 1/1997; *Boehncke et al.,* 1997)

- Coking plants and secondary recovery plants
- Refineries and fuelling areas
- Formation of benzene during chemical processes
- Transfer of petrol/gasoline and benzene (loading and unloading of tanker vehicles and tanker vessels)
- Cleaning, maintenance and repair of tanks and tank fittings (raw benzene, petrol/gasoline)
- Foundries: thermal disintegration during the casting of synthetic resin-bonded moulds (furan and phenolic resins) results in the production of benzene (casting line, demoulding)
- Use as a basic material for synthesis in the chemical industry (transfer, operation of the machine, maintenance, repair, inspection patrols)
- Vehicle construction, automotive workshops, filling stations:
  Inspection, maintenance, repair, servicing of vehicles (passenger cars, goods vehicles, construction machinery); work on lines carrying fuel, replacement of fuel gauges and fuel filters, engine test benches, repair of filling pumps; in the past: adjustment of carburettors, removal of carburettors, use of petrol/gasoline for the cleaning of vehicle parts and engine cleaning, fuelling by filling-pump attendants. Dermal and respiratory exposure to petrol/gasoline containing benzene was greater

Benzene in petrol/gasoline:

In the mid-1950s, the benzene content of petrol/gasoline was approximately 15% by volume (ARAL). In subsequent years, the benzene content decreased, and was approximately 10% by volume in the late 1970s (BP). Since 1985, the oil industry has closely

observed the benzene content in petrol and gasoline on the market, in order to dispel suspicion that the removal of lead has been compensated for by the addition of benzene. According to these studies, the average benzene content fell between 1985 and 1996 from 2.5 to 1.8% by volume.

Benzene content of special boiling-point gasoline in the German Democratic Republic (GDR):

The actual situation in the GDR regarding the benzene content of formulations was highly diverse. Precise figures can however be stated for the special boiling-point gasolines which were produced by superfractionation of straight-run gasoline B (Leuna) (Table 9).

Benzene in lacquers and thinners:

Sporadic studies conducted by the BGIA in the 1970s and representative inspections by the BAuA in the 1980s revealed that benzene had virtually ceased to be relevant as a solvent in lacquers and thinners.

Benzene contents measured as impurities in lacquers and solvents were › 0.5% until around 1951, ‹ 0.5% until around 1969, and approximately ‹ 0.1% until 1981. Vessels specially labelled “Benzene” or “Contains benzene” were a special case. Substantially higher benzene concentrations than the percentages stated above were to be assumed for these products. In 1954, the labelling threshold (regulation on solvents)

Table 9:
Benzene content of special boiling-point gasolines in the German Democratic Republic according to GL 6428, “Flüssige Brennstoffe (Vergaserkraftstoffe)”, 1 January 1973 onwards

Type	Benzene content in %	Area of application
SB 30/85	2.7	Plastics industry, footwear chemicals, base material for medical-grade benzine
Medical-grade benzine	3.8	Medical purposes
SB 60/85	7.6	Solvents in the oil and margarine industry
SB 80/100	1.7	Solvents and extraction agents for the rubber industry and for dry-cleaning
SB 80/120	1.3	Catalytic petrol/gasoline (gas fires)
SB 100/140	Traces	Solvents for the rubber, lacquer, asphalt and tar-products industries
SB 135/200	Traces	Solvents in the paints and lacquers industry

for benzene was 5%, and in 1982 still 1%. The products thus labelled had benzene contents above these percentages.

Since 1981, the benzene content of the solvents used for lacquer formulations has generally been below 0.01%, and below 0.001% in the case of "special boiling products" (SBPs).

Table 10:
MEGA – Benzene, DL = analytical detection limit;
‹ DL: No percentile concentration is calculated because there are more values below the analytical detection limit (DL) then would be represented by the percentage of this percentile

Group of areas of work	Number of measurement data	Number of plants	50th percentile value in mg/m³	90th percentile value in mg/m³
Period to which data refer: 1985 to 1991				
Cold/hot moulding of plastics	82	40	‹ DL *	‹ DL *
Transfer/filling up of petrol/gasoline	31	17	‹ DL *	3.0
Repair/maintenance/test bench	153	43	‹ DL *	13.0[1)]
Thermal processing methods	67	45	‹ DL *	‹ DL *
Mechanical processing methods	34	24	‹ DL *	‹ DL *
Bonding/coating/lacquer application	118	64	‹ DL *	‹ DL *
Cleaning (excluding cleaning of buildings)	11	9	‹ DL *	‹ DL *
Laboratories	14	7	‹ DL *	4.6
Foundry (with existing moulding process)	99	44	‹ DL *	5.0

Table 10:
(Continuation)

Group of areas of work	Number of measure-ment data	Number of plants	50th percentile value in mg/m³	90th percentile value in mg/m³
Period to which data refer: 1992 to 1997				
Cold/hot moulding of plastics	69	41	‹ DL **	‹ DL **
Transfer/filling up of petrol/gasoline	54	27	‹ DL **	3.7
Repair/maintenance/test bench	344	102	‹ DL **	3.3
Thermal processing methods	159	84	‹ DL **	‹ DL **
Mechanical processing methods	73	35	‹ DL **	‹ DL **
Bonding/coating/lacquer application	133	73	‹ DL **	‹ DL **
Cleaning (excluding cleaning of buildings)	13	8	‹ DL **	‹ DL **
Cleaning of/in tanks and vessels (raw benzene, motor fuels, heating oil)	61	15	2.1	34.0
Laboratories	25	14	‹ DL **	‹ DL **
Foundry (with existing moulding process)	69	29	‹ DL **	4.1
Period to which data refer: 1998 to 2002				
Cold/hot moulding of plastics	28	16	‹ DL **	‹ DL **
Transfer/filling up of petrol/gasoline	27	15	‹ DL **	3.4
Repair/maintenance/test bench	114	36	‹ DL **	0.7
Thermal processing methods	54	36	‹ DL **	‹ DL **
Mechanical processing methods	16	12	‹ DL **	‹ DL **
Bonding/coating/lacquer application	46	26	‹ DL **	‹ DL **
Cleaning (excluding cleaning of buildings)	19	15	‹ DL **	‹ DL **
Cleaning of/in tanks and vessels (raw benzene, motor fuels, heating oil)	100	7	‹ DL **	2.2
Laboratories	14	8	‹ DL **	0.8
Foundry (with existing moulding process)	43	25	‹ DL **	1.2

* Detection limit around 1.0 mg/m³
** Detection limit around 0.1 mg/m³
1) Repair of filling pumps

Note that exposure data in this table for areas of work evaluated **across sectors** cannot necessarily be applied in all cases to areas of work and tasks in **specific sectors.**

4.2 Butanone

Identification criteria
(BGIA, 2006)

Synonyms:
Methyl ethyl ketone, ethyl methyl ketone, MEK, 2-butanone

CAS No.: 78-93-3

Selected physical and chemical data
(BGIA, 2006)

Boiling point: 79.57 °C (1,013 hPa)

Vapour pressure:
105 hPa (20 °C)
167 hPa (30 °C)
370 hPa (50 °C)

Chronology of the German occupational exposure limit
(BGIA, 2006; DFG, 1958 to 2003)

1958
Introduction of the MAK value of 740 mg/m³ (250 ml/m³)

1960
Reduction of the MAK value to 590 mg/m³ (200 ml/m³)

2000
Adjustment of the MAK value to 600 mg/m³ (200 ml/m³)

Uptake routes

The primary uptake route for butanone is the respiratory tract. Approximately 41 to 56% of the inhaled butanone is absorbed in the lung (BGIA, 2006).

Data exist for relatively good absorption via the digestive tract and the skin. Studies performed on test subjects (application of butanone to an area of approximately 90 cm² on the forearms) revealed that damp skin is penetrated more easily than dry skin. Absorption rates for butanone in the region of 0.3 to 0.6 mg · cm^{-2} · h^{-1} were calculated from the test results (BGIA, 2006).

Use/areas of application
(BGIA, 2006; *Henschler,* 1996; *Ullmann,* 1983)

After acetone, butanone is the ketone of greatest technical importance:

- Solvent properties for lacquers, plastics, adhesives, natural and synthetic resins in many branches of industry
- Manufacture of artificial leather
- Manufacture of transparent paper
- Manufacture of printing inks (flexography and rotogravure package printing)
- Cleaning and degreasing of metal surfaces (no longer used for this purpose)

- Extraction of fats, oils, waxes and natural resins
- Deparaffinization of mineral oils

Exposure values

Table 11:
MEGA – Butanone

Group of areas of work	Number of measure-ment data	Number of plants	50th percentile value in mg/m³	90th percentile value in mg/m³
Period to which data refer: 1985 to 1997				
Production of formulations	434	114	10	140
Cleaning, degreasing of metal, wood and plastic items	374	181	5	152
Bonding	1,009	337	< DL	101
Brush application, hand-painting	191	84	6	113
Spray-painting	1,754	778	< DL	24
Surface coating, mechanical, by machine (laminating, impregnating, immersion coating, curtain coating, printing)	1,117	423	< DL	120
Period to which data refer: 1998 to 2002				
Production of formulations	63	20	16	218
Cleaning, degreasing of metal, wood and plastic items	78	55	< DL	181
Bonding	209	97	13	58
Brush application, hand-painting	38	23	< DL	146
Spray-painting	175	133	< DL	< DL
Surface coating, mechanical, by machine (laminating, impregnating, immersion coating, curtain coating, printing)	173	94	< DL	102

Note that exposure data in this table for areas of work evaluated **across sectors** cannot necessarily be applied in all cases to areas of work and tasks in **specific sectors.**

4.3 Dichloromethane

Identification criteria
(BGIA, 2006)

Synonyms:
Methylene dichloride

CAS No.: 75-09-2

Selected physical and chemical data
(BGIA, 2006)

Boiling point: 40.67 °C (1,013 hPa)

Vapour pressure:
460.9 hPa (20 °C)
689.4 hPa (30 °C)
1,500.0 hPa (50 °C)

Chronology of the German occupational exposure limit
(BGIA, 2006; DFG, 1958 to 2003)

1958
Introduction of a MAK value of 1,750 mg/m³ (500 ml/m³)

1975
Reduction of the MAK value to 720 mg/m³ (200 ml/m³)

1982
Reduction of the MAK value to 360 mg/m³ (100 ml/m³)

1986
Classification as a III-B substance

1996
Classification as carcinogenic K3 (substances which give cause for concern owing to a possible carcinogenic effect in humans but for which sufficient information does not yet exist for a satisfactory assessment. Indicators exist from relevant animal tests, but are not sufficient for classification of the substance as more hazardous).

2000
Adjustment of the MAK value to 350 mg/m³ (100 ml/m³)

2005
Suspension of the limit value

2007
260 mg/m³
German occupational exposure limit (TRGS 900)

1982
Specification of a BAT value for dichloromethane:
5% CO haemoglobin, measured in the blood
1 mg/l dichloromethane, measured in the blood

1989
Additional BAT value for dichloromethane:
1 mg/l dichloromethane, measured in the blood

Uptake routes

Dichloromethane is absorbed primarily via the respiratory tract. Under exposure in the range between 180 and 720 mg/m³, an ini-

tial rapid increase in the dichloromethane concentration in the blood is followed within approximately 4 hours by stabilization of the level. Under conditions of physical inactivity, approximately 70 to 75% of the inhaled dose is absorbed. Under physical exertion, the retained proportion of the dose drops comparatively; the absorbed quantity increases however, owing to the elevated ventilation rate. The uptake of dichloromethane is also dependent upon the body weight/fat content: adipose persons retain up to 30% more dichloromethane than do slim individuals (BGIA, 2006).

Dichloromethane is also absorbed through intact skin, but to only a small degree compared to the respiratory uptake. Following immersion of the thumb in liquid dichloromethane for 30 minutes, a test on a subject yielded a dichloromethane content in the exhaled air of 3.1 ml/m³ (10.9 mg/m³). This value fell within 2 hours to 0.7 ml/m³ (2.5 mg/m³) (BIA, 03/1997).

Use/areas of application
(BGIA, 2006; BUA, 1986; BG Chemie, 1988; BMA, 1998; *Römpp,* 1989 to 1992)

- Solvent and extraction agents in the food industry (fatty oils, caffeine from coffee and tea, cocoa butter, hops, spices)
- Solvent for chemical synthesis
- Extraction agent for the purification of montan wax (recovered from lignite)
- Constituent of a solvent employed for the coating of pills in the pharmaceutical industry
- Cleaning agent for moulds in which polyurethane and polystyrene have been cast (open contact prohibited in accordance with the 2nd Ordinance for the Implementation of the German Federal Immission Control Act [2nd BImSchV])
- Cleaning agent for plant components such as spray nozzles in which polyester or polyurethane foams have been manufactured or handled
- Constituent of adhesives for polyurethane foam and PVC mouldings
- Stripping agent and façade cleaners in the construction industry
- Degreasing agent in the film and electronic industries
- Degreasing and cleaning agent in the textile industry. Since enactment of the 2nd Ordinance for the Implementation of the German Federal Immission Control Act (2nd BImSchV) on 10 December 1990, its use in dry-cleaning and textile finish-ing installations has been prohibited. This prohibition does not apply to degreasing installations for animal coats
- Degreasing and stripping agent and solvent in the leather, metals and plastics industries. Since enactment of the 2nd BImSchV on 10 December 1990, restric-

tions upon use have been in force: the open application of dichloromethane is prohibited, and its application is now permitted only in enclosed installations with controlled emissions

- Cold stripping agent: owing to its high capacity to dissolve chlorinated rubber, PVC, polystyrene, and many natural and synthetic resins, dichloromethane is employed in paste and liquid form in stripping agents
- Solvent and propellant component, for example for anti-spatter welding sprays
- Solvent and propellant component in sprays (restricted to 35% in cosmetic products by the EU Cosmetics Directive)
- Component in fire extinguishing agents
- Insecticidal fumigant for cereals
- Refrigerant
- Component in special adhesives
- Solvent for gold-plating formulations for glass and ceramics
- Rotogravure package printing and flexography
- Basic material for organic synthesis
- Recycling product recovered from solvents containing dichloromethane

Substitutes for dichloromethane as a paint remover and stripping agent:

Detailed information on substitutes can be found in the Technical Rules for Hazardous Substances TRGS 612.

Exposure values

No trend over time was observed. Since enactment of the 2nd Ordinance on the Implementation of the German Federal Immission Control Act on 10 December 1990 (2nd BImSchV), open use of the substance has been prohibited in certain sectors.

Table 12:
MEGA – Dichlormethane

Group of areas of work	Number of measure-ment data	Number of plants	50th percentile value in mg/m³	90th percentile value in mg/m³
Period to which data refer: 1985 to 1997				
Production of formulations	123	67	71	536
Cleaning, degreasing, stripping	440	202	159	932
Mould foaming	185	95	36	233
Bonding/coating (plastics/rubber/timber/ upholstered furniture industry)	679	246	50	413
Bonding/coating (ceramics/glass/metal/ footwear/electrical industry)	902	388	18	287
Period to which data refer: 1998 to 2002				
Production of formulations	34	17	40	153
Cleaning, degreasing, stripping	44	25	60	1,054
Mould foaming	30	12	33	480
Bonding/coating (plastics/rubber/timber/ upholstered furniture industry)	121	48	104	658
Bonding/coating (ceramics/glass/metal/ footwear/electrical industry)	119	56	24	309

Note that exposure data in this table for areas of work evaluated **across sectors** cannot necessarily be applied in all cases to areas of work and tasks in **specific sectors.**

4.4 Ethanol

Identification criteria
(BGIA, 2006)

Synonyms:
Ethyl alcohol, alcohol, methylcarbinol

CAS No.: 64-17-5

Selected physical and chemical data
(BGIA, 2006)

Boiling point: 78.33 °C (1,013 hPa)

Vapour pressure:
59.0 hPa (20 °C)
100.0 hPa (30 °C)
280.0 hPa (50 °C)

Chronology of the German occupational exposure limit
(BGIA, 2006; DFG, 1958 to 2003)

1958
Introduction of the MAK value of
1,900 mg/m³ (1,000 ml/m³)

2003
Reduction of the MAK value to 960 mg/m³
(500 ml/m³)

Uptake routes

At the workplace, the primary uptake route for ethanol in the respiratory/dermal comparison is the respiratory tract (BGIA, 2006). Dermal absorption is substantially lower than that for methanol. In a diffusion chamber test involving female chest skin preparations, an uptake rate of 1.1 mg · cm^{-2} · h^{-1} was measured (*Ursin et al.*, 1995).

Use/areas of application
(BGIA, 2006; Ullmann, 1983)

- Alcoholic beverages
- Solvent for fats, oils and resins, particularly in the manufacture of lacquer and adhesives, and for the manufacture of essences
- Solvent for printing inks in rotogravure package printing and flexography
- Solvent for scents (80 to 90% by weight) and cosmetics (after-shave, hair lotion (40 to 60% by weight)
- Fuel in the form of methylated spirit or hard spirit
- Engine fuel in mixtures with petrol/gasoline
- Synthetic base material for a large number of chemicals such as diethyl ether, chloroform, chloroethane, colourings, pharmaceutical preparations, etc.
- Preservatives and disinfectants
- Foundries: production of cold-box cores and the application of mould coatings (immersion in ethanol/2-propanol alcohol wash)

Exposure values

Table 13:
MEGA – ethanol

Group of areas of work	Number of measure-ment data	Number of plants	50th percentile value in mg/m³	90th percentile value in mg/m³
Period to which data refer: 1985 to 1991				
Production of formulations	306	89	17	469
Cleaning, degreasing (excluding cleaning of buildings)	233	114	27	413
Bonding (excluding flooring work)	84	35	5	48
Bonding (flooring work)	189	82	15	179
Brush application, hand-painting	75	43	6	46
Spray-painting	504	253	4	29
Surface coating (curtain coating, immersion coating, lamination)	195	96	8	165
Surface coating (impregnation, printing)	369	118	28	551
Period to which data refer: 1992 to 1997				
Production of formulations	510	166	13	310
Cleaning, degreasing (excluding cleaning of buildings)	375	184	< DL	194
Bonding (excluding flooring work)	360	138	< DL	16
Bonding (flooring work)	272	130	9	157
Brush application, hand-painting	136	79	< DL	61
Spray-painting	1,059	486	< DL	18
Surface coating (curtain coating, immersion coating, lamination)	335	165	< DL	66
Surface coating (impregnation, printing)	643	240	< DL	210

Table 13:
(Continuation)

Group of areas of work	Number of measure-ment data	Number of plants	50th percentile value in mg/m³	90th percentile value in mg/m³
Period to which data refer: 1998 to 2002				
Production of formulations	400	115	8	91
Cleaning, degreasing (excluding cleaning of buildings)	226	121	20	213
Bonding (excluding flooring work)	120	58	‹ DL	30
Bonding (flooring work)	66	18	207	523
Brush application, hand-painting	49	27	‹ DL	54
Spray-painting	298	136	‹ DL	30
Surface coating (curtain coating, immersion coating, lamination)	108	55	10	146
Surface coating (impregnation, printing)	386	144	16	202

Note that exposure data stated in this table concerning areas of work evaluated **across sectors** cannot necessarily be applied in all cases to **sector-specific** areas of work and tasks.

More detailed information on exposure in the construction sector can be found in Section II.3.2.2.

4.5 n-Heptane

Identification criteria
(BGIA, 2006)

Synonyms:
heptane

CAS No.: 142-82-5

Selected physical and chemical data
(BGIA, 2006)

Boiling point: 98.43 °C (1,013 hPa)

Vapour pressure:
48 hPa (20 °C)
76 hPa (30 °C)
190 hPa (50 °C)

Chronology of the German occupational exposure limit
(DFG, 1958 to 2003; BGIA, 2006; *Greim,* 1982)

The German occupational exposure limit applies only to heptane (all isomers):

1958
Introduction of the MAK value of 2,000 mg/m³ (500 ml/m³)

1985
This value was reviewed and is still valid in accordance with the Technical Rule for Hazardous Substances TRGS 900

2000
Adjustment of the MAK value to 2,100 mg/m³ (500 ml/m³)

Uptake routes

The primary uptake route for n-heptane is the respiratory tract. Approximately 25% (± 5%) of inhaled n-heptane is absorbed in the lung. Absorption through the skin may be considered minor (DGMK, 1986).

Use/areas of application
(*Henschler,* 3/1996; *Ullmann,* 1983; *Greim,* 1995; DGMK, 1986)

Standard commercial heptanes and special boiling-point gasolines containing heptane have the following n-heptane content:

Technical heptane (30 to 45%) and special boiling-point gasoline 80/110 (10 to 30%) are employed as:

- Thinners in the manufacture of paints and lacquers
- Constituents of adhesives, primarily in the rubber industry
- Care and cleaning agents (for example for furniture polishes, flooring care products)
- Extraction agents for animal fats and oils in flaying houses, bone mills and fish-meal plants

- Degreasing agents in tanning plants, wool scouring plants, and in the metalworking industry
- A component of cleaning agents used in offset and letterpress printing
- Extraction agents employed in the manufacture of cosmetic and vegetable active agents

Pure n-heptane is employed as a solvent in laboratories and as a reference substance for determination of the octane number of petrol/gasoline (octane number = 0).

Table 14:
n-Heptane content of heptanes and special boiling-point gasolines

Name	Boiling point range in °C	n-Heptane content in %
Heptane, industrial	94 to 100	30 to 40
Heptane, industrial	85 to 105	30 to 45
Special boiling-point gasoline 80/110	83 to 107	10 to 30
50 thinner	98 to 105	65
80 thinner	97 to 142	6.6

Exposure values

Table 15:
MEGA – n-Heptane

Group of areas of work	Number of measure-ment data	Number of plants	50th percentile value in mg/m³	90th percentile value in mg/m³
Period to which data refer: 1985 to 1991				
Production of formulations	112	42	< DL	36
Cleaning, degreasing (excluding cleaning of buildings)	116	74	< DL	49
Bonding (plastics/rubber industry)	100	30	18	52
Bonding (timber/upholstered furniture industry)	477	66	28	101
Bonding (leatherwork/footwear manufacture)	234	39	12	40
Bonding (flooring work)	72	32	13	50
Brush application, hand-painting	77	41	6	51
Spray-painting (metalworking)	70	42	< DL	5
Spray-painting (timber/upholstered furniture industry)	47	25	5	41
Surface coating (plastics/rubber industry)	65	28	7	45
Surface coating (metals/electrical industry/ precision mechanics)	66	33	< DL	8
Surface coating (timber/upholstered furniture industry)	26	17	7	16
Printworks	10	5	< DL	5
Period to which data refer: 1992 to 1997				
Production of formulations	104	45	3	16
Cleaning, degreasing (excluding cleaning of buildings)	172	107	6	60
Bonding (plastics/rubber industry)	102	38	7	44
Bonding (timber/upholstered furniture industry)	349	95	23	82
Bonding (leatherwork/footwear manufacture)	413	93	9	83
Bonding (flooring work)	83	36	17	70
Brush application, hand-painting	113	57	3	18
Spray-painting (metalworking)	124	77	<DL	10

Table 15:
(Continuation)

Group of areas of work	Number of measure-ment data	Number of plants	50th percentile value in mg/m³	90th percentile value in mg/m³
Spray-painting (timber/upholstered furniture industry)	113	58	3	10
Surface coating (plastics/rubber industry)	67	36	3	16
Surface coating (metals/electrical engineering/ precision mechanics)	75	40	<DL	13
Surface coating (timber/upholstered furniture industry)	154	58	9	85
Printworks	71	24	5	23
Period to which data refer: 1998 to 2002				
Production of formulations	54	22	4	17
Cleaning, degreasing (excluding cleaning of buildings)	131	73	11	68
Bonding (plastics/rubber industry)	37	17	21	46
Bonding (timber/upholstered furniture industry)	73	24	20	48
Bonding (leatherwork/footwear manufacture)	83	20	10	36
Bonding (flooring work)	*	*	*	*
Brush application, hand-painting	48	27	3	24
Spray-painting (metalworking)	51	31	2	8
Spray-painting (timber/upholstered furniture industry)	80	36	5	14
Surface coating (plastics/rubber industry)	20	11	4	15
Surface coating (metals/electrical engineering/ precision mechanics)	14	11	5	9
Surface coating (timber/upholstered furniture industry)	*	*	*	*
Printworks	19	11	4	46

* Insufficient data are available for statistical evaluation.

Note that exposure data in this table for areas of work evaluated **across sectors** cannot necessarily be applied in all cases to areas of work and tasks in **specific sectors.**

More detailed information on exposure in the construction sector can be found in Section II.3.2.2.

4.6 n-Hexane

Identification criteria
(BGIA, 2006)

Synonyms:
hexane

CAS No.: 110-54-3

Selected physical and chemical data
(BGIA, 2006)

Boiling point: 68.74 °C (1,013 hPa)

Vapour pressure:
160 hPa (20 °C)
248 hPa (30 °C)
540 hPa (50 °C)

Chronology of the German occupational exposure limit
(BGIA, 2006; DFG, 1958 to 2003; *Greim,* 1982)

1958
Introduction of the MAK value of 1,800 mg/m³ (500 ml/m³)

1974
Reduction of the MAK value to 360 mg/m³ (100 ml/m³)

1982
Reduction of the MAK value to 180 mg/m³ (50 ml/m³)

1988
Specification of a BAT value of 9 mg/l for n-hexane,
2,5-hexanedione plus 4,5-dihydroxy-2-hexanone are measured in the urine at the end of exposure/end of the shift

1993
Reduction of the BAT value to 5 mg/l

Uptake routes

The primary uptake route for n-hexane is the respiratory tract. n-Hexane is absorbed well via the alveoli of the lung when inhaled. Following inhalation, the alveolar retention rate is relatively low, at 16%. During longer exposure, the retention value was even seen to fall, to 5.5%, in the second hour. Tidal volume, respiratory frequency, body weight and body fat content may increase absorption. Dermal absorption is probably minor (BGIA, 2006).

Use/areas of application
(BGIA, 2006; BG Chemie, 2/1997; *Ullmann,* 1983)

n-Hexane can be obtained from suitable raw materials (light naphtha, BTX raffinate) by fractionated distillation or molecular sieving. n-Hexane is a constituent of low-boiling-point mineral-oil fractions from which solvents and thinners are manufactured for the lacquer and adhesives industry.

Pure n-hexane:

- Extraction agent for vegetable oils (food industry)

n-Hexane as a component of the low-boiling-point mineral-oil fraction:

- Formulating agent for lacquers. Prior to 1992, the n-hexane content in these fractions was up to 5% (boiling-point range 80/110). Since the early 1990s, the n-hexane content in fractions of the 80/95 and 100/140 range has not exceeded 1%, with an average of around 0.6%
- Mineral-oil fractions with a boiling point of around 60 °C may still (1997) contain up to 4.5% n-hexane. Such gasoline fractions are employed in the wire insulating varnish industry (fast-drying)
- Fast-drying adhesives for the bonding of floorings in buses and goods vehicles now contain approximately 1% n-hexane. The n-hexane content in thinners may also be approximately 1%
- Contact adhesives in the construction sector contain up to 3% n-hexane, adhesives for domestic use approximately 1.5 to 2%, and correction fluids containing solvents also approximately 1.5 to 2%
- Elution agent and solvent used in thin-layer chromatography and spectroscopy
- Test substance for determining the octane rating of petroleum/gasoline
- Solvent for vinyl resins and nitrocellulose
- Reactant employed during polymerization for the manufacture of plastics and synthetic rubber
- Component in cleaning agents for use in metalworking and precision engineering

Prior to 1989, lacquers containing up to 13% n-hexane and thinners containing up to 20% n-hexane were employed in the German Democratic Republic.

Exposure values

Table 16:
MEGA – n-Hexane

Group of areas of work	Number of measure-ment data	Number of plants	50th percentile value in mg/m³	90th percentile value in mg/m³
Period to which data refer: 1985 to 1991				
Manufacture of formulations (mixing, agitating, transfer/filling)	125	46	2	40
Brush application, hand-painting	12	10	‹ DL	‹ DL
Bonding (plastics, metals, electrical, timber, upholstered furniture industries)	575	119	7	39
Bonding (leather, footwear industry)	153	30	13	35
Period to which data refer: 1992 to 1997				
Manufacture of formulations (mixing, agitating, transfer/filling)	99	49	1	22
Brush application, hand-painting	22	14	‹ DL	‹ DL
Bonding (plastics, metals, electrical, timber, upholstered furniture industries)	460	153	3	14
Bonding (leather, footwear industry)	327	78	4	18
Period to which data refer: 1998 to 2002				
Manufacture of formulations (mixing, agitating, transfer/filling)	44	26	2	12
Brush application, hand-painting	*	*	*	*
Bonding (plastics, metals, electrical, timber, upholstered furniture industries)	89	40	4	12
Bonding (leather, footwear industry)	40	14	5	24

* Insufficient data are available for statistical evaluation

Note that exposure data in this table for areas of work evaluated **across sectors** cannot necessarily be applied in all cases to areas of work and tasks in **specific sectors.**

4.7 2-Hexanone

Identification criteria
(BGIA, 2006)

Synonyms:
methyl butyl ketone, MBK, MNBK, butyl methyl ketone

CAS No.: 591-78-6

Selected physical and chemical data
(BGIA, 2006)

Boiling point: 127.2 °C (1,013 hPa)

Vapour pressure:
3.5 hPa (20 °C)
7.33 hPa (30 °C)
26.7 hPa (50 °C)

Chronology of the German occupational exposure limit
(BGIA, 2006; DFG, 1958 to 2003)

1958
Introduction of the MAK value of 410 mg/m³ (100 ml/m³)

1960
Reduction of the MAK value to 21 mg/m³ (5 ml/m³)

1988
Specification of a BAT value:
9 mg/l 2,5-hexanedione + 4,5-dihydroxy-2-hexanone, measured in the urine

1993
Reduction of the BAT value:
5 mg/l 2,5-hexanedione + 4,5-dihydroxy-2-hexanone, measured in the urine

Uptake routes

The primary uptake route for 2-hexanone is the respiratory tract. In kinetic studies conducted on test subjects, approximately 75 to 92% of the inhaled dose was absorbed at hexanone concentrations of 10 to 50 ml/m³ (42 to 210 mg/m³) over 7.5 hours and 100 ml/m³ (420 mg/m³) over 4 hours (BGIA, 2006).

Absorption rates amounting to 0.25 to 0.48 $mg \cdot cm^{-2} \cdot h^{-1}$ were measured following application of 15 ml 2-hexanone to the forearm skin of test persons and with exclusion of inhalation (BGIA, 2006).

Use/areas of application
(BGIA, 2006; *Ullmann,* 1983)

- Solvents for natural and synthetic resins (hot-spray and coil-coating lacquers)

Exposure values

Evaluation of 157 items of BGMG measurement data in the MEGA database of the BGIA revealed that 98.7% of the 2-hexanone concentrations measured in the period from 1985 to 2002 failed to reach the analytical limit of detection of the methods employed. The measurements were performed at 55 different workplaces in a number of sectors.

4.8 Methanol

Identification criteria
(BGIA, 2006)

Synonyms:
Carbinol, methyl alcohol, wood spirit

CAS No.: 67-56-1

Selected physical and chemical data
(BGIA, 2006)

Boiling point: 64.51 °C (1,013 hPa)

Vapour pressure:
128.6 hPa (20 °C)
216.7 hPa (30 °C)
552.0 hPa (50 °C)

Chronology of the German occupational exposure limit
(BGIA, 2006; DFG, 1958 to 2003)

1958
Introduction of the MAK value of 260 mg/m³ (200 ml/m³)

1983
Specification of a BAT value for methanol: 30 mg/l methanol in the urine, measured at the end of a working week/in the second half of a shift

2000
Adjustment of the MAK value to 270 mg/m³ (200 ml/m³)

Uptake routes

The uptake route for methanol is via the respiratory tract and the skin.

60 to 70% is absorbed when inhaled in the form of its vapours (BGIA, 2006).

Uptake of toxic quantities through the skin is possible. The absorption rate of liquid methanol through the skin of the human forearm is in the order of 12 mg · cm^{-2} · h^{-1}. Accordingly, immersion of one hand in methanol for two minutes may result in absorption of a quantity equivalent to eight hours' respiratory uptake at approximately 50 mg/m³ (*Grandjean*, 1990). According to another source, the absorption rate via the human hand is 8.1 ± 3.7 mg · cm^{-2} · h^{-1} (*Batterman and Franzblau*, 1997). Higher absorption rates may be anticipated for solvent mixtures containing methanol (e.g. petrol/gasoline and methanol) (BGIA, 2006).

Use/areas of application
(BGIA, 2006; *Henschler*, 3/1996)

Methanol is currently used in the following areas:

- Solvent in chemical laboratories
- Solvent in spectroscopy
- Solvent for lacquers and resins
- Stripping agent in the metals industry: together with dichloromethane or in the form of a methanolic potassium hydroxide

solution, methanol is employed as a paint-stripper; degreasing installations employing alcohol/methanol are not known

- As extraction agent and for the purification of synthesis gas
- Refrigerants
- Filling of fuel cells
- In small quantities, as a colouring-pasting agent
- Permitted on a limited scale for use in cosmetics
- In stripping products
- In adhesives, including flooring adhesives
- Fuels or mixture components for special boiling-point gasolines
- Energy carriers
- Raw material for synthesis
- Source of carbon for petro-protein
- Adhesives

Exposure values

Table 17:
MEGA – Methanol

Group of areas of work	Number of measure-ment data	Number of plants	50th percentile value in mg/m³	90th percentile value in mg/m³
Period to which data refer: 1985 to 1991				
Production of formulations	47	22	23	140
Cleaning, degreasing (excluding cleaning of buildings)	66	39	22	145
Bonding (excluding flooring work)	11	8	1	10
Bonding (flooring work)	212	97	35	467
Brush application, hand-painting	16	13	1	14
Spray-painting	72	46	1	8
Surface coating (lamination, immersion coating, curtain coating, impregnating, printing)	85	41	7	232

Table 17:
(Continuation)

Group of areas of work	Number of measure-ment data	Number of plants	50th percentile value in mg/m³	90th percentile value in mg/m³
Period to which data refer: 1992 to 1997				
Production of formulations	19	11	9	260
Cleaning, degreasing (excluding cleaning of buildings)	32	23	8	103
Bonding (excluding flooring work)	18	9	< DL	20
Bonding (flooring work)	126	56	148	693
Brush application, hand-painting	11	10	< DL	< DL
Spray-painting	71	41	< DL	14
Surface coating (lamination, immersion coating, curtain coating, impregnating, printing)	319	176	< DL	68
Period to which data refer: 1998 to 2002				
Production of formulations	14	10	3	38
Cleaning, degreasing (excluding cleaning of buildings)	13	11	10	190
Bonding (excluding flooring work)	16	10	< DL	22
Bonding (flooring work)	*	*	*	*
Brush application, hand-painting	*	*	*	*
Spray-painting	18	13	< DL	4
Surface coating (lamination, immersion coating, curtain coating, impregnating, printing)	42	26	4	73

* Insufficient data are available for statistical evaluation.

Note that exposure data in this table for areas of work evaluated **across sectors** cannot necessarily be applied in all cases to areas of work and tasks in **specific sectors.**

More detailed information on exposure in the construction sector can be found in Section II.3.2.2.

4.9 2-Methoxyethanol

Identification
(BGIA, 2006)

Synonyms:
Ethylene glycol monomethyl ether, methyl glycol, glycol methyl ether

CAS No.: 109-86-4

Selected physical and chemical data
(BGIA, 2006)

Boiling point: 124.6 °C (1,013 hPa)

Vapour pressure:
8.1 hPa (20 °C)
16.2 hPa (30 °C)
42.0 hPa (50 °C)

Chronology of the German occupational exposure limit
(BGIA, 2006; DFG, 1958 to 2003)

1980
Introduction of the MAK value of 80 mg/m³ (25 ml/m³)

1983
Reduction of the MAK value to 15 mg/m³ (5 ml/m³)

2000
Adjustment of the MAK value to 16 mg/m³ (5 ml/m³)

Uptake routes

The principal uptake routes are the respiratory tract and the skin (BGIA, 2006). The absorption rate for preparations from human skin ("in vitro") is stated as 2.8 mg · cm^{-2} · h^{-1} (*Gingell et al.*, 1994) which correlates closely with more recent in-vivo results (forearm of volunteer test subjects: (2.9 ± 2.0 mg · cm^{-2} · h^{-1}). Immersion of both hands and forearms for one hour in liquid 2-methoxyethanol thus results in a substance uptake which is higher by up to two powers of ten than that which may be anticipated for exclusively respiratory exposure to methoxyethanol vapours at a concentration of 15 mg/m³ respiratory air per eight-hour shift (*Kezic et al.*, 1997). 2-Methoxyethanol in gas form is also absorbed easily through the skin. Experiments have shown that under whole-body exposure to methoxyethanol vapours, dermal and respiratory uptake are approximately equally high (*Kezic et al.*, 1997).

Use/areas of application
(BGIA, 2006; *Ullmann,* 1983)

- Solvents for lacquers, fats, oils, resins, celluloid, cellulose acetates and cellulose nitrates, and chlorinated rubber
- Antifreeze
- Softening agents

Exposure values

Table 18:
MEGA – 2-Methoxyethanol

Group of areas of work	Number of measure-ment data	Number of plants	50th percentile value in mg/m³	90th percentile value in mg/m³
Period to which data refer: 1985 to 1991				
Production of formulations	31	9	< DL	17.8
Cleaning, degreasing (excluding cleaning of buildings)	15	7	< DL	2.2
Coating: spray-painting, curtain coating, brush-coating	224	85	< DL	< DL
Coating with (plastic-)impregnating/ immersion coating lacquers	22	5	18	56
Period to which data refer: 1992 to 1997				
Production of formulations	27	9	< DL	12.4
Cleaning, degreasing (excluding cleaning of buildings)	17	11	< DL	3.9
Coating: spray-painting, curtain coating, brush-coating	106	58	< DL	< DL
Coating with (plastic-)impregnating/ immersion coating lacquers	14	7	7.0	18.8
Period to which data refer: 1998 to 2002				
Production of formulations	*	*	*	*
Cleaning, degreasing (excluding cleaning of buildings)	14	8	< DL	< DL
Coating: spray-painting, curtain coating, brush-coating	76	53	< DL	< DL
Coating with (plastic-)impregnating/ immersion coating lacquers	*	*	*	*

* Insufficient data are available for statistical evaluation.

Note that exposure data in this table for areas of work evaluated **across sectors** cannot necessarily be applied in all cases to areas of work and tasks in **specific sectors.**

More detailed information on exposure in the construction sector can be found in Section II.3.2.2.

4.10 Styrene

Identification criteria
(BGIA, 2006)

Synonyms:
Vinyl benzene, phenylethylene, styrol

CAS No.: 100-42-5

Selected physical and chemical data
(BGIA, 2006)

Boiling point: 145.14 °C (1,013 hPa)

Vapour pressure:
6.24 hPa (20 °C)
11.4 hPa (30 °C)
32.9 hPa (50 °C)

Chronology of the German occupational exposure limit
(BGIA, 2006; DFG, 1958 to 2003)

1958
Introduction of a MAK value of 420 mg/m³ (100 ml/m³)

1987
Reduction of the MAK value to 85 mg/m³ (20 ml/m³)

1983
Specification of a BAT value for styrene:
BAT value = 2 g/l mandelic acid in the urine,
BAT value = 2.5 g/l mandelic acid plus phenylglyoxylic acid in the urine, measured at the end of exposure/end of the shift.

1997
BAT value = 600 mg mandelic acid plus phenylglyoxylic acid per gramme of creatinine, measured at the end of exposure/end of the shift.

2000
Adjustment of the MAK value to 86 mg/m³ (20 ml/m³)

Uptake routes

Styrene is absorbed in humans primarily via the respiratory tract, approximately 60 to 90% being absorbed. Following inhalation, 2 to 3% of the uptake quantity is exhaled again (BUA, 1990; BGIA, 2006).

Styrene can also be absorbed to a limited degree via the skin. A liquid styrene absorption rate of 60 ± 30 µg · cm^{-2} · h^{-1} has been measured for the human hand *in vivo*. Substantially higher values known from older literature could not be confirmed (*Berode et al.*, 1985).

Studies on test subjects wearing respiratory protective devices and exposed to styrene vapours at up to three times the MAK value (i.e. approximately 258 mg/m³) revealed a dermal absorption expressed in blood styrene concentrations of, on average, between 30 and 56 µg l^{-1}. This corresponds to approximately 14 to 25% of the blood value measured following eight hours of respiratory styrene exposure at the level of the MAK value (*Woitowitz and Knecht,* n.d.).

Use/areas of application
(BUA, 1990; BGIA, 2006; *Ullmann*, 1983)

Styrene is employed solely for the manufacture of polymer products, and together with ethene, propene and vinyl chloride, is one of the most significant monomers. It serves as a basic material for thermoplastics, elastomers, duroplastics and dispersions.

Styrene production groups and their areas of application:

Polystyrene:

Packaging, domestic refrigeration appliances, other electrical appliances, domestic goods, furniture, toys, insulation materials

Styrene copolymers:

Automotive components (SAN, ABS)*, electrical domestic appliances, radio, TV, electronics, telephones, domestic refrigeration appliances, packaging, domestic goods, toys, pipes, fittings, ion exchange resins

Synthetic rubber:

Tyres, rubber goods, rubber-modified impact-resistant polystyrene, coatings, adhesives, textile coatings, carpet backing

Unsaturated polyester (UP) resins:

Pipes, vessels, boats, sheets, pressings for the automotive and electrical industry, unsaturated polyester resin concrete, fillers, acidproof construction, glassfibre reinforced plastic (GRP)

Styrene acrylates:

Coatings, lacquers, high-quality construction materials

The use of reaction resins containing styrene for the manufacture of plastic components (see also Section II.3.2.5)

* SAN = styrene acrylonitrile copolymers; ABS = acrylonitrile butadiene styrene copolymers

Exposure values

Table 19:
MEGA – Styrene

Group of areas of work	Number of measure-ment data	Number of plants	50th percentile value in mg/m³	90th percentile value in mg/m³
Period to which data refer: 1985 to 1997				
Hot moulding of polystyrene	306	154	< DL	8
Hot-pressing	182	43	46	141
Mixers, agitators	163	66	46	165
Filling, smoothing	156	82	18	116
Stoneworking (filling, cementing)	32	12	22	245
Production of polymer concrete	60	17	67	230
Open work over large areas in plastics processing	3,638	766	65	264
Open work over large areas in the construction industry	235	47	99	340
Period to which data refer: 1998 to 2002				
Hot moulding of polystyrene	83	49	< DL	24
Hot-pressing	48	14	37	98
Mixers, agitators	40	18	37	163
Filling, smoothing	38	27	12	42
Stoneworking (filling, cementing)	*	*	*	*
Production of polymer concrete	*	*	*	*
Open work over large areas in plastics processing	1,060	244	56	224
Open work over large areas in the construction industry	56	15	45	253

* Insufficient data are available for statistical evaluation.

Note that exposure data in this table for areas of work evaluated **across sectors** cannot necessarily be applied in all cases to areas of work and tasks in **specific sectors.**

More detailed information on exposure in the construction sector can be found in Section II.3.2.2.

4.11 Tetrachloroethylene

Identification criteria
(BGIA, 2006)

Synonyms:
Perchloroethylene, ethylene perchloride, ethylene tetrachloride

CAS No.: 127-18-4

Selected physical and chemical data
(BGIA, 2006)

Boiling point: 121.20 °C (1,013 hPa)

Vapour pressure:
18.9 hPa (20 °C)
32.0 hPa (30 °C)
84.0 hPa (50 °C)

Chronology of the German occupational exposure limit
(BGIA, 2006; DFG, 1958 to 2003)

1958
Introduction of a MAK value of 1,350 mg/m³ (200 ml/m³)

1960
Reduction of the MAK value to 670 mg/m³ (100 ml/m³)

1982
Reduction of the MAK value to 345 mg/m³ (50 ml/m³)

2006
Suspension of the limit value

1988
Classification as a IIIB substance (substance with substantiated suspicion of being potentially carcinogenic)

1997
Classification as carcinogenic K3 (substances which give rise to concern owing to a possible carcinogenic effect in humans but for which sufficient information does not yet exist for a satisfactory assessment. Some indicators exist from relevant animal tests, but are not sufficient for the substance to be classified as carcinogenic)

1982
Specification of a BAT value for tetrachloroethylene:
1.0 mg/l tetrachloroethylene, measured in the blood
64 ml/m³ tetrachloroethylene, measured in the alveolar air

1984
Reduction of the BAT value to 9.5 ml/m³ tetrachloroethylene, measured in the alveolar air

Uptake routes

The primary uptake route for tetrachloroethylene is via the respiratory tract and the skin.

Tetrachloroethylene is absorbed easily via the lungs (up to approximately 20%); the quantity absorbed is dependent primarily upon the atmospheric concentration, and less upon the duration of exposure (BGIA, 2006).

The high dermal absorption of tetrachloroethylene has been demonstrated in animal tests (*Greim*, 1997).

Use/areas of application
(BG Chemie, 10/1988; *Roth*, 1996; *Ullmann*, 1983)

Tetrachloroethylene is employed primarily (65%) in the area of surface treatment, i.e. as a solvent for coatings or for cleaning and degreasing, for example of metal parts. The second major area of application is that of dry-cleaning.

In accordance with the 2nd Ordinance for the Implementation of the German Federal Immission Control Act of 10 December 1990, tetrachloroethylene may be used for example in dry-cleaning and metal-degreasing installations only if certain technical requirements are satisfied.

Dry-cleaning:

- Since expiration of the last transitional provisions on 1 January 1995, all dry-cleaning installations employing tetrachloroethylene as the solvent must satisfy the requirements of the 2nd Ordinance for the Implementation of the German Federal Immission Control Act of 10 December 1990 (2nd BImSchV). In accordance with these provisions, the operation of dry-cleaning installations must be monitored continually by inspection with reporting to the authority, third-party inspection and in-plant monitoring. This provision is intended to prevent further operation of installations in the event of malfunctions which promote emissions. As a result of these measures, the measurement results for installations which satisfy the requirements of the 2nd BImSchV are substantially below 1/10 of the limit value. The measurement results obtained during the performance of tasks at workplaces some distance from the installation are lower.

Metals industry, formerly:

- Vapour degreasing installations
- Degreasing installations (hot dipping, hot spraying), with/without peripheral exhaust, with/without cover, in combination with ultrasonic cleaning, high-pressure rinsing or spray-cleaning systems
- Cold cleaning (with/without peripheral exhaust)
- Safe solvent cleansers, i.e. hydrocarbon mixtures to which a certain percentage of tetrachloroethylene or trichloroethylene has been added in order to suppress the flashpoint, frequently used in washstands, for example in the automobile sector

- Lubrication units, solutions of corrosion-protection oils and waxes in tetrachloroethylene
- Component of lacquer solvents and thinners
- Solvent in aerosol cans (brake cleaners, anti-spatter welding sprays, etc.)
- Solvent for assembly foams

Metals industry, currently:

- Only fully enclosed vapour degreasing systems are permissible; these are used for example for the cleaning of small turned parts (decorative trim for furniture, threaded inserts, studs, etc.) with narrow gaps, pores, bores/blind holes, which are rotated continually in baskets within the vapour chamber. Owing to its very low surface tension and viscosity, tetrachloroethylene assures very effective contact with the workpiece during cleaning.

With the exception of the maintenance personnel for the vapour degreasing systems, which are fully enclosed, personnel in the metals industry no longer have contact with the substance.

Other sectors of industry:

- Extraction agent for animal and vegetable fats and oils
- Solvent for waxes and resins
- Sporadically up until the late 1980s, use in flaying houses as a solvent for the separation of fat

Exposure values

Table 20:
MEGA – Tetrachloroethylene

Group of areas of work	Number of measure-ment data	Number of plants	50th percentile value in mg/m³	90th percentile value in mg/m³
Period to which data refer: 1985 to 1991				
Production of formulations	20	9	11	61
Cleaning, degreasing (excluding cleaning of textiles and buildings)	658	279	90	499
Dry-cleaning (textiles)*	1,350	1,319	85	275
Surface coating (curtain coating, immersion coating, lamination, bonding, spray-painting, printing)	133	73	< DL	114
Period to which data refer: 1992 to 1997				
Production of formulations	14	7	14	27
Cleaning, degreasing (excluding textiles and cleaning of buildings)	309	128	33	211
Dry-cleaning (textiles)* +	93	24	22	89
Surface coating (curtain coating, immersion coating, lamination, bonding, spray-painting, printing)	60	38	< DL	30
Period to which data refer: 1998 to 2002				
Production of formulations	**	**	**	**
Cleaning, degreasing (excluding textiles and cleaning of buildings)	106	50	25	161
Dry-cleaning (textiles)*	60	10	23	62
Surface coating (curtain coating, immersion coating, lamination, bonding, spray-painting, printing)	22	14	< DL	13

\+ The figures include exposure in Eastern Germany. Measurement results of up to half the limit values were recorded during operation of the special machines in use there.
* Measurements were performed only if clear indicators of elevated exposure existed, for example in the course of an investigation into a suspected case of occupational disease.
** Insufficient data are available for statistical evaluation.
Note that exposure data in this table for areas of work evaluated **across sectors** cannot necessarily be applied in all cases to areas of work and tasks in **specific sectors.**
More detailed information on exposure in the construction sector can be found in Section II.3.2.2.

4.12 Toluene

Identification criteria
(BGIA, 2006)

Synonyms:
Toluol, methylbenzene, phenylmethane

CAS No.: 108-88-3

Selected physical and chemical data
(BGIA, 2006; *Roth*, 1996)

Boiling point: 110.63 °C (1,013 hPa)

Vapour pressure:
27.8 hPa (20 °C)
45.2 hPa (30 °C)
109.0 hPa (50 °C)

Chronology of the German occupational exposure limit
(BGIA, 2006; DFG, 1958 to 2003)

1958
Introduction of a MAK value of 750 mg/m³ (200 ml/m³)

1985
Reduction of the MAK value to 375 mg/m³ (100 ml/m³)

1994
Reduction of the MAK value to 190 mg/m³ (50 ml/m³)
This value is still valid in accordance with the Technical Rule for Hazardous Substances TRGS 900

1981
Specification of a BAT value for toluene: 3.4 g/l toluene, measured in the blood

1986
Reduction of the BAT value to 1.7 mg/l toluene, measured in the blood

1996
Extension of the examination: BAT value = 1.0 mg/l toluene, measured in the blood, BAT value = 3.0 mg/l o-cresol, measured in the blood, measured at the end of exposure/end of the shift

Uptake routes

The primary uptake route for toluene in humans is the inhalation of vapours (BGIA, 2006).

Systematic intoxication by percutaneous absorption of liquid toluene is unlikely, unless large areas of skin are moistened with the substance over a longer period. Approximately 0.17 mg of toluene per cm² of skin is absorbed per hour (BGIA, 2006); another source states 0.08 ± 0.07 mg · cm^{-2} · h^{-1} (*Ursin et al.*, 1995). Up to 0.2 to 0.5 mg of toluene per litre of blood was found in the arms of test subjects who had immersed the hand of the other arm in liquid toluene for five minutes. This blood concentration is almost as high as that attained by inhalation of a toluene atmosphere of 380 mg/m³ breathing air. A second study revealed blood values, following immersion of one hand in toluene for half an hour, which were approximately one-quarter

of those measured following inhalation of toluene vapours in a concentration of 380 mg/m³ breathing air for four hours (*Grandjean*, 1990). Toluene is absorbed even more effectively through the skin in mixtures with methanol (*Tsuruta*, 1996).

Exposure to toluene vapours in a concentration of 2,280 mg/m³ over 3.5 hours led to dermal absorption which was lower than 1% of the pulmonary uptake (*Grandjean*, 1990).

Use/areas of application
(BGIA, 2006; *Roth*, 1996; *Ullmann*, 1983)

- Solvents for various natural and synthetic resins (urea, melamine, phenol-formaldehyde resins)
- Solvents for publication rotogravure inks
- Initial product for the manufacture of trinitrotoluene (TNT), toluene diisocyanates as starting products for polyurethane, benzene, cresoles, phenol, benzoic acid, caprolactam and colourings
- Construction industry:
  Solvent component of epoxy resins, stone strengtheners, parquet and other seals, wood putty, and in primers and adhesives
- Metals industry:
  Solvent component of lacquers, lacquer thinners, primers and adhesives (e.g. polyurethane adhesives), extenders in cellulose nitrate lacquers and synthetic resins
- Component of various hydrocarbon mixtures (AII/AIII) for cleaning and degreasing in enclosed installations and in open application
- Component of solvent cleansers (e.g. on washstands in the automotive sector)
- Component of petrol/gasoline and diesel fuels (in the mid-1950s, toluene accounted for approximately 20% by volume; in 1991/92, for 4.4 to 15.1% by mass)
- Component of non-dearomatized punching and drawing oils and corrosion-protection oils (for sheet-metal forming, drawing, punching)
- Component of epoxy resins (casting and lamination of epoxy resins)

Exposure values

Table 21:
MEGA – Toluene

Group of areas of work	Number of measure-ment data	Number of plants	50th percentile value in mg/m³	90th percentile value in mg/m³
Period to which data refer: 1985 to 1991				
Production of formulations	522	128	10	102
Cleaning, degreasing: manual +	381	188	6	101
Cleaning, degreasing: by machine +	50	22	8	96
Bonding (plastics/rubber industry)	163	62	11	138
Bonding (timber/upholstered furniture industry)	389	71	7	137
Bonding (leatherwork/footwear manufacture)	477	68	41	188
Bonding (flooring work)	375	130	79	438
Brush application, hand-painting	557	188	‹ DL	117
Spray-painting (metalworking)	497	254	‹ DL	24
Spray-painting (timber/upholstered furniture industry)	799	301	8	43
Spray-painting (construction industry)	123	28	4	48
Surface coating (plastics/rubber industry)	158	64	‹ DL	76
Surface coating (electrical industry, precision mechanics, metalworking)	146	63	‹ DL	47
Surface coating (timber/upholstered furniture industry)	362	131	18	116
Period to which data refer: 1992 to 1997				
Production of formulations	545	137	4	51
Cleaning, degreasing: manual +	319	181	4	89
Cleaning, degreasing: by machine +	54	33	7	21
Bonding (plastics/rubber industry)	217	79	‹ DL	37
Bonding (timber/upholstered furniture industry)	263	100	‹ DL	49
Bonding (leatherwork/footwear manufacture)	431	93	13	135
Bonding (flooring work) *	238	98	11	280
Brush application, hand-painting	489	227	‹ DL	36

Table 21:
(Continuation)

Group of areas of work	Number of measure-ment data	Number of plants	50th percentile value in mg/m³	90th percentile value in mg/m³
Spray-painting (metalworking)	559	306	< DL	19
Spray-painting (timber/upholstered furniture industry)	1,423	535	3	29
Spray-painting • Construction industry, painting work	255	53	10	64
Spray-painting • Construction industry, corrosion-protection work	43	10	< DL	9
Surface coating (plastics/rubber industry)	214	89	< DL	55
Surface coating (electrical industry, precision mechanics, metalworking)	150	73	4	31
Surface coating (timber/upholstered furniture industry)	608	203	4	72
Publication rotogravure	1,430	15	47	198
Period to which data refer: 1998 to 2002				
Production of formulations	347	86	2	37
Cleaning, degreasing: manual +	224	90	< DL	51
Cleaning, degreasing: by machine +	41	22	2	36
Bonding (plastics/rubber industry)	49	23	4	37
Bonding (timber/upholstered furniture industry)	55	17	< DL	47
Bonding (leatherwork/footwear manufacture)	94	21	21	80
Bonding (flooring work) *	**	**	**	**
Brush application, hand-painting	140	75	4	74
Spray-painting (metalworking)	247	137	3	29
Spray-painting (timber/upholstered furniture industry)	407	157	4	21
Spray-painting • Construction industry	60	28	2	14
Surface coating (plastics/rubber industry)	104	40	6	151

Table 21:
(Continuation)

Group of areas of work	Number of measure-ment data	Number of plants	50th percentile value in mg/m³	90th percentile value in mg/m³
Surface coating (electrical industry, precision mechanics, metalworking)	82	42	2	51
Surface coating (timber/upholstered furniture industry)	160	56	6	62
Publication rotogravure	2,133	15	29	176

\+ Not buildings cleaning

* Up to 1993; then change in recipe, 90th percentile value 1/10 to 1/4 limit value

** Insufficient data are available for statistical evaluation.

Note that exposure data in this table for areas of work evaluated **across sectors** cannot necessarily be applied in all cases to areas of work and tasks in **specific sectors.**

More detailed information on exposure in the construction sector can be found in Section II.3.2.2.

4.13 1,1,1-Trichloroethane

Identification criteria
(BGIA, 2006)

Synonyms:
Methyl chloroform, methyl trichlormethane, 1,1,1-TCE

CAS No.: 71-55-6

Selected physical and chemical data
(BGIA, 2006)

Boiling point:
73.7 °C (1,013 hPa)

Vapour pressure:
133 hPa (20 °C)
200 hPa (30 °C)
445 hPa (50 °C)

Chronology of the German occupational exposure limit
(BGIA, 2006; DFG, 1958 to 2003)

1958
Introduction of a MAK value of 2,700 mg/m³ (500 ml/m³)

1962
Reduction of the MAK value to 1,080 mg/m³ (200 ml/m³)

1983
Specification of a BAT value for 1,1,1-trichloroethane: 550 µl/l 1,1,1-trichloroethane, measured in the blood; 20 ml/l 1,1,1-trichloroethane, measured in the alveolar air

1998
Withdrawal of the BAT value for 1,1,1-trichloroethane of 20 ml/l, measured in the alveolar air

2000
Adjustment of the MAK value to 1,100 mg/m³ (200 ml/m³)

Uptake routes

The primary uptake route for 1,1,1-trichloroethane is inhalation. Approximately 90% of the inhaled quantity is absorbed in the lung (BGIA, 2006).

1,1,1-Trichloroethane is also absorbed percutaneously (BUA, 1995). 1,1,1-Trichloroethane was applied to volunteers over an area of skin measuring 12.5 cm², and the affected area sealed airtight for two hours in order to prevent evaporation loss. The 1,1,1-trichloroethane concentration in the exhaled air corresponded to that measured following two hours of respiratory exposure to 1,1,1-trichloroethane vapours in the range from 54 to 108 mg/m³ air (*Grandjean,* 1990). Further experiments showed that immersion of both hands for half an hour in 1,1,1-trichloroethane resulted in a peak concentration of the substance in the exhaled air corresponding to that for 30 minutes' respiratory exposure to vapour in the range between 540 and 2,700 mg/m³ air (*Stewart and Dodd,* 1964).

Gaseous 1,1,1-trichloroethane is absorbed percutaneously only in small quantities (*McDougal et al.,* 1990).

Use/areas of application
(BGIA, 2006; *Roth,* 1996; *Ullmann,* 1983)

Up to 1991, 1,1,1-trichloroethane was increasingly used as a substitute for trichloroethylene and tetrachloroethylene. In accordance with the 2nd Ordinance for the Implementation of the German Federal Immission Control Act of 10 December 1990 (2nd BImSchV) and the fluorochlorinated hydrocarbon/halon Prohibitory Regulation of 6 May 1991, the use of 1,1,1-trichloroethane is prohibited. The prohibition is not limited to cleaning and degreasing work in the metals industry, but also applies to bonding work or tasks in other sectors, such as the timber and plastics industry and the garments trade. 1,1,1-Trichloroethane has been completely replaced by substitutes. Production is expected to cease by 2005.

Former areas of application:

- Solvent for lacquers, oils, fats, waxes, resins
- Use as an extraction agent in asphalt and construction-material laboratories
- Degreasing, cleaning and stripping agent in various areas of industry (e.g. the automotive, aircraft, metals and plastics industries), cleaning in closed and semi-open installations (with peripheral exhaust and cover) or open, large-area cleaning with cloths, brushes or high-pressure equipment
- Solvent for oils, fats and waxes in lubrication units
- Degreasing agent in the electronics industry, soldering flux remover
- Propellant and solvent for assembly foams (e.g. polyurethane foams) in compressed gas packaging
- Paper industry: carrier solution for silicon and other protective coatings
- Textile industry: cloth examining
- Garments industry: stain removers (cold spotting)
- Glues/adhesives industry: component for example of special polyurethane adhesives
- Cleaning agent in book/offset printing (up to 1991)

Exposure values

Table 22:
MEGA – 1,1,1-Trichloroethane

Group of areas of work	Number of measure-ment data	Number of plants	50th percentile value in mg/m³	90th percentile value in mg/m³
Period to which data refer: 1985 to 1991				
Foaming	97	40	18	218
Cleaning, degreasing (manual, by machine)+	359	203	107	634
Bonding/coating (plastics/metals/upholstered furniture industries)	586	200	56	421
Laboratories	26	7	57	138
Foundries	65	30	3	16
Period to which data refer: 1992 to 1997				
Foaming	****	****	****	****
Cleaning, degreasing (manual, by machine)+	23	13	‹ DL	278*
Bonding/coating (plastics/metals/upholstered furniture industries)	136	72	21	397**
Laboratories	***			
Foundries	***			
Period to which data refer: 1998 to 2002				
No differentiation	39	19	‹ DL	10

\+ Not buildings cleaning
* Up to 1992
** Up to 1995
*** All contact ceased
**** Insufficient data are available for statistical evaluation

Note that exposure data in this table for areas of work evaluated **across sectors** cannot necessarily be applied in all cases to areas of work and tasks in **specific sectors.**

4.14 Trichloroethene

Identification criteria
(BGIA, 2006)

Synonyms:
Ethylene trichloride, TRI, trichloroethylene

CAS No.: 79-01-6

Selected physical and chemical data
(BGIA, 2006)

Boiling point: 86.7 °C (1,013 hPa)

Vapour pressure:
77.1 hPa (20 °C)
128 hPa (30 °C)
290 hPa (50 °C)

Chronology of the German occupational exposure limit
(BGIA, 2006; DFG 1958 to 2003)

1958
Introduction of a MAK value of 1,050 mg/m³ (200 ml/m³)

1960
Reduction of the MAK value to 520 mg/m³ (100 ml/m³)

1970
Reduction of the MAK value to 270 mg/m³ (50 ml/m³)

2004
Formulation of a TRK value of 165 mg/m³ (30 ml/m³)

2005
Suspension of the TRK value

1976
Classification as a IIIB substance (substance with substantiated suspicion of being potentially carcinogenic)

1997
Classification as carcinogenic K3 (substances which give rise to concern owing to a possible carcinogenic effect in humans but for which sufficient information does not yet exist for a satisfactory assessment. Some indicators exist from relevant tests on animals but are not sufficient for classification of the substance as carcinogenic). (Trichloroethylene has been classified by the DFG senate commission as Category IIIA 1; in the toxicology advisory group, classification in Group K1 is currently under discussion)

1981
Specification of a BAT value for trichloroethylene: 5 mg/l trichloroethanol, measured in the blood

1985
5 mg/l trichloroethanol, measured in the blood
100 mg/l trichloroacetic acid, measured in the urine

Uptake routes

The primary uptake route for trichloroethylene is inhalation. In humans, the pulmonary absorption rate is dependent upon the trichloroethylene concentration

in the breathing air and upon the tidal volume (and therefore the physical constitution) (BGIA, 2006).

Immersion of one hand in liquid trichloroethylene for half an hour led to absorption corresponding to approximately one-third of that attained via the respiratory tract following four hours' presence within a trichloroethylene vapour with a concentration of 540 mg/m³ breathing air. Dermal absorption of toxic quantities need not be anticipated during normal contact with trichloroethylene (*Grandjean,* 1990; BGIA, 2006).

Use/areas of application
(BGIA, 2006; BUA, 6/1991; *Roth,* 1996; VCI, 1997)

In accordance with the 2nd Ordinance for the Implementation of the German Federal Immission Control Act of 10 December 1990 (2nd BImSchV), trichloroethylene may be employed, for example in metals degreasing installations, only if certain technical criteria are met.

According to a report by the VCI, approximately 2,000 tons of trichloroethylene was in use in 1986. Consumption fell by approximately 75% by 1992.

- Glass industry: cleaning, degreasing and extraction agent
- Extraction apparatus: decaffination of coffee, extraction of carotene from palm oil
- For use in the metals industry, see tetrachloroethylene. The decision whether to employ trichloroethylene or tetrachloroethylene is left to the operator of the degreasing installation. The advantage of trichloroethylene is primarily its low boiling point, i.e. the energy costs are low. Conversely, tetrachloroethylene is more stable. A further advantage of tetrachloroethylene is its low price.

Use as:

- Solvent for fats, oils, waxes, resins and rubber
- Solvent component in the use of plastics in manufacturing
- Paper industry: production of board
- Use as an extraction agent in asphalt and construction-material laboratories
- Preparation of gas purification products and other products containing sulphur
- Cleaning agent in book/offset printing (up to 1990)

Exposure values

Table 23:
MEGA – Trichloroethene

Group of areas of work	Number of measure-ment data	Number of plants	50th percentile value in mg/m³	90th percentile value in mg/m³
Period to which data refer: 1985 to 1991				
Production of formulations	40	17	16	212
Cleaning, degreasing+	748	267	83	547
Surface coating in the plastics/rubber industry (curtain coating, immersion coating, lamination, bonding, spray-painting, printing)	76	28	27	365
Surface coating (metals/leather/upholstered furniture/electrical industry) (curtain coating, immersion coating, lamination, bonding, spray-painting, printing)	115	59	< DL	255
Period to which data refer: 1992 to 1997				
Production of formulations	25	13	17	185
Cleaning, degreasing+	198	84	61	285*
Asphalt and construction-material laboratories	56	25	47	146
Surface coating in the plastics/rubber industry (curtain coating, immersion coating, lamination, bonding, spray-painting, printing)	62	28	55	384
Surface coating (metals/leather/upholstered furniture/electrical industry) (curtain coating, immersion coating, lamination, bonding, spray-painting, printing)	41	25	< DL	41
Period to which data refer: 1998 to 2002				
Production of formulations	**	**	**	**
Cleaning, degreasing+	61	30	30	122
Asphalt and construction-material laboratories	100	38	72	491
Surface coating in the plastics/rubber industry (curtain coating, immersion coating, lamination, bonding, spray-painting, printing)	25	14	53	405

Table 23:
(Continuation)

Group of areas of work	Number of measure-ment data	Number of plants	50th percentile value in mg/m³	90th percentile value in mg/m³
Surface coating (metals/leather/upholstered furniture/electrical industry) (curtain coating, immersion coating, lamination, bonding, spray-painting, printing)	24	20	‹ DL	350

\+ Not buildings cleaning

* Up to 1992

** Insufficient data are available for statistical evaluation.

Results of exposure measurements from legacy or improper, open extraction of asphalt by means of hot trichloroethylene, and the cleaning of machine parts fouled with bitumen: see Section II 3.2.3.

4.15 Xylene (isomer mixture consisting of o-, m-, p-xylene)

Identification criteria
(BGIA, 2006)

Synonyms:
Dimethylbenzene, Xylol

CAS No.: 1330-20-7

Selected physical and chemical data
(BGIA, 2006)

Standard commercial xylene consists of a mixture of the isomers o-xylene (20 to 25%), m-xylene (50 to 60%) and p-xylene (20 to 25%). Owing to the close proximity of their boiling points, separation of the isomers does not generally occur. Commercial xylene described as "pure xylene" contains approximately 25% ethyl benzene.

Boiling points:
o-xylene: 144.41 °C (1,013 hPa)
m-xylene: 139.10 °C (1,013 hPa)
p-xylene: 138.35 °C (1,013 hPa)

Vapour pressure:

o-xylene	6.7 hPa (20 °C)
	12.0 hPa (30 °C)
	32.2 hPa (50 °C)
m-xylene	8.0 hPa (20 °C)
	14.7 hPa (30 °C)
	40.0 hPa (50 °C)
p-xylene	8.2 hPa (20 °C)
	16.0 hPa (30 °C)
	43.0 hPa (50 °C)

Chronology of the German occupational exposure limit
(BGIA, 2006; DFG, 1958 to 2003)

1958
Introduction of a MAK value of 870 mg/m³ (200 ml/m³)

1983
Reduction of the MAK value to to 440 mg/m³ (100 ml/m³)

1984
Specification of a BAT value for xylene: 1.5 mg/l of xylene in the blood or 2,000 mg/l methyl hippuric acid in the urine, measured at the end of exposure/end of the shift.

Uptake routes

The primary uptake route for xylene is the respiratory tract. Approximately 60 to 70% of the inhaled quantity is absorbed via the lung (BGIA, 2006).

The dermal absorption rate for liquid m-xylene is stated as being in the range from 42 to 260 $\mu g \cdot cm^{-1} \cdot h^{-1}$; higher values are in some cases also found in the literature. Immersion of both hands in liquid m-xylene for 15 minutes yielded an uptake of approximately 35 mg, which corresponds approximately to the quantity which would be taken up via the respiratory tract in the same period through respiratory exposure to a vapour concentration of 440 mg/m³. The absorption rates for o-xylene and p-xylene are likely to be in the same order of magnitude (*Grandjean,* 1990).

The absorption of xylene in vapour form through the skin is comparatively minor (BGIA, 2006; *McDougal,* 1990).

Use/areas of application
(BGIA, 2006; BG Chemie, 10/1988; *Ullmann,* 1983)

- Component of petrol/gasoline for internal-combustion engines, by which the octane number is raised
- Solvent for lacquers, paints, adhesives, waxes, resins, fats
- Surface treatment
- Petrochemical sector
- Coking plants
- Special disinfectant agents (for example in antiseptic soaps)
- Component of herbicide and insecticide formulations
- Component of ageing inhibitors for rubber
- Terpentine substitutes
- Base product for a number of polyester resins (in the same way as mesitylene, cumene, cymene and styrene)
- Special solvent

Exposure values

Table 24:
MEGA – Xylene

Group of areas of work	Number of measure-ment data	Number of plants	50th percentile value in mg/m³	90th percentile value in mg/m³
Period to which data refer: 1985 to 1991				
Production of formulations	831	201	39	188
Cleaning, degreasing *	482	237	11	162
Coatings – plastics industry	369	137	3	33
Coatings – metals processing and use	1,603	530	8	125
Coatings – electrical engineering/precision mechanics	630	249	5	43
Coatings – wood processing and use, upholstered furniture	1,295	379	7	35
Coatings – leatherwork/footwear manufacture	39	10	2	5
Coatings – ceramics industry	124	45	1	33
Coatings – construction trade	936	225	11	183
Laboratories	39	20	12	48
Foundries	67	35	1	26
Period to which data refer: 1992 to 1997				
Production of formulations	951	227	23	132
Cleaning, degreasing *	435	239	5	86
Coatings – plastics industry	429	161	< DL	15
Coatings – metals processing and use	1,737	701	6	68
Coatings – electrical engineering/precision mechanics	631	261	2	35
Coatings – wood processing and use, upholstered furniture	2,320	705	3	27
Coatings – leatherwork/footwear manufacture	61	18	< DL	8
Coatings – ceramics industry	273	101	2	19
Coatings – construction industry, painting work	1,246	349	25	521
Coatings – construction industry, corrosion-protection work	213	29	174	938

Table 24:
(Continuation)

Group of areas of work	Number of measure-ment data	Number of plants	50th percentile value in mg/m³	90th percentile value in mg/m³
Period to which data refer: 1992 to 1997 (Continuation)				
Laboratories	91	53	2	24
Foundries	66	29	7	84
Period to which data refer: 1998 to 2002				
Production of formulations	585	148	18	130
Cleaning, degreasing +	340	149	‹ DL	87
Coatings – plastics industry	183	69	2	18
Coatings – metals processing and use	1,102	433	7	63
Coatings – electrical engineering/precision mechanics	293	153	4	49
Coatings – wood processing and use, upholstered furniture	667	227	5	34
Coatings – leatherwork/footwear manufacture	20	8	2	16
Coatings – ceramics industry	152	62	‹ DL	25
Coatings – construction industry, painting work	301	112	8	85
Coatings – construction industry, corrosion-protection work	22	10	129	1,040
Laboratories	70	38	2	24
Foundries	47	19	31	136

+ not buildings cleaning

Note that exposure data in this table for areas of work evaluated **across sectors** cannot necessarily be applied in all cases to areas of work and tasks in **specific sectors.**

More detailed information on exposure in the construction sector can be found in Section II.3.2.2.

5 Mixtures of neurotoxic solvents

The 15 solvents listed in Chapter II.1 may occur in products in all mixture combinations containing two, three or more solvents. Products are seldom two-component mixtures; frequently, they comprise four or more components, generally also including other substances of relevance to occupational medicine (BAuA, 1988). Above a certain percentage by weight, the solvents must be stated in the material safety data sheets in accordance with their classification (see Table 1).

5.1 Possible solvent mixtures

Owing to their similarity in their chemical and physical behaviour, the aromatic hydrocarbons toluene and xylene very often occur in products as a mixture combination. Combinations of aromatic hydrocarbons involving ethanol and methanol or containing 2-butanone are also common. The aliphatic hydrocarbons hexane and heptane, however, are rarely employed as pure components in products. They are found in products in the form of the corresponding crude-oil distillate cuts.

Mixtures containing the chlorinated hydrocarbons dichloromethane, 1,1,1-trichloroethane, trichloroethylene and tetrachloroethylene are found only sporadically in products. This is primarily a consequence of the reduced use of chlorinated hydrocarbons, owing to the restrictions imposed upon their use by the 2nd Ordinance for the Implementation of the German Federal Immission Control Act (2nd BImSchV).

5.2 Hydrocarbon/solvent mixtures

The hydrocarbon compounds n-hexane, n-heptane, benzene[1], toluene, xylene and styrene contain six, seven or eight carbon atoms, and boil in the range between 68 and 146 °C (aliphatic hydrocarbons, boiling-point range 68 to 99 °C; aromatic hydrocarbons, boiling-point range 80 to 146 °C). The discussion below will therefore be limited to hydrocarbon solvents which may contain these six compounds.

Since the components of the product are frequently expressed by the names of fractions of the crude-oil distillation, it is not immediately apparent whether the product contains the stated hydrocarbon compounds. The aliphatic hydrocarbons n-hexane and n-heptane in particular are therefore declared only in a small number of the products which may actually contain them.

Styrene also has a certain special status. It is employed as a solvent (*Römpp,* 1989 to 1992) and co-reactant for unsaturated polyester resins, and for styrenation. Styrene is

[1] Benzene has now ceased to be relevant except as a process impurity. The use of hazardous substances with a benzene mass component equal to or greater than 0.1% is prohibited. Exceptions are governed by Annex IV (4) of the German Hazardous Substances Ordinance.

therefore more accurately described as a reactive solvent than as an organic or hydrocarbon solvent.

Common terms are generally applied to the various fractions of the crude-oil distillation which provide no indication of the discrete components, as for example *Römpp,* 1989 to 1992; VCI, 1997.

Light naphtha

Fraction of the atmospheric distillation of the crude oil, with boiling points of between 70 and 90 °C (primarily n-hexane and n-heptane)

Pyrolysis gasoline (Pygas)

Aromatics-rich hydrocarbon mixture produced during the steam cracking of naphtha, boiling point between 60 and 160 °C

Heavy naphtha

Fraction of the atmospheric distillation of crude oil with a higher boiling point, at 100 to 200 °C; synonym: heavy gasoline or mineral turpentine. Light gasoline (light naphtha) and heavy gasoline (heavy naphtha) are frequently grouped together under naphtha

Special boiling-point spirits (SBPs)

These are naphtha cuts with low aromatic content and boiling points of between 60 and 140 °C.

Mineral turpentine

Also termed “white spirit” or “Stoddard solvent”, this term refers to gasoline fractions with a higher boiling point (of between 130 and 200 °C, and a flash point › 21 °C) which generally have an aromatics component of approximately 20%.

These terms are assigned in the material safety data sheets to the CAS numbers of industrial mixtures. Depending upon the distillate cut, however, manufacturers use several different names for one and the same CAS number, and also several different CAS numbers for the same name.

The common names are frequently extended by numerical combinations which, depending upon the chemical structure of the hydrocarbons (VCI, 1997):

- Characterize the boiling-point range (e.g. special boiling-point spirits 60/95, boiling-point range 60 to 95 °C) from the group of light aliphatic hydrocarbon mixtures (35 to 140 °C)
- Describe the flash point (e.g. naphtha 21, boiling-point range 135 to 180 °C, flash point 21 °C) from the group of the heavy aliphatic hydrocarbon mixtures (135 to 330 °C)
- Indicate the rising nature of the boiling-point ranges (e.g. solvent naphtha 100: boiling-point range 165 to 180 °C; solvent naphtha 150: boiling-point range 180 to

210 °C) from the group of the aromatic hydrocarbon mixtures (165 to 310 °C).

The names of the industrial mixtures indicate the origin of the fraction from the industrial process. A chemical characterization corresponding to the name and CAS number can be found in Annex 1 of the applicable version of EU Directive 67/548/EEC; this is not stated for the majority of products, however.

The chemical characterization frequently takes the following structure:

- Origin from the industrial process
- Chemical structure of the hydrocarbons (e.g. aliphatic, alicyclic, aromatic, naphthenic, olefinic or paraffinic)
- Indication of the number of carbon atoms of which the hydrocarbons are primarily composed
- Boiling-point range

Accordingly, any industrial hydrocarbon mixture may be relevant to occupational disease No. 1317 if its characterization applies to the hydrocarbon solvents discussed here. Annex 1 of the Directive 67/548/EEC classifies approximately 700 industrial hydrocarbon mixtures. Based upon their chemical characterization, approximately 140 of these mixtures may contain the above hydrocarbon solvents.

Table 25:
Light aliphatic hydrocarbon mixtures (VCI, 1997)

Light aliphatic hydrocarbon mixtures Boiling-point range 35 to 40 °C The aromatics content is probably below 1%		Possible solvents (aromatics [A])
Special boiling-point spirit 60/95 CAS No. 64742-49-0	Boiling-point range 63 to 100 °C	n-Hexane, n-heptane (benzene [A], toluene)
Special boiling-point spirit 80/110 CAS No. 64742-49-0	Boiling-point range 78 to 113 °C	n-Heptane (benzene [A], toluene)
Special boiling-point spirit 100/140 CAS No. 64742-49-0	Boiling-point range 98 to 140 °C	n-Heptane (benzene [A], toluene, xylene)
Petroleum ether CAS No. 8032-32-4 EC No. 232-453-7 (also CAS No. 64742-49-0)	Complex combination of hydrocarbons from the rectification of crude oil. This fraction boils in the range between around 20 and 135 °C.	n-Hexane, n-heptane (benzene [A], toluene)
Rubber solvent	C5-C8 hydrocarbons, boiling-point range 45 to 125 °C	n-Hexane, n-heptane (benzene [A], toluene)

[A] Benzene has now ceased to be relevant except as a process impurity. The use of hazardous substances with a benzene mass component equal to or greater than 0.1% is prohibited. Exceptions are governed by Annex IV (4) of the German Hazardous Substances Ordinance.

Table 26:
Heavy aliphatic hydrocarbon mixtures (VCI, 1997)

Heavy aliphatic hydrocarbon mixtures Boiling-point range 135 to 330 °C		Possible solvents Classification by boiling point and number of carbon atoms
Mineral turpentine, general	Boiling-point range 135 to 330 °C Characterization by indication of the flash point, e.g. naphtha 21	Xylene
Mineral turpentine, containing aromatics	Boiling-point range 135 to 330 °C	Xylene
Mineral turpentine, free of aromatics	Boiling-point range 135 to 330 °C	
Naphtha 21	Boiling-point range 135 to 180 °C	Xylene

Table 27:
Aromatic hydrocarbon mixtures

Aromatic hydrocarbon mixtures Boiling-point range 136 to 310 °C		Possible solvents Classification by boiling point and number of carbon atoms
Solvent naphtha (coal), light; light-oil redistillate CAS No. 85536-17-0; EC No. 287-498-5	Low boiling point	
Solvent naphtha (coal), containing coumarone/styrene; Light-oil redistillate CAS No. 85536-19-2; EC No. 287-500-4	Medium boiling point	Styrene
Solvent naphtha (coal), xylene-styrene cut; light-oil redistillate CAS No. 85536-20-5; EC No. 287-502-5	Medium boiling point	Xylene, styrene

5.3 Uses of solvent mixtures

The use of only a single solvent in a product is the exception. As a rule, solvent mixtures consisting of two to six solvents are employed in products.

The reasons for this include the following:

- The desired product properties can be achieved only by the use of mixtures.
- Industrial mixtures of hydrocarbon solvents are cheaper than the pure substances.

Accordingly, mixtures of solvents are used in virtually all areas of application. The list below of solvent mixtures and their areas of application is intended to provide an indication of the broad range of application, and should not be considered exhaustive.

Areas of application for hydrocarbon mixtures
(BUA, 1988; VCI, 1997)

- Thinners in the lacquer and paint industry
- Solvents in printworks
- Solvents for fast-drying adhesives
- Paper industry
- Adhesive tape, sticking plasters, rubber solutions
- Cleaning and degreasing agents
- Dewaxing
- Degreasing of metals
- Solvents used in dry-cleaning

- Stain-removal agents used during textile and garment manufacture
- Adjustment substances for modern analytic methods
- Extraction agents and reaction media

Areas of application of solvent mixtures

In the following products, used for example in the construction industry:

Primers and adhesives

- Dispersion products
- Epoxy resin products
- Products with a high solvent component
- Polyurethane products

Wood putties and sealants

- Parquet sealants
- Primer sealants
- Oil-based synthetic-resin sealants
- Polyurethane sealants
- Acid-hardening sealants

House paints

Wood-preserving agents, insecticides

Forming oils

Epoxy resins

Hydrophobing agents, stone strengtheners, stone polishing creams

In the following products, used for example in metalwork, electrical engineering, precision mechanics, and the upholstered furniture and timber industries:

Surface-cleaning agents

- Cleaning agents containing non-water-soluble solvents:
  Solvent cleansers containing chlorinated hydrocarbons
  Solvent cleansers free of chlorinated hydrocarbons
  Cellulose thinners

Adhesives

Paints, lacquers

In the following products, used in the printing industry:

Solvents in offset printing

- Naphthas

Solvents in silk-screen printing

- Toluene, n-heptane, xylene, naphthas

In the following products, used in the footwear industry:

Shoe manufacture/shoe repairs

Adhesives

- Toluene, n-heptane, butanone

Shoe finish, thinner

- Xylene

Sole solvent

- Toluene, dichloromethane*, 1,1,1-trichloroethane*, trichloroethylene*

Parting agents

- Dichloromethane*

* No longer contained, for environmental reasons (Fluorochlorinated hydrocarbon/halon Prohibitory Regulation, 2nd Ordinance for the Implementation of the German Federal Immission Control Act)

III. Recommendations for medical assessment

1 Clinical picture and diagnosis

1.1 Polyneuropathy

1.1.1 Definition

Polyneuropathies are diseases of the peripheral nervous system which affect motor, sensory and autonomic fibres in the same or in different ways. Their clinical manifestation differs according to whether the polyneuropathy is of the symmetrical or asymmetrical distribution type. A distinction is drawn between distal symmetrical purely sensory neuropathies, sensory-motor or motor-sensory neuropathies, and more rarely exclusively motor and autonomic neuropathies. Cases with asymmetric distribution may be focal or multifocal neuropathies, i.e. complex polyneuropathies. From a histopathological perspective, neuropathies may be distinguished according to whether the small myelinated and unmyelinated fibres or primarily the large, strongly myelinated fibre calibres are affected. In consideration of the data from the neurophysiological examination, a distinction is drawn between a lesion type which is primarily axonal or primarily demyelinating.

1.1.2 Synonyms and differentiation from other disorders

The term “polyneuritis” refers exclusively to inflammatory disorders of the peripheral nervous system, particularly autoimmune neuropathies and polyradiculitis. The term “neuropathy” is frequently used as a synonym for polyneuropathy.

A distinction must be drawn between this condition and radicular syndromes, nerve-root irritations caused by intervertebral disks, compression injury to peripheral nerves, arterial circulation disorders of the extremities, and other neurological clinical pictures, such as restless-legs syndrome.

1.1.3 Cardinal symptoms of polyneuropathy

The typical symptoms concern: sensory disorders of the stocking-glove pattern (superficial and deep sensation, sense of pain and touch, temperature sensation, position sense and vibratory sensation, two-point discrimination and graphesthesia, deterioration or failure of the muscular proprioceptive reflexes (hyporeflexia/areflexia), muscle paresis and muscular atrophies, functional neurovegetative disorders). In some cases, the clinical picture of polyneuropathy may include disorders of the cranial nerves.

1.1.4 Information on etiology and differential diagnosis

The etiopathogenesis of the polyneuropathies is diverse and concerns clinical pictures which are hereditary, inflammatory (viral, bacterial and parainfectious), immunological in origin, metabolic, vascular, toxic, and paraneoplastic. A solvent neuropathy is typically manifested as a distal symmetrical sensory or sensory-motor polyneuropathy. Asymmetrical, multifocal, purely motor or autonomic neuropathies are not typical where solvents are the cause. The same applies to a primary infection of the cranial nerves. Only in sporadic cases have disorders of the cranial nerves, for example of the trigeminal nerve, been observed following exposure to trichloroethylene.

Owing to the particular importance for differential diagnosis, attention is drawn explicitly to the fact that restless-legs syndrome is not a clinical picture in the context of formally recognized occupational disease No. 1317 (*Benes,* 2000; *Oertel et al.,* 2000)

1.1.5 Diagnostic criteria for polyneuropathy

Symptoms of polyneuropathy typically concern the distal parts of the extremities, i.e. the soles of the feet, tips of the fingers and toes, and palms of the hands. The sensory disorders spread, rising from distal to proximal. In addition, the symptoms typically become more severe at night, as nocturnal paresthesias. Frequent incidence of calf cramps is a further common attendant phenomenon. Dysaesthesia throughout the body, "from head to toe", general itching of the skin, are not typical symptoms of a neuropathy, and can be differentiated by suitable anamnestic questioning.

Objective pathological findings for the diagnosis of a solvent polyneuropathy are:

- Distal symmetrical sensory or sensory-motor neuropathy
- Hyporeflexia/areflexia of the lower extremities
- Distal symmetrical pareses
- Dystal symmetrical sensory disorders of the stocking-glove pattern for esthesia, algesia, vibratory and temperature sensation, position sense, two-point discrimination
- Concomitant neurovegetative symptoms such as hypohidrosis or hyperhidrosis of the soles of the feet, hyperkeratosis, and alterations in the nail bed
- Decrease in nerve conduction velocity and prolonging of distal latencies as verified by electroneurography, and/or decrease in the amplitude of the sensory nerve-action potential or of the motor compound action potential, and/or signs of an acute or chronic neurogenic degenerative process on the electromyogram

The significance of the progress of the disease is addressed in Section III.3.4.

1.2 Encephalopathy

1.2.1 Definition

Encephalopathy refers to noninflammatory disorders of the brain or to brain damage of diverse origin. Strictly speaking, an encephalopathy is neither an entity nor a diagnosis, but a generic term for structural damages to and functional disorders of the brain.

A toxic encephalopathy is a clinical picture resulting from direct or indirect damage to the brain or parts of the brain caused by neurotoxic substances which are absorbed exogenously or produced by the metabolism.

The clinical picture of toxic encephalopathy does not differ in its essential symptoms from other forms of encephalopathy. The core symptoms are: impaired concentration, weak memory, difficulties in the registering and retention of information, affective and impulse disorders with loss of initiative, elevated irritability, dysphoria and changes to the primary personality, and exceptional fatigability or rapid exhaustibility.

1.2.2 Synonyms and differentiation from other disorders

Terms such as “pseudoneurasthenic syndrome”, “organic psychosyndrome”, “organic brain syndrome”, “cerebral function disorder”, “organic personality change” and “dementia” are used as synonyms. The diversity in terminology for the condition illustrates the problems presented by the nomenclature.

Owing to the vagueness of the symptoms, swift and reliable diagnosis is difficult, particularly in the early stages: the complaints are only mild at the onset of the condition, and vary widely from one individual to another. Depending upon the circumstances of the case in question, various neuropsychiatric, psychopathological and prognostic aspects must be considered for the diagnostic classification. The mild stages of the disease can therefore generally be diagnosed with adequate certainty only by longer-term observation of the progress.

1.2.3 Information on etiology and differential diagnosis

Since mental illness is widespread in the population as a whole and the etiology of organic disorders is generally multifactoral, an adequate differential diagnosis is particularly important. Differentiation must be made from other diseases, particularly in the areas of neuropsychiatry and internal medicine.

Such diseases are, in this context:

- Primary degenerative dementia and presenile dementia
- Multi-infarct dementia and other cerebrovascular diseases
- Alcoholic encephalopathy
- Morbus Parkinson and Parkinson Sndyrome

- Organic neuropsychological disorders due to other causes are:
  - Brain damage in early childhood
  - Post-traumatic personality disorder
  - Hydrocephalus
  - Compressive processes
  - Conditions resulting from meningoencephalitis and other encephalitides (AIDS)
  - Drug addiction
  - Conditions resulting from endocrinological, hepatic and renal disorders
- Affective disorders (formerly: endogenous depression)
- Anxiety and phobic disorders
- Reaction and stress disorders
- Somatoform disorders (formerly: psychosomatic disorders)
- Sleep apnea syndrome (obstructive, central or mixed form)

For the purpose of classification as occupational disease No. 1317, encephalopathy disorders caused by other potentially neurotoxic listed substances must also be considered. In accordance with the current list of formally recognized occupational diseases, this applies to the following listed substances:

- Lead and its compounds, particularly organic lead compounds (occupational disease No. 1101)
- Mercury and its compounds (occupational disease No. 1102)
- Manganese and its compounds (occupational disease No. 1105)
- Carbon monoxide (occupational disease No. 1201)
- Carbon disulphide (occupational disease No. 1305)
- Organic phosphorous compounds (phosphoric acid ester) (occupational disease No. 1307)

Encephalopathies caused by benzene and its homologues and styrene or by methanol fall under occupational disease No. 1317 (and not Nos. 1303 or 1306 as previously).

1.2.4 Degrees of severity of the toxic encephalopathy

It has proved practical to divide the clinical picture of toxic encephalopathy into three degrees of severity. The division below represents a synopsis of the scientific literature, the recommendations of international working groups, and many years' experience in occupational medicine and neurotoxicology (for overviews, see *Cranmer and*

Goldberg, 1986; WHO, 1985; *Triebig and Grobe,* 1987). The degree of severity II (intermediate form) is subdivided again in the official code of practice for occupational disease No. 1317 (see Section III.6.4) and in the recommendations of the present Occupational Disease Report concerning assessment of the reduction in earning capacity (see Section III.4.2), in order for appropriate allowance to be made for differences in the conditions' intensity and their impacts in various areas of working life.

Degree of severity I (mild form)

Degree of severity I encompasses vague subjective disorders such as increased tiredness, deterioration in memory and initiative, impaired concentration and greater irritability. The symptoms are vague and frequent. Generally, objectifiable indicators of a functional deficit in cognitive ability and personality changes which can be verified consistently by neuropsychiatric methods are absent. In the mild form of the encephalopathy, neuropsychological symptoms must be identified by anamnestic questioning. The patient may exhibit difficulties in coping with life which are to be regarded as an affective disorder of medical relevance.

Degree of severity II (intermediate form)

In degree of severity II, the symptoms are more pronounced and sustained. They are primarily tiredness, impaired concentration and (short-term) memory, emotional instability, impulse disorders and changes in mood and motivation, i.e. a sustained personality impairment.

These symptoms and personality changes generally determine the clinical picture, and should be verified by means of standardized methods. They are often linked with mild functional impairments which can be defined objectively in the area of attention, short-term memory and psychomotor speed.

The clear impairments of intellectual functions referred to above may also determine the clinical picture, whereas the subjective symptoms and personality changes which are experienced are less readily detected.

In addition, unspecific neurological observations in the form of co-ordination disorders may be present which are associated with nondirectional ataxia, rest tremor and intention tremor, and/or dysdiadochokinesia. The concomitant objective impairments in the performance of cognitive functions particularly concern the areas of attention and memory. More pronounced tendencies towards social withdrawal also occur at this degree of severity.

During assessment of the progress of a toxic encephalopathy, differentiation should, if possible, be made between the mental disorders of organic origin and the symptoms and syndromes which are not organic in origin. It has to be emphasized that subjective disorders may be less pronounced with increasing cerebral functional impairment, and may therefore lead to incorrect estimation of the actual degree of severity.

Evidence of a diffuse or localized cerebral atrophy neither supports nor excludes assumption of a toxic encephalopathy of intermediate severity. According to recent scientific findings, a causal relationship between chronic exposure to solvent at the workplace and a diffuse cerebral atrophy beyond the subject's age has not been clearly demonstrated.

Evidence of cerebrovascular disorders is not consistent with the typical clinical picture of toxic encephalopathy. Instead, a finding of this kind must be considered in the differential diagnosis. A normal SPECT finding does not justify exclusion of toxic encephalopathy.

Degree of severity III

Degree of severity III corresponds to the clinical picture of severe dementia with pronounced global impairment of intellectual performance and memory. In the severe form of toxic encephalopathy, the patient may exhibit a diffuse internal and external cerebral atrophy. The cerebral atrophic changes do not necessarily correlate in their scale with the clinical picture or the neuropsychological deficits. Severe toxic encephalopathy, accompanied in some cases by cerebral atrophy, has been observed in solvent sniffers following many years of substance abuse. Under the prevailing exposure conditions, such a level of severity is unlikely to have occupational causes.

1.2.5 Diagnostic criteria for encephalopathy

Pathological/anatomical verification of the diagnosis is not possible, for obvious reasons.

The following objective symptoms and findings are relevant:

- Demonstration of typical core symptoms (see Section III.1.2.1) which cannot be attributed to other causes
- Typical deficits in cognitive performance
- Typical signs of affective disorders of organic origin
- Evidence of tremor, ataxia and co-ordination disorders

Symptoms of a neuropathy which cannot be explained by other causes may also support the assumption of a toxic encephalopathy.

No specific biomarkers for solvent-induced encephalopathy have been known until now.

The significance of the progress of the disease is addressed in Section III.3.4.

2 Expert examination

2.1 Interdisciplinary assessment

Diagnosis of solvent-induced encephalopathy necessitates an interdisciplinary approach. Besides the occupational physician with overall responsibility for assessment of the causality, the following medical disciplines are of particular importance:

- Neurology
- Psychiatry
- Neuropsychology
- Neuroradiology

The annex of Chapter III (Section 6) contains a proposal for formulation of an application for assessment. The application for assessment is generally made to an occupational physician, with consideration for the insured individual's entitlement to select the assessor (German Social Code VIII, 200 [2]). The occupational physician holds primary responsibility for determining the causality. The accident insurance institution commissions the necessary supplementary assessments in the areas of neurology, neuroradiology/psychiatry or neuropsychology. The entitlement to select assessors must also be considered in the commissioning of supplementary assessments. For assessment of an encephalopathy and its intensity, a clinical neuropsychologist is assigned the task of producing a supplementary psychological assessment in cases where the neurological/psychiatric assessor is not qualified to produce a neuropsychological assessment him or herself.

The neuropsychologist's input is not limited to the mere evaluation of tests and the description of deficits, since assessment must be made not only of the impairment of mental performance, but also of possible personality changes of organic origin caused by the toxic encephalopathy.

Organic mental disorders must therefore be differentiated in neuropsychological and neuropsychiatric assessments from those which are not organic in origin. Conversely, assessment of the causality is an interdisciplinary medical task, overall responsibility for which lies primarily with the occupational physician. Based upon the supplementary neurological, psychiatric and neuropsychological assessments, a substantiated proposal must be made in the overall occupational medical assessment for estimation of the reduction in earning capacity in consideration of the scope for employment on the wider labour market which has been lost as a result of the disablement.

The conclusiveness of the assessments must be reviewed by the administration commissioning them. The institution for statutory accident insurance and prevention is responsible for determining whether the criteria for recognition are met, and the form and scale of benefits in accordance with the relevant legislation.

2.2 Medical history

The general medical history should be examined with particular consideration for hereditary stresses in the form of neuropsychiatric disorders, craniocerebral trauma, intake of medication, consumption of alcohol, smoking habits, etc., and drug use. During examination of the medical history, patients must also be questioned concerning sleeping disorders, snoring, interruption to breathing during sleep, excessive daytime sleepiness, and associated functional disorders.

In the detailed work history, attention must be paid above all to the form of exposure (respiratory, dermal), its duration, and the level of solvent concentration in the workplace atmosphere. In addition, attention must be paid to typical prenarcotic symptoms coinciding closely with the exposure to solvents. Irritation of the skin and mucous membranes may also serve as indicators of exposure.

Since investigation of exposure is primarily the task of the accident insurance institution, the observations of the prevention service should be exploited. If the results of the physician's consultation of the patient differ substantially from these observations, it has to be mentioned in the evaluation (cf. 3.6).

2.3 General examination

The general physical examination is supplemented by the specific examinations listed under 2.4 to 2.7, and if necessary, by an electrocardiogram performed both at rest and under strain.

2.4 Clinical/chemical and occupational medical/toxicological examination

Particular attention must be paid to:

- Blood count and differential blood count
- Basic parameters for liver and kidney function
- Thyroid hormones (according to indication)
- Vitamin B12 serum level, folic acid
- Biomonitoring for organic solvents and for further neurotoxic agents (such as lead, mercury, manganese; cf. under 1.2.3)

In the biomonitoring indication, attention must be paid to the short biological half-lives of organic solvents, which are in the order of minutes and hours, and at most a few days.

2.5 Neurological examination

- Complete neurological examination status, including cranial nerve status, examination of the motor functions, strength test, reflex status, examination of all sensory qualities
- Electroencephalography
- Electroneurography (motor and sensory nerve conduction velocities and distal latencies) and electromyography in accor-

dance with the standards of the DGKN (German society of clinical neurophysiology)

An examination of the autonomic nervous system is necessary only where indicators exist of autonomic polyneuropathy (e.g. heart-rate variation analysis, sympathetic skin response). Measures such as the following are not required for verification of occupational disease No. 1317; at most, they serve the purpose of differential diagnosis for differentiation from other diseases in exceptional cases:

- Brain mapping (spectral EEG)
- Electronystagmography
- Vestibular function tests (e.g. posturography)

Imaging methods:

- Cranial computer tomography (CCT), or according to indication cranial magnetic resonance tomography (MRT). Where available, preference should be given to MRT, owing to its lower radiation burden and greater sensitivity. Evaluation of the results demands particular experience and care, however. The use of functional magnetic resonance tomography (FMRT) or magnetic resonance spectroscopy (MRS) is not indicated at the present level of knowledge.

Not required, according to present knowledge, are:

- Single photon emission computed tomography (SPECT)
- Positron emission tomography (PET)

For differential diagnostics purposes:

- When indicated, a differential diagnostic confirmation of (for example) intervertebral disk injuries, lumbar and cervical root irritations (x-ray examination of the spine), other diseases of the nervous system (more detailed neurophysiological examinations), arterial circulatory disorders (sonography), and also sleep apnea syndrome (polysomnography)

2.6 Psychiatric examination

The neurologist or psychiatrist should have particular experience in the assessment of organic mental disorders. The difficulties of differential diagnostics associated with the problem at hand thus generally place high demands upon the investigating physician.

Beyond the psychiatric questioning, the assessor must also have the freedom to select supplementary methods (e.g. a structured interview, diagnosis checklists, operationalized psychodynamic diagnosis, biographical personality interview, questionnaire).

Comprehensive presentation of the psychological finding (consciousness, orientation, attention, concentration, perceptiveness, adaptability, memory, train of thought and thought content, cognition, mood and affectivity, impulse, psychomotricity, behaviour, critical faculty, interests, compliance, addiction behaviour) is essential.

Information must also be obtained in all cases from close relatives or other persons of reference (third-party case history). The modes of behaviour observed during the neurological examination – which provide a valuable indication of compliance or behaviour – must be considered in the psychiatric assessment in the same way as the results and evaluation of the psychological and neuropsychological examinations.

2.7 Neuropsychological examination

The neuropsychological examination should record not only the instantaneous neurocognitive performance profile and the affective status, but also the premorbid cognitive status and the premorbid personality. The exposure-related changes to these aspects must be shown. The task is not that of viewing the general strain ensuing from the vocation in its influence upon the neurocognitive and personality development, but of acknowledging the potential neurotoxic aspect of the contact with working agents. The neuropsychological study must encompass the following areas (refer in this context also to *Hartman,* 1995; *Berent and Albers,* 2005):

Medical history

Acute complaints associated with the work are recorded, as are changes to them during recovery phases (at the end of the shift, during the weekend or vacation). In this context, general signs of exhaustion from (generally) physical work must be differentiated from the effects peculiar to working agents (symptoms of intoxication, the effect of odours, acute hypersomnia, changes in activities following the shift).

Premorbid intelligence

During evaluation of the premorbid intelligence, consideration must be given in the first instance to the educational and vocational history and the socio-economic status of the individual under assessment. These data can be supplemented by test methods which are considered relatively insensitive to noxious substances. Vocabulary tests are generally employed for this purpose. More recent studies (*Satzger et al.,* 2002) however reveal a tendency for multiple-choice methods to result in the linguistic intelligence level being significantly overestimated. The "vocabulary" sub-test from the *Wechsler* intelligence test for adults is therefore preferable for this purpose.

Motor functions

In the area of motor functions, methods such as the finger-tapping test are suitable for testing the motor speed. Fine-motor co-ordination with visual monitoring can be examined by means of a number of peg-

board tasks (such as the Grooved Pegboard and Purdue Pegboard). The results may assist in differentiation between motor and cognitive aspects of slowdown.

Attention

An essential distinction is drawn in neuropsychological and cognitive concepts of attention between three aspects:

1. Activation of attention, including sustained attention and vigilance

2. Selective attention, including division of attention

3. Executive attention

Modern computer-based test batteries are available for these functions from which suitable sub-tests can be selected (such as the TAP test battery for attention testing). Attention questionnaires supplement the objective test data with the insured individual‘s subjective estimation.

Learning and memory

Learning and memory are complex concepts involving, on the one hand, processes such as encoding, consolidation, storing and retrieval, and on the other, structural concepts such as short-term and long-term memory. Working memory has a particular status. In order for learning ability and memory performance to be examined, at least the memory span (such as the repeating of numbers forwards), the working memory (such as the repeating of numbers backwards), the learning ability (such as tasks involving the learning of word lists over several passes) and the memory performance should be examined after several brief intervals of different length. A large number of test batteries (such as the revised version of the *Wechsler* Memory Scale, WMS-R) and discrete tests (such as the California Verbal Learning Test, CVLT) are available for use in the examination.

Executive functions

The concept of the executive functions encompasses not only a large number of functions which are required for new planning and problem-solving tasks, such as anticipatory thinking, flexibility, adaptability, strategy development and error monitoring, but also social competencies on the behavioural level, such as the ability to receive social signals and to exploit them for guidance of one’s own activity; communication behaviour is also part of this function. For the first of these areas, neuropsychologists have a range of methods at their disposal, such as Behavioural Assessment of the Dysexecutive Syndrome (BADS) and the Regensburg Word fluency Test (RWT). For evaluation of dysexecutive behavioural abnormalities, the examiner is dependent upon his observations during testing; in addition, he may have recourse to observations from the closer social environment of the insured individual.

Visual perceptive and visual constructive functions

For the basic functions (such as angle and length estimates), a range of test batteries are available which permit cost-efficient study of such functions by means of selected sub-tests (such as Visual Object and Space Perception, VOSP). Generally however, it is more practical to begin with complex testing, such as the mosaic test from the *Wechsler* intelligence test for adults, and if necessary, to examine the basic functions in addition should abnormalities be observed.

Emotional status and personality characteristics

Standardized measurement of the emotional status and personality is recommended, in order for neurotoxic developments to be detected as a background to the complaints, and for possible psychosomatic tendencies to be clarified during processing of them. Tendencies towards emotional instabilization, which is frequently observed, should be recorded. The measurement of personality characteristics which prompt a change in perception of the disorder independent of exposure, is also recommended. For this purpose, personality inventories are suitable (such as the Freiburg Personality Inventory, FPI-R; Minnesota Multiphasic Personality Inventory, MMPI 2). Methods such as the Symptom Check List (SCL-R 90) can be employed for evaluation of the instantaneous mental state, as can a range of depression questionnaires.

Ability and compliance

The results of examinations depend not only upon the objective state of health, but also upon the subject's compliance. A situation should be avoided in which the results of an examination are distorted by inadequate compliance. Conversely, care must be taken to avoid complaints caused by illness and impairments to performance such as elevated fatigability, rapid exhaustibility and lack of motivation being misinterpreted as a lack of compliance.

Test procedures now exist in neuropsychology by which the possibility of a lack of compliance, particularly in the area of learning and memory, can be examined with a high degree of accuracy. This is all the more important given that anamnestic functions may be impaired by neurotoxic factors. Inadequate compliance may however also be a factor in other areas of neurocognitive functions. The neuropsychological assessor should consider these aspects in his conclusions.

Typical chronic complaints

A neuropsychological examination for toxic encephalopathy cannot be based solely upon the recording of impairments in mental performance, or their exclusion.

Degree of severity I is characterized by complaints. Since these complaints, in the form of high fatigability, exhaustibility, and poor attention and motivation, may have a wide range of causes, the selection of specific

methods is recommended, the validity of which has been demonstrated for the neurotoxic problem (psychological/neurological questionnaire, Q 16). Profile observations of the complaints are particularly valuable.

Comments on evaluation

Mental performance:

The number of "abnormal" findings in the test variables must be evaluated. The level of reduced performance must be discussed with reference to the anticipated values associated with the premorbid intelligence. A trend towards change in the mental performance which is organic in origin should be substantiated.

- Complaints:

  Chronic complaints of fatigue, memory deficits, concentration and attention disorders, and difficulties in coping with life may be regarded as an expression of affective disorders. The level and profile of the complaints, measured for example by means of a pschological-neurological questionnaire, can provide information by which the neurotoxic specificity of the complaints can be evaluated.

- Covariation of exposure and psychologically recorded change:

  Diagnosis of toxic encephalopathy requires a consistent picture of the personality to be perceptible. Changes of personality characteristics should be timely related to changes of exposure.

- Coping with life:

  The relationship between the complaints described and the reduction in performance on the one hand and the coping with social and occupational demands on the other must be discussed. Phenomena of social withdrawal generally form part of the clinical picture. Should the subject have no difficulty coping with daily life, a toxic encephalopathy can probably be excluded. Vague signs of fatigue and reductions in motivation are not in themselves sufficient to satisfy the criteria for toxic encephalopathy.

- Differentiation from other diseases:

  Encephalopathy caused by alcohol abuse is generally associated with reductions in mental performance which are similar to those following prolonged occupational exposure to solvents. The two clinical pictures differ however in the subjective experience of the complaints. Alcoholics generally do not complain as much as persons who have suffered long-term solvent exposure. Developments of neurotic diseases may lead to complaints being experienced in similar ways to those caused by long-term occupational solvent exposure.

3 Criteria for the legal and medical assessment of formally recognized occupational disease No. 1317

3.1 General legal information

Assessment of whether a subject is suffering from occupational disease No. 1317 primarily involves examination of the relationship between the exposure to solvents during insured tasks and the observed clinical picture. If this relationship is deemed confirmed, the next question is that concerning the reduction in earning capacity caused by the occupational disease. The model form for assessment reproduced in the annex considers both aspects of the assessment.

Request for evidence – certainty and probability

Exposure to solvents or to mixtures containing them must be established with certainty (conclusive evidence). This does not mean that proof must exclusively take the form of documentation supported by results of measurement performed at the actual workplace; findings from comparable workplaces and experience may dispel doubts that exposure occurred and thus provide validation. One of the diseases named in occupational disease No. 1317, i.e. polyneuropathy or encephalopathy, must therefore be present beyond all doubt. A tentative diagnosis is not sufficient.

Equally, it is not sufficient for the insured person to have "possibly" been exposed. The finding that exposure "probably" occurred is also not sufficient in this case, since the facts upon which the claim is based (insured activity, exposure, disease) must be proven.

Probability is acceptable as a standard of proof only when – based upon satisfaction of these basic criteria – a causal relationship between the exposure to solvents and the disease is reviewed.

Causality may then be considered probable when, in acknowledgement of all circumstances in the case in question, the grounds for a relationship predominate.

Essential criterion

Not to be confused with the standard of proof, which as stated above is defined differently for the different elements of the decision, is the question of whether a cause is an essential criterion in the context of the statutory accident insurance.

Where a disease has several possible causes, it must be established which of these are essential causes. A disease is to be recognized as occupational when the exposure stated in the list of occupational diseases is at least a significant causal element of the damage to health.

Essential is not synonymous with predominant; a cause which is not equivalent may still be essential.

These general principles also apply in the assessment of cases of occupational disease No. 1317. The clinical pictures stated

for this disease are unspecific. In order to permit evaluation of which causes are essential, the causes must first be identified which may scientifically be considered in the first instance. On the one hand, it must be established whether, in accordance with the above principles concerning proof, occupational exposure occurred which is capable in principle of causing the disease. On the other hand, it must be established whether specific factors exist in the lifestyle or disposition of the individual which might equally explain the incidence of the clinical picture.

Both the occupational exposure and the non-occupational factors must be identified specifically for an evaluation of which are essential. If only the occupational factor or only a non-occupational factor is proven, the question regarding which factor is of essential relevance does not arise.

Conversely, if several causes are identified for a polyneuropathy, evaluation is necessary of whether the occupational exposure made an essential contribution to the genesis, deterioration or acceleration of the disease.

The lower the occupational exposure in qualitative and quantitative terms and the more apparent the non-occupational risk (e.g. diabetes mellitus, alcohol abuse), the safer the conclusion that the non-occupational cause is of primary importance. Thus, the occupational exposure can be regarded merely as a marginal factor which made no essential contribution. The reverse applies in equal measure.

3.2 Work-related criteria

On the one hand, it must be established that the solvents employed were neurotoxic; on the other hand, it must be established that exposure to them occurred in a sufficiently high concentration.

3.2.1 Neurotoxic solvents

Confirmed neurotoxic solvents are:

- Aliphatic hydrocarbons: n-hexane, n-heptane
- Ketones: 2-butanone (= methyl ethyl ketone), 2-hexanone (= n-butyl methyl ketone)
- Alcohols: methanol, ethanol, 2-methoxyethanol (= methyl glycol)
- Aromatic hydrocarbons: benzene, toluene, xylene, styrene
- Chlorinated aliphatic hydrocarbons: dichloromethane, 1,1,1-trichloroethane, trichloroethylene, tetrachlorethylene

Solvent mixtures are considered in particular when they contain an adequate quantity of at least one neurotoxic solvent (for indicators in this context, refer to the differentiated threshold values stated in Sections III.6.2 and III.6.3). For less recent exposure, the precise composition will generally no longer be ascertainable. In this case, it must be considered that in the past, the mixtures frequently contained neurotoxic solvents.

In consideration of the various neurological clinical pictures which are grouped under occupational disease No. 1317, a more far-reaching differentiation is necessary with regard to the neurotoxic action of these solvents.

Based upon current scientific knowledge of neurotoxicity, only some of the listed substances are capable in principle of causing polyneuropathy, generally following chronic and elevated exposure. These substances specifically include:

- n-Hexane
- 2-Hexanone (n-butyl methyl ketone)

The neurotoxic action of n-hexane and 2-hexanone may be exacerbated by simultaneous exposure to 2-butanone (methyl ethyl ketone).

For the other substances, the effects upon the central nervous system (encephalopathy) are the primary decisive factor. Further details can be found in Annex 6.2.

3.2.2 Level of exposure

During evaluation of the exposure for investigation into a case of solvent-induced polyneuropathy or encephalopathy, the limit values stated in the substance dossiers (Section II.4), which are relevant to prevention activity, are not necessarily a suitable measure for comparison. Besides the fact that such limit values cannot generally be extrapolated to compensation, it must be considered that during the definition of limit values for preventive activity, all health hazards must be taken into account, and that effects upon the nervous system are not the primary issue for all solvents.

For evaluation of a case of occupational disease No. 1317, the exposure conditions must be known under which, with reference to existing medical findings, neurotoxic effects were (first) observed.

In Annex 6.2, "neurotoxic threshold values" are deduced for the atmospheric concentration of certain neurotoxic solvents, and the literature references listed upon which they are based. The studies upon which these threshold values are based differ in their density and validity. Not all substances have been addressed by studies involving large numbers of cases and relatively precise measurements of the exposure; in some cases, the deductions are based upon studies involving smaller numbers and casuistic statements, and therefore exhibit uncertainty.

The neurotoxic threshold value is the concentration of a substance in the workplace atmosphere below which neurotoxic effects serving as a criterion for the condition have not yet been observed or described. With regard to combined effects, particular attention must be paid to 2-butanone (methyl ethyl ketone, MEK), since simultaneous exposure to n-hexane or 2-hexanone (n-butyl methyl ketone) gives rise to a supra-additive combined effect.

This exception aside, the effect of individual components in solvent mixtures is assumed in the first instance to be additive. The deduction of "neurotoxic threshold values" for mixtures is more difficult than for single substances, owing to the heterogeneity of the studies. Annex 6.3 refers to data from studies of long-term exposure to organic solvent mixtures, and formulates the possible conclusions from them. Owing to the incomplete or total lack of exposure data in the studies, only the evaluation index in accordance with the technical rules TRGS 403 was calculated; differentiation between neurotoxic and other components was not possible. For assessment in specific cases, the neurotoxic potential of the solvent mixtures employed must be considered during interpretation of the exposure data.

An important indicator that the "threshold concentration" is exceeded is the indication of prenarcotic symptoms occurring during or shortly after the exposure. Under normal workplace conditions, respiratory uptake is the primary uptake route. Direct contact of the liquid with larger areas of the skin and for longer periods may however lead to elevated internal exposure to the solvent. This particularly applies to the substances denoted as percutaneously absorbable (H) in the current list of limit values. This specifically applies to the following neurotoxic solvents: 2-butanone, 2-hexanone, methanol, 2-methoxyethanol, benzene, toluene, xylene, 1,1,1-trichloroethane, tetrachlorethylene.

Where available, biomonitoring data are particularly useful in these cases for quantification.

3.2.3 Duration of exposure

Besides the level of exposure, its duration is also relevant to the neurotoxicity of solvents.

Epidemiological studies show that toxic encephalopathy generally develops only after a period of exposure of ten years or longer. Where exposure is unusually high (several times the threshold value), toxic encephalopathy may arise after shorter periods of exposure.

Conversely, toxic polyneuropathy may often be observed after only a few months' exposure. Exposure lasting for ten years is the exception.

3.2.4 At-risk workplaces

Some workplaces are known from the past to be associated with considerable solvent exposure. Examples are:

- Fitting work on scrubbers
- Solvent immersion baths
- Spraying work in the furniture industry
- Lacquer spraying work
- Bonding workplaces in indoor footwear manufacture

- Cardboard industry involving PER
- Optical industry involving PER
- Tank cleaning
- Cleaning work in shipyards

The exposure must however always be investigated on a case-by-case basis.

3.3 Clinical picture

Polyneuropathy and encephalopathy constitute mutually independent diseases (*Albers et al.,* 1999; *Dietz et al.,* 2002). Coincidence is possible, but has been observed only in a minority of cases (*Dietz et al.,* 2002). A substance-specific evaluation of causality must be performed in each case.

The diseases "toxic polyneuropathy" or "toxic encephalopathy" defined above must be confirmed. Other diseases, such as lesions of the cranial nerves or disorders of the autonomic nervous system, may be considered in addition provided one of the two diagnoses defined above is confirmed.

Occupational origin of sleep apnea syndrome is the subject of scientific discussion. The data are inconsistent with regard to an association between sleep apnea syndrome and solvent exposure. Occupational disease No. 1317 does not encompass sleep apnea syndrome, however.

During assessment of subjective disorders and their significance, both general and individual aspects must be considered. General aspects are experience regarding reversibility and the possibilities of and prognoses for adequate therapy. For proper assessment of the case under consideration, the constraints imposed by the disease upon the general ability to cope with life must be considered. The functional constraints or the disruption to activities which the patient cannot complete in the manner considered "normal" in his or her social environment are important here. In this context, it must be noted that the evaluation of "normality" is characterized by expectations which are subject to continual change within society.

A subjective disorder can be rated as a toxic encephalopathy when a consistent pattern of complaints and personality changes are confirmed which can be related in their coincidence and toxic causality to the elevated risk of illness resulting from the contact with solvent. Possible further influences upon the change in mental state (occupational stress, loss of the workplace, conflict, ageing-related changes, elevated anxiety, elevated sensitivity to environmental stimuli, reactive or endogenous depression, organic diseases) must be considered.

3.4 Progress of the disease

Polyneuropathy and encephalopathy differ in their progress and in their prognoses.

The exposure giving rise to the disease and the onset of the latter coincide closely in time, i.e. the disease develops during or shortly after occupational exposure. A longer

interval between the end of exposure and the onset of the disease is not plausible for toxicological reasons, not least owing to the short biological half-lives of the neurotoxic solvents.

This does not rule out the possibility of the disease not being perceived as serious by the subject until a later stage, and correspondingly not being diagnosed medically until later.

Polyneuropathy

The severity of a case of toxic polyneuropathy is determined among other things by the persistence or capacity for reversal of the symptoms of peripheral neurological deficits and irritation. The results of significant longitudinal studies, which can also be found in the official code of practice for occupational disease No. 1317 (BMGS, 2005), are presented below in greater detail (Table 28, see Page 136 ff.).

Table 28:
Publications concerning diagnosis of toxic polyneuropathy in studies involving repeat examinations

Random sample	Number of repeat examinations	Repetition rate of the tests
n-Hexane-induced PNP in workers in paper production industry	N = 11 2 with sensory PNP 9 with sensory-motor PNP, moderate to severe PNP in all cases	Duration: 4 years without exposure (in the first 2 years monthly, in the third year every two months, in the fourth year every 3 months)
n-Hexane-induced PNP in workers in the footwear industry	N = 90 with diagnosis of n-hexane-induced PNP	First examination at least one year after diagnosis and cessation of exposure. Follow-up examination: Group A: N = 63, less than 10 years after the first examination Group B: N = 27, over 10 years after the first examination
n-Hexane-induced PNP in workers in a ball-production plant	N = 4 women, exposure ranging from 3 to 108 months	Monitoring of the progress: clinical examination at fortnightly intervals – electrophysiology 4 to 5 times in total
PNP in workers following chronic exposure to n-hexane	N = 102 Primarily sensory PNP, lower incidence of motor symptoms	

Change in complaints	Change in electrophysiology	Source	Evaluation
5 patients reported further deterioration in strength up to 2 to 3 months following cessation of exposure; 6 patients with initially severe PNP and indication of muscle stiffness were still reporting morning cramps in the calf at the end of the study into the progress of the condition; 2 developed increased reflexes in the legs with no increase in tone	6 patients exhibited a deterioration in the motor NCV parameters; in 5 patients, deterioration in the sensory NCV parameters in each case following cessation of exposure (exact progress not documented)	*Chang*, 1990	Overall prognosis positive; all patients, including one tetraplegic, recovered strength almost completely. Sensory disorders with a sensory-motor component subside much earlier than motor disorders (besides also occurring earlier), generally within 3 to 4 months; changes in the electrophysiology did not always correlate with the clinical complaints. Some constraints imposed by the method: limited documentation of the progress over time, in particular of the neurophysiological parameters
Clinical symptoms among up to 30% of the examined patients; no difference in PNP symptoms between Groups A and B; no progression	In the follow-up examination, all patients exhibited complete recovery of the motor NCV; sensory NCV remained significantly pathological compared to the normal group, but generally significantly improved compared to the previous examination; no progression	*Valentino et al.*, 1996	Prognosis generally favourable; no progression; motor nerve fibres recover fully, whereas sensory fibres recover more slowly and residual damage may remain over 10 years following anti-infective measures; method: an issue was that at the time of the study, many patients in Group B were seeking compensation
Further deterioration in strength over 1 to 2 months following cessation of exposure, then a plateau of 2 to 5 months, followed by almost complete recovery after 1 year; improvement in the emotional disturbance after 3 to 5 months	Initially, deterioration of the NCV over 3 months; improvement of all NCV values within 16 months; in some patients however, residual pathological NCV parameters remained after 15 months	*Huang et al.*, 1989	Biphasic progress of the polyneuropathy, with favourable prognosis; methodological constraints: only n = 4 patients
All 102 patients exhibited complete reversal of the PNP symptoms following cessation of exposure		*Kuang et al.*, 2001	Prognosis positive without exception; limitation: method and differentiated results only partially comprehensible

Table 28:
(Continuation)

Random sample	Number of repeat examinations	Repetition rate of the tests
n-Butyl methyl ketone-induced PNP in workers in plastics processing	N = 86 Of which: Medium to severe PNP: N = 11 Mild PNP: N = 38 Minimal PNP: N = 37	Follow-up examination with questionnaire, clinical examination and electrophysiology at irregular intervals
Toxic PNP among printworkers	Once cases of illness became apparent, 1157 workers were examined by means of EMG, NCV study and questionnaires. 192 employees exhibited abnormalities (following between 5 weeks‘ and 27 years‘ exposure)	Division into groups 1. Normal 2. No clear signs of PNP 3. Suspected PNP 4. PNP certain The progress was observed of only 38 patients
Toxic PNP among workers in the footwear industry	N = 122 PNP groups 1) Severe NCV change: N = 37 2) Moderate NCV change: N = 42 3) Normal NCV/EMG change: N = 43	Groups 1 and 2 Clinical and electrophysiological examinations every 3 to 6 months until normal values reached Group 3 1 year following the first examination Duration: 30 months
Toxic PNP among workers in the footwear industry	N = 53 Group 1 10 medium to severe PNP Group 2 24 mild PNP Group 3 19 clinically virtually unimpaired, but with electrophysiological abnormalities	Every 3 months in the first year Annually until normalization or stabilization of the values Duration: 8 years (max.)

Legend:
EMG: = electromyograph
NCV = nerve conduction velocity
PNP = polyneuropathy

Change in complaints	Change in electrophysiology	Source	Evaluation
Medium to severe group: all exhibited improvements following cessation of exposure Mild group: 86% improvement, 11% no change, 1 patient slight deterioration Minimal group: 71% improvement, the remainder unchanged or with minimal deterioration after 8 months		*Allen et al.*, 1975	Up to 3 to 8 months following cessation of exposure, continued progression in either symptoms or electrophysiology; generally improvement; method: no differentiation between clinical and electrophysiological parameters, since the overall score was compared; the progress in the patient groups which were not severely affected cannot therefore be considered more precisely (see footnote)
22 of the 38 improved clinically following cessation of the exposure; no progression	16 of the 38 improved only electrophysiologically; no progression in any cases following cessation of the exposure	*Billmaier et al.*, 1974	No progression, cessation of exposure generally followed by recovery; method: vague description; studies of the progress only very limited; description tending to be of the state
Clinical reversal generally within 3 years, in some cases with residual complaints; no clear progression; altogether, onset insidious with general premonitory symptoms: anorexia, loss of weight, headaches, nausea, GIT complaints	Deterioration in the electrophysiology up to a maximum of 4 months following cessation of exposure, then recovery of most patients, with isolated residual NCV changes after 30 months	*Cianchetti et al.*, 1976	Primarily favourable prognosis following possible initial deterioration; no progression; method: variation between individuals in time between onset of the symptoms and cessation of exposure
General improvement in the progress; no PNP progression Groups 1 and 2: neurological symptoms still present in up to 50% of the patients after 5-6 years Clinical symptoms still present in 6 out of 7 patients in Group 1 even after 7-8 years	General recovery in the progress; no PNP progression; EMG changes persist in some cases even 8 years after cessation of exposure; NCV generally recovered after 6-24 months with mild PNP and after 12-36 months with severe PNP	*Passero et al.*, 1983	Prognosis generally favourable depending on the severity of the PNP; no progress of the PNP; method: no distinction between possible concomitant diseases (see footnote)

Remarks:
Allen et al.: It remains incomprehensible that in the patient groups which were clinically mildly affected, a slight deterioration is described in some cases following cessation of exposure, whereas all (!) patients in the severely affected group exhibited improvements.

Passero et al.: Development of symptoms affecting the CNS with increasingly frequent spastic symptoms after 2-5 (!) years following cessation of exposure in all severity groups (no differentiation from other/competing disorders)

Chang (1990) reports observation of the progress of eleven cases of n-hexane-induced polyneuropathy over a period of up to four years. Following signs of a deterioration in the motor disorders in the first three months following cessation of exposure in some cases, the symptoms improved in the subsequent progress in all cases, including in tetraplegic patients; the improvement was observed earlier in the sensory disorders. The prognosis according to *Chang* for n-hexane-induced polyneuropathy is therefore invariably positive. The author points out explicitly that changes in the electrophysiology do not always correlate with clinical complaints.

In a comparable long-term study on 90 workers in the footwear industry with n-hexane-induced polyneuropathy, *Valentino et al.* (1996) did not observe progression of the symptoms in any of the cases. In follow-up examinations conducted in some cases over ten years after cessation of exposure, complete recovery from the motor deficit symptoms and virtually complete recovery from sensory disorders was observed.

In a close-meshed study, *Huang et al.* (1989) examined four women with n-hexane-induced polyneuropathy over a period of 15 months. In this case, the symptoms were seen to increase over a period of one to three months following cessation of exposure, with a plateau phase after approximately two to five months, followed by virtually complete recovery in the clinical symptoms and neurophysiological parameters. This author therefore also confirms a favourable prognosis for n-hexane-induced polyneuropathy.

The same estimation of a principally favourable prognosis for this condition can be found in a recent study by *Kuang et al.* (2001) who studied 102 workers with n-hexane-induced polyneuropathy. In all cases, complete reversal of the symptoms was observed in the progress following cessation of exposure.

Allen et al. (1975) report on the follow-up examination of 86 patients with polyneuropathy following exposure to n-butyl methyl ketone. All patients in the clinically moderately to severely affected group exhibited an improvement in symptoms following cessation of exposure. In the group with "mild PNP", 1 of the 38 patients exhibited a slight deterioration, and isolated minimal deteriorations were also reported in the group with "minimal PNP". Since the study performed by *Allen* employed an overall score and no differentiation was made between clinical and electrophysiological parameters, further differentiation of these changes is not possible retrospectively.

Billmaier et al. (1974) studied 38 printworkers with toxic polyneuropathy; a progression was observed neither clinically nor neurophysiologically. In the majority of cases, the symptoms improved in the progress. This study is of only limited use, since a description was made primarily of the present condition, and a description of the progress was conducted only for a small number of patients.

A study of the progress conducted by *Cianchetti at al.* (1976) on 122 workers in the footwear industry with toxic polyneuropathy describes a temporary impairment in the clinical symptoms and in the electrophysiology within a period of at most four months following cessation of exposure. In the subsequent progress a reversal of the symptoms, which varied between the individuals over time, was observed over a period of up to 30 months. Progression of the symptoms was not observed in any of the cases.

The progress of toxic polyneuropathy in 53 workers from the footwear industry was studied by *Passero et al.* (1983) over a period of up to eight years. In the severely affected individuals in particular, the symptoms were observed to deteriorate in the initial months following cessation of exposure. In the long-term observation, a general improvement occurred during the progress; in some cases, peripheral neurological symptoms and in particular neurophysiological changes persisted. A progression of the PNP symptoms was not observed in any of the cases. It is notable that between two and five years following cessation of exposure, symptoms classified as affecting the central nervous system termed "spasticity and hyperreflexia" are described with increasing frequency in all severity groups. The method made no differentiation from competing disorders. With regard to the polyneuropathy initially described for these patients, the development of a vigorous reflex level may be interpreted clearly as a clinical improvement in the peripheral neurogenic damage. The authors discuss whether the findings relating to the central nervous system are changes of toxic origin which were initially eclipsed by the peripheral symptoms. The latency of up to five years before the onset of these symptoms in the central nervous system suggests that this is not the case. In view of clear deficiencies in the method of this study, and without comparable confirmation by other occupational epidemiological studies, this question must remain unanswered.

The method of the study by *Ørbæk and Lindgren* (1988), also listed in the code of practice (BMGS, 2005), is clearly geared in its description of the results and its discussion towards observation of the progress of toxic encephalopathy. Although clinical findings concerning the peripheral nervous system and neurographic findings are also reported in a table, these results are not considered in the discussion, and in particular are not discussed with regard to polyneuropathy with consideration for competing factors. This study therefore appears to offer little information for evaluation of the progress of toxic polyneuropathy.

Altogether, the available studies presented here can be described as very disparate in terms of the quality of their methods. The older studies, such as those of *Billmaier et al.* (1974) or *Allen et al.* (1975), for example, primarily contain instantaneous descriptions of the condition, and only a partially standardized study of the progress. The available studies are therefore of only limited comparability from a methodical perspective. A significant consistency is that in the majority of studies over a period of, on

average, some three to four months following cessation of exposure, the pathological, clinical and neurophysiological changes were seen to increase. The available studies were further consistent in that in the long term, with the exception of isolated cases, further deterioration of the symptoms invariably did not occur; rather, a complete or in some cases incomplete reduction in the previous peripheral neurogenic or neurophysiological changes took place.

With critical consideration of the methodical constraints already referred to, the following core conclusion of the available studies may be formulated: following cessation of exposure, a case of toxic polyneuropathy may exhibit a deterioration in the symptoms for a period limited to a few months, but in the long term, further deterioration does not occur; instead, the clinical and neurophysiological symptoms have decreased virtually completely, although in individual cases, residual disorders may persist, particularly in patients initially severely affected.

Encephalopathy

The first signs of toxic encephalopathy (such as poor concentration and memory, tiredness) are frequently not consciously registered by those affected, or are misinterpreted. As a result, mild encephalopathy may initially remain undetected, and the subjective connection between the symptoms and the solvent exposure not made until later.

Evaluation of the progress of the condition must give consideration to normal ageing processes and changes in occupational and private lifestyles. These include, for example, a change in or loss of occupational activity or changes in family ties and circumstances. A general prognostic evaluation of the development in patient health must consider both changes in exposure and in living conditions. Limitation of the consideration to specific aspects, such as the indicated symptoms, clinical finding, mental functions, neurophysiological measurements or information from imaging methods, does not permit an overall prognosis.

The persistence or reversibility of the effects is an important aspect in evaluation of the severity of the toxic encephalopathy. The results of several longitudinal studies (Table 29, see page 146 ff.) support the observation that the cognitive deficits in particular do not undergo progression following cessation of exposure.

Follow-on studies of 32 diagnosed cases of toxic encephalopathy after four years – exposure had ceased – for example revealed a slight attenuation of the symptoms and no significant change in the test performance (*Ørbæk and Lindgren,* 1988). The same conclusion can be drawn from a survey of 25 cases of toxic encephalopathy 2 1/2 years after the first examination (*Jensen et al.,* 1984).

In a study encompassing 21 cases which were reappraised after an average of two years' exposure-free activity, 43% (9 out of 21) exhibited an improvement, 52% (11 out of 21) no change, and 5% (1 out of 21) a deterioration in the test results (*Dryson and Ogden,* 2000). In another progress study, once again primarily no change: only in 2 out of 26 cases were reductions in cognitive performance observed after two exposure-free years. Progression of the clinical picture was explicitly excluded (*Bruhn et al.,* 1981). A further study with a five-year interval and a total of 111 cases confirms this estimation, provided the re-examined persons had not been subjected to further exposure (*Edling et al.,* 1990).

Two more available studies (*Leira et al.,* 1990; *Lauritsen et al.,* 1985) present problems with regard to method, since some 30% of those who were examined again remained subject to exposure. In the study by *Leira et al.* (1990), 24 chronic and 36 subacute cases of toxic encephalopathy were re-examined after an interval of three to five years; the methods however were not consistent. Trends in changes were interpreted without reasonable statistics: in the chronic cases, a trend towards a "negative" change was observed, in the subacute cases, a trend towards a "positive" change. In the study by *Lauritsen et al.* (1985), 69 cases of encephalopathy of varying severity were re-examined after an interval of three years. The symptoms stated do not increase significantly in the medium-severity cases, and increase significantly in three of twelve symptoms among the mild toxic encephalopathy cases; the test results remain largely constant, with a trend towards a slight improvement.

The studies cited up to this point have relatively short repetition intervals. A study is available with an interval of 18 years following the first examination. Floor-layers subjected to solvent exposure were compared with exposure-free carpenters. In ten neuropsychological tests, no significant reductions in test performance were observed in exposed subjects beyond those observed in the controls (*Nordling Nilson et al.,* 2002). The principal result of this study thus correlates with the results cited above.

Deficits in memory performance, perception speed and attention were observed in a sub-group of older floor-layers with very high exposure, both in comparison with the group as a whole, and as a dose-effect relationship. These deficits were interpreted as an interaction between age and high exposure, i.e. an exacerbation of the effect. The stated quantities of solvents employed in the flooring adhesives in past years are exceptionally high in this group (› 10 l/day over 10 to 20 years) and substantially exceed the › 30 l/day-years presented by *Mikkelsen et al.* (1988) as risk-enhancing for toxic encephalopathy.

In conclusion, it can be surmised that persistence or slight attenuation in the perceived symptoms and persistence or slight attenuation of the existing mental performance deficits following cessation of exposure is the most frequently observed progress of the disease. Progression of the subjective

symptoms and of the reduction in mental performance was not observed in a clear majority of the methodically validated studies. The progression of toxic encephalopathy following cessation of exposure is therefore not the probable progress of this disease. Only in cases involving very high and long exposure to solvents should mutual exacerbation of ageing and exposure effects be considered as an explanation for progression.

Table 29:
Publications concerning diagnosis of toxic encephalopathy in studies involving repeat examinations

Random sample	Number of repeat examinations	Repetition rate	Change in complaints
Chronic toxic encephalopathy patients	N = 32, previous exposure over 26 years	4 years after first examination, without exposure	10/17 neurasthenic symptoms evaluated in summary: significant reduction from an average of 7 to 5 symptoms
Chronic toxic encephalopathy patients	N = 25; first examination 3 months after cessation of exposure, 14.9 years of exposure	2 ½ years after first examination	19 symptoms; "stability"; trend in change: reduction for 17 symptoms, same frequency for 2 symptoms
Chronic toxic encephalopathy patients	N = 21	2 years after first examination, exposure score, classification according to severity of the disease n = 15 without, 6 with reduced exposure	10 unchanged 7 symptoms improved 3 deteriorated 1 no indication
Chronic toxic encephalopathy in housepainters	N = 26, first examination 1 year after cessation of exposure; previously 28 years' exposure	2 years after first examination, without exposure	13 symptoms: with respect to all data at first examination: "unchanged" 67% "no longer present" + "improved" 28% "increased" 5%
Chronic toxic encephalopathy patients	N = 65 only symptoms (Type I) N = 46 (Type IIb)	5 years after first examination: 16 still exposed 32 in work without exposure 52 with compensation 14% with exposure at follow-up examination	14 symptoms: increase in 4 symptoms with Type IIb vs. Type I; significant deactivation more with Type IIb

Change in performance	Source	Evaluation
12 tests summarized in 6 function areas: N = 9/32 unchanged N = 13/32 deterioration in performance in 1 or more tests N = 6/32 improvement in 1 or more tests N = 4/32 deteriorations and improvements	*Ørbæk and Lindgren,* 1988	Subjective improvement experienced, increases in performance observed when initial situation low, deterioration in performance when high. Psychometry suggests no progressive development following cessation of exposure
Numerous tests for categories: evaluation of level of reduction at first/second examination, "worse/better/unchanged" Psychomotor speed 4/2/19 Attention, concentration 4/4/17 Learning/memory 3/7/15 Complete intellectual ability 4/ 4/17	*Jensen et al.,* 1984	Performance constant, but slight attenuation in stated symptoms Progression negated
Evaluated cognitively and "psychologically": 11 unchanged 9 improved 1 deteriorated The stronger the impairment at the first examination, the greater the improvement at the second examination	*Dryson and Ogden,* 2000	Condition predominantly unchanged or improved; no evidence of progression Tendency towards the centre, as described by *Ørbæk and Lindgren*
11 test scores: in 10 scores, no significant change; one significant attenuation presented as "probably not relevant" Overall individual evaluation: in 24/26 unchanged; in 2/26 attenuation of the performance level	*Bruhn et al.,* 1981	Persistence or attenuation of symptoms predominates; no significant change in performance; reversibility and progression evaluated by authors as "not observed"
8 tests from 5 areas, diagnoses determined by tests: Of 65 Type I unchanged n = 59, 3 deteriorated to Type IIb (3 lost) Of 46 Type IIb unchanged n = 28, 12 improved to Type I (6 lost)	*Edling et al.,* 1990	Mild cases with recovery effect; more severe cases with persistence; in the absence of exposure, no progression of the disease

Table 29:
(Continuation)

Random sample	Number of repeat examinations	Repetition rate	Change in complaints
Chronic/subacute toxic encephalopathy patients	N = 24 chronic N = 36 subacute Partial evaluation n = 47	3-5 years following diagnosis 13/47 still exposed 19/47 in employment without exposure 15/47 in retirement 28% with exposure at follow-up examination!	First examination with free statement of symptoms; second examination employing structured questions (9 symptoms): Chronic: deterioration Subacute: reduction in symptoms No statistics!
Persons exposed to solvents with clinical referral	N = 69: 15 medium-severity toxic encephalopathy 29 light toxic encephalopathy 9 other encephalopathy 16 no encephalopathy	3 years following first examination: 4/69 still subject to same exposure 17/69 still exposed but with reduced exposure 30% with exposure at follow-up examination!	12 symptoms: Medium-severity encephalopathy: Slight increase (not significant) Mild encephalopathy: in 3/12 increase in symptoms Other encephalopathy: no change No encephalopathy: significant reduction
Floor-layers vs. carpenters, long vs. short vocational experience The same exposed persons with the highest exposure	N = 21 › 20 years‘ exposure N = 20 5-10 years‘ exposure 18 controls with long, 22 with brief occupational experience 10 with highest alcohol-based 10 with highest contact-adhesive-based vs. 18 with long vocational experience	18 years‘ further work, exposure indices (l/day; cumulative) Subgroup of older employees and with highest exposure vs. older non-exposed	Not addressed Not addressed

Change in performance	Source	Evaluation
First examination 8 tests (comprehensive); second examination abridged versions? No significant changes; indication of "negative tendency" in chronic cases, of "positive tendency" in subacute cases	*Leira et al.*, 1990	Method presents difficulties. First/second examinations not consistent; "changes" evaluated in some cases without statistics: trends in changes in chronic cases different to those in subacute cases
5 tests with 9 evaluation variables: "largely identical median and percentile values" A tendency towards improvement in the test values is observed in all groups; a tendency towards attenuation also in all groups, but substantially less frequent	*Lauritsen et al.*, 1985	Indicated symptoms increase in groups with medium-severity and mild encephalopathy, but predominantly not significantly Test performances constant, with strong tendency towards improvement
12 tests ANOVA: 11 tests without exposure effect All tests without age-exposure interaction Digit-symbol test significant Alcohol: 1/12 tests with significant exposure effect, 4/12 with evident tendency, exposure-time interaction 3/2 significant Contact adhesive: 1/12 tests exposure effect, 3/12 tendency evident	*Nordling Nilson et al.*, 2002	No exposure effect Exposure effect among individuals with highest exposure in some tests, interaction with age

3.5 Other causes and personal susceptibility

Other occupational causes are decreasing in their relevance when compared to previous decades. Lead and mercury exposure must in particular still be considered at the present time.

Non-occupational causes are addressed above under "differential diagnosis" (cf. Sections 1.1.4 and 1.2.3).

For the evaluation of non-occupational contributory causes in the occupational disease legislation, see Section III.3.1.

The incidence of toxic effects differs from one individual to the next (personal susceptibility) owing to genetic variability, which is relevant for the expression of enzymes which metabolize foreign substances. Despite numerous positive research results, substantial deficits remain, particularly where different polymorphisms are considered in combination. The determination of polymorphisms of different enzymes which metabolize foreign substances is not therefore currently a suitable instrument for personal risk assessment. The same applies to neurotoxic effect markers such as paraoxonase polymorphism, with the result that valid biomarkers for personal diagnosis cannot be stated at this time.

3.6 Synoptic assessment

The legal framework described under Section III.3.1 must be considered for the synoptic assessment.

A criterion for formal recognition of a case of occupational disease No. 1317 is that regular exposure to neurotoxic solvents at an adequate level and for an adequate duration must be validated (i.e. the work-related criteria must be met). The diagnosis of encephalopathy or polyneuropathy must also be confirmed (the medical criteria for occupational disease No. 1317 must be met).

Questions concerning the type and scale of exposure should be clarified if at all possible at the beginning of the assessment. The insurance institution is responsible for establishing the facts and circumstances of exposure. Detailed personal consultation of the insured individual by the prevention service during on-site investigation in the plant may help to prevent contradictory results. Should the exposure be estimated differently by the insured individual themselves, this is recorded in the prevention service's report. Within the scope of his particular expertise, the assessor will also consult the insured individual regarding the exposure conditions. Should the information on exposure obtained by the assessor differ from the circumstances recorded by the insurance institution in aspects with a bearing upon the decision, the assessor may not simply base his vote upon it; he must either attempt to establish the circumstances more conclusively by consultation of the accident insurance institution, or perform an alternative assessment (*Köhler,* 1998). The alternative assessment also generally requires further investigation of the circumstances by the accident insurance institution, in order for uncertainty concerning the exposure which

is relevant to the decision to be eliminated as far as possible.

Evidence that the symptoms had already occurred during the period of exposure to solvents or at most only shortly after its cessation reinforces the argument for a causal relationship.

The test criteria for case-specific causal analysis may be summarized as follows:

1. Arguments for occupational origin are:
   - Typical clinical picture
   - High exposures (prenarcotic effects occurring repeatedly at work are indicative)
   - Long duration of exposure, generally of over ten years in the case of encephalopathy
   - Exclusion of known non-occupational causes
   - Demonstration of solvent-induced effects in other organs (consecutive symptoms)
   - Manifestation of the disease during or shortly after cessation of exposure
2. Arguments against occupational disease No. 1317 are:
   - Atypical clinical picture
   - Low exposure
   - Brief duration of exposure, particularly in the case of encephalopathy
   - Long latency period between the cessation of exposure and the onset of the disease
3. Where present, competing causes do not exclude a contributory effect from solvents; careful consideration of the overall circumstances is however necessary. Aggravation of the disease in its long-term progress following cessation of the activity presenting the risk is atypical of toxic polyneuropathy or encephalopathy, but does not exclude a contributory effect by earlier exposure to solvent.

If the exposure to neurotoxic solvents is probably the cause of or a substantial contributing factor for the clinical picture, the components of solvent inducement and non-solvent inducement cannot normally be separated, unless specific findings enable unrelated damage to be differentiated.

4 Evaluation of the reduction in earning capacity

In accordance with Volume VII, 56 of the German Social Code (SGB), insured persons are entitled to an accident insurance pension should their earning capacity be reduced by at least 20% as a result of an occupational accident or disease. A reduction in earning capacity of 10 or 15% gives rise to an entitlement to a pension when further insurance claims or equivalent compensation claims also give rise to a reduction in earning capacity of at least 10%.

The concept of the reduction in earning capacity is defined by law as follows (Volume VII 56 (2) of the German Social Code):

The reduction in earning capacity is based upon the scale of the reduced opportunity for employment on the entire labour market ensuing from the impairment in physical and mental performance.

The definition takes account of the personal impairment to health resulting from the insured damage and its repercussions for the individual's capacity for employment on the wider labour market. The reduction in earning capacity and if applicable an entitlement to a pension are assessed independently of whether the individual was gainfully employed or suffered loss of income. Since the reduction in earning capacity is measured against the opportunities for work on the wider labour market, the degree of reduction in earning capacity is also by definition independent of the occupation previously pursued and of the insured individual's current level of qualification, age, sex, and place of residence. Legacy disabilities or health impairments may result in the reduction in earning capacity being ranked higher or lower should a functional inter-action exist between the damage to health of occupational origin and the existing injury.

The medical assessor establishes the loss of functions caused by the occupational disease, evaluates the scale of the resulting impairment to performance, and submits a proposal for evaluation of the reduction in earning capacity. The insurance institution reaches its decision with consideration for this evaluation, and is responsible for the observance of statutory requirements.

Recommendations for reductions in earning capacity are based upon empirical values and are intended to contribute to the creation of consistent criteria for the assessment and evaluation of the consequences of clinical pictures which occur regularly and exhibit a typical progress.

How these criteria for evaluation of the consequences of occupational accidents and diseases are to be developed and made part of a cohesive overall assessment system is the subject of review. At the Hennef Colloquium on the subject of reductions in earning capacity, held on 10 January 2001, this issue was discussed intensively with employers' and employees' representatives and with experts from a range of disciplines in medicine, jurisprudence, and labour

market and occupational research. A general consensus was reached that tables of reductions in earning capacity constitute important sources of information. As qualified empirical values, they can be accepted when they enjoy the support of a majority of experts in the field concerned. No standardized procedure exists however by which, in particular, consideration can be given specifically to the conditions on the labour market during investigation of the degree of reduced earning capacity of particular functional impairments.

The recommendations reproduced here are based upon the consensus of the experts involved from the various disciplines. The Institute for Employment Research at the German Federal Employment Services in Nuremberg was also consulted. The result has confirmed that the scale of remaining or closed opportunities for work from which a reduction in earning capacity could be calculated cannot be deduced from statistical data.

The percentages stated below for the reduction in earning capacity are based upon the experience of the experts involved and are consistent with evaluations for comparable traumatic injury which can be found in standard works in the assessment literature. The bands indicated for encephalopathy provide scope for individual grading which is in turn necessary in order to accommodate the wide variety of forms of the brain and nerve damages under consideration.

4.1 Polyneuropathy

For estimation of the reduction in earning capacity caused by solvent-induced polyneuropathy, the significant element is the scale of the motor and in particular sensory disorders. Reflex findings and the results of the additional diagnoses obtained by technical means (e.g. EEG, neurography, needle electromyography, evoked potentials) are of secondary importance for assessment of performance, in contrast to their relevance in diagnosis.

The following are suitable guidelines:

- Very mild polyneuropathy

  Clinically minor polyneuropathy, with mild sensory disorders including irritation, without functional impairment
  Reduction in earning capacity below 10%

- Mild polyneuropathy

  Sensory disorders including irritation and/or the onset of motor disorders at the extremities, which overall do not yet essentially impair the affected person‘s ability to walk or stand
  Reduction in earning capacity 10%

- Mild to medium-severity polyneuropathy

  Sensory disorders, including adverse irritation and/or minor motor disorders with a minor impact upon the affected person‘s ability to walk or stand
  Reduction in earning capacity 20%

- Medium-severity polyneuropathy

  Pronounced sensory disorders and/or sensory irritation and distal motor disorders with a clear impact upon the affected person's ability to walk or stand
  Reduction in earning capacity 30%

Higher levels of evaluated reduction in earning capacity may only rarely occur for solvent-induced polyneuropathy.

During estimation of the reduction in earning capacity, consideration must also be given to the potential for recovery from solvent-induced polyneuropathy, on the basis of which it can be anticipated that the estimated reduction will be phased over time.

Where polyneuropathic disorders are persistent, causes unrelated to the occupational disease must be examined which compete in legal terms with the occupational cause; such causes may become more prominent as the time interval from the cessation of exposure increases.

4.2 Encephalopathy

For estimation of the reduction in earning capacity within the statutory accident insurance system, a general principle is that brain damage with a minor impairment in performance is assigned a reduction in earning capacity of 10 to 20%, that with a medium impairment in performance a reduction of 30 to 50%, and that with a severe impairment in performance a reduction in earning capacity of 60 to 100%.

As with other disorders, the estimated reduction in earning capacity for cases of solvent-induced encephalopathy must involve an overall assessment of the neurological/neuropsychological and psychopathological findings, including those from psychological tests, in terms of their impact upon gainful employment in the context of the wider labour market.

With reference to the classification of severity of toxic encephalopathy, the following bands are recommended in consideration of the evaluation criteria normally applied in the statutory accident insurance system:

- Mild encephalopathy

  Vague pattern of complaints, the pronouncement of which may be highly individual, without adequately specific changes in personality or impairments to cognitive performance of organic/psychological origin
  Reduction in earning capacity up to 10%

- Mild to medium-severity encephalopathy

  Clear subjective disorders and personality changes with motivational and affective disorders are verifiable; the personality changes may be accompanied by minor cognitive impairments in performance of organic/mental origin
  Reduction in earning capacity 20 to 30%

- Medium-severity encephalopathy

  Clear impairments in cognitive performance of organic/mental origin are confirmed. Accompanied by subjective disorders, personality changes are also generally evident. In many cases, neurological findings (atactic disorders, tremors) are also present
  Reduction in earning capacity 40 to 50%

- Severe encephalopathy

  Substantially pronounced psychopathological disorders, for example of long-term and short-term memory, attention, and also of a personality change, with further disorders of the central nervous system
  Reduction in earning capacity 60 to 100%
  This level of severity is generally unlikely with solvent-induced encephalopathy of occupational origin.

Combined clinical picture

An overall estimation of cases of solvent-induced encephalopathy and polyneuropathy is reached not by addition of the listed rates for the reduction in earning capacity, but by an overall evaluation of the performance in consideration of the various forms of functional disorder.

5 Information on rehabilitation

Following cessation of exposure, solvent-induced polyneuropathy is generally associated with gradual spontaneous recovery from the sensory disorders and the motor disorders; solvent-induced encephalopathy likewise generally exhibits a slow improvement in the disorder pattern once exposure has ceased.

Treatment is focused on the symptoms and the disorders.

The exposure to neurotoxic substances must of course cease.

The avoidance of unfavourable consumption of drinks and tobacco, and in particular alcohol is of great importance, as is the optimum treatment of concomitant diseases, particularly metabolic disorders such as diabetes mellitus, liver diseases, hyperuricemia, etc.

Physiotherapy may be beneficial in the treatment of polyneuropathy. The effectiveness of both neurotropic vitamins (vitamin B complex) and alpha-lipoic acids against solvent-induced polyneuropathy is not validated. Therapy involving drugs may in principle be indicated for adverse sensory irritation.

The form of treatment of solvent-induced encephalopathy is also selected according to the symptoms, as a function of the disorder syndrome. Neuropsychological or behavioural neurological training measures for example may particularly be considered, as may supporting psychotherapeutic measures for coping with the disease; these may be accompanied in some cases by psychopharmacological treatment, for example with thymoleptic agents in the case of depressive disorders, low dosages being prescribed in

such cases in consideration of the organic origin. Where symptoms include headaches, treatment in accordance with the procedures for the treatment of migraine may be indicated. Care should be taken to avoid secondary chronification of headaches by the regular use of painkillers.

Generally, out-patient neurological psychiatric treatment must be conducted, supported by neuropsychological and psychotherapeutic measures. Only in more severe cases will forms of in-patient treatment (particularly neuropsychological, behavioural medical, and in a supporting function psychotherapeutic) be appropriate.

No evidence exists that in-patient medical rehabilitation measures are more effective than out-patient treatment for mild encephalopathy, nor should this be expected for polyneuropathy.

Therapeutic measures should be selected in consideration of the individual case, monitored and co-ordinated by the practising neurologist if at all possible, since the most suitable treatment must be geared not only to the health disorders of the patient in question, but also to the regional circumstances. Essentially, the basic rules for neurotraumatological rehabilitation of victims of head and brain injuries may be applied.

All suitable means are employed for rehabilitation, in consideration however of their suitability and cost-effectiveness; particular consideration must be given to this aspect in the case of expensive treatment concepts the efficiency of which is not adequately validated.

6 Annex

6.1 Model for an assessment for the occupational disease No. 1317

Dear Dr ...,

Mr/Ms X is to be examined with regard to whether he/she is suffering from an occupational disease caused by exposure to organic solvents, either as single substance or as mixture.

We ask you for an expert assessment based upon your personal examination. Please inform us of the need for any additional assessments, such as neurological, psychological, neuropsychological examination, in order for us to commission them with consideration for the legislation governing the freedom of choice of assessor (German Social Code Volume VII, 200 [2]).

Please state your opinion on the following questions:

1. *What health problem is being complained about?*

2. *What is the clinical finding?*

3. *Do the results of the neurological/psychiatric examination indicate polyneuropathy/encephalopathy?*

4. *What information does the psychological examination provide on deficits and possible causes?*

5. *What diagnosis follows from the overall assessment?*

6. *Is the condition an occupational disease in accordance with No. 1317 of the list of formally recognized occupational diseases (polyneuropathy or encephalopathy caused by organic solvents, either as single substance or as mixture), and if so, what single substance or mixtures were the cause of the occupational disease?*

7. *What are the present consequences of the occupational disease?*

8. *What date can be stated for the onset of the occupational disease (first treatment or incapacity for work owing to the occupational disease)?*

9. *Since when and to what level did or does a quantifiable reduction in the capacity for gainful employment (at least 10%) exist owing to the consequences of the occupational disease? How can this reduction be graded retrospectively over time in line with the progress of the disease?*

10. *May changes in the consequences of the occupational disease be anticipated in the future, and if so, for when should a review be planned?*

11. *Are prevention or rehabilitation measures necessary, and if so, what measures do you propose?*

We request that the report of the assessment observe the recommendations for the assessment of solvent-induced occupational diseases which are published in the report on occupational disease No. 1317 in the publications of the German Social Accident Insurance (DGUV), and that detailed reasons be stated for any deviation.

Yours sincerely,

6.2 Substance-specific information and estimation of neurotoxic threshold values for the listed substances

Preliminary remarks

In Section III.3.2.2 (Level of exposure), reasons were stated why the Occupational Exposure Limit Values relevant to occupational medical prevention activity (TRGS 900 airborne limit values, MAK maximum workplace concentration values, BAT biological tolerance values) are of only limited suitability for ascertainment of whether exposure to organic solvents may in principle be capable of causing polyneuropathy or encephalopathy.

For this reason, "neurotoxic threshold values" are proposed below which serve as points of reference for the magnitude of the solvent concentrations which are to be considered.

A relationship between the "neurotoxic threshold value" and the NOEL (No Observed Effect Level) or NOAEL (No Observed Adverse Effect Level) commonly used in toxicology exists when the neurotoxicity of interest here corresponds to the level of action associated with the limit value. In all other cases, deviations are possible to the effect that the "neurotoxic threshold value" must be estimated as being higher than the NOEL/NOAEL and the limit values derived from them (TRGS 900, 903, MAK maximum workplace concentration, BAT biological tolerance value).

The "neurotoxic threshold values" are based upon publications in the relevant literature and on the latest scientific rationales for the MAK maximum workplace concentration values issued by the commission for working agents (*Greim* [ed.], 2006).

It must first be noted in this context that the body of scientific data differs widely. The data for some organic solvents are based solely on further casuistics, the generalized conclusions of which are severely limited owing to possible individual peculiarities. Conversely, comprehensive field or experimental studies have been conducted by various working groups which owing to valid records of the exposure, permit substantiated conclusions regarding the level of "neurotoxic threshold values". The inconsistent scientific quality of the publications must be taken into account where specific conclusions are drawn on a case-by-case basis.

Legacy and concomitant diseases, coexposure to other substances with neurotoxic action, both at the workplace and elsewhere, must be given appropriate consideration in

evaluation of each specific case. The extent to which the incidence of a case of occupational disease No. 1317 can be attributed to increased individual sensitivity owing to genetically determined polymorphisms of metabolizing enzymes is the subject of current and future studies.

n-Heptane

Acute exposure to n-heptane and heptane isomer vapours induces toxic effects in the central nervous system.

Whether n-heptane is capable of triggering clinically apparent polyneuropathy cannot be determined conclusively owing to the lack of systematic studies. From a toxicokinetic study on test subjects and laboratory animals it can be concluded that exposure to 2,5-heptanedione (the primary metabolite of n-heptane) resulting from n-heptane exposure of up to 500 ppm = 2,100 mg/m³ does not induce peripheral neuropathy (*Störmer et al.*, 1995).

Indicators for occupational exposure to n-heptane as a cause of chronic encephalopathy cannot be found in the literature.

Evaluation:

The lack of data prevents deduction of a "neurotoxic threshold value".

The current workplace limit value is 2,100 mg/m³ (500 ppm heptane, all isomers); a BAT value has not yet been defined (TRGS 900).

n-Hexane

Comprehensive and up-to-date rationales for the MAK maximum workplace concentration value are available for the neurotoxicity of n-hexane, most recently from 1992 and 1997 (*Greim* [ed.], 2006).

Numerous casuistic reports and epidemiological studies consistently show that n-hexane concentrations of more than 200 ppm = 716 mg/m³ induce significant changes in the peripheral nervous system.

According to a study by *Sanagi et al.* (1980), an average NOEL of 58 ppm = 208 mg/m³ (in the range between 40 and 88 ppm = 143 to 315 mg/m³) may be assumed.

Chang et al. (1993) reported subclinical signs of neuropathy at an average air concentration of 63 ppm = 226 mg/m³ (range between 30 and 110 ppm = 107 to 394 mg/m³). In addition to n-hexane, 2-propanol and toluene were present. Acute neurotoxic effects in the central nervous system involving dizziness, nausea and headaches occurred at concentrations above of 500 ppm = 1,790 mg/m³.

Longitudinal studies have shown that the prognosis for n-hexane-induced polyneuropathy is favourable following cessation of exposure. Even severe clinical symptoms, such as forms of paralysis, have improved over the course of a number of months to at most two years (*Chang*, 1990 and 1991).

No indicators exist that n-hexane is capable of causing chronic encephalopathy under the occupational exposure conditions described.

With the simultaneous presence of 2-butanone (methyl ethyl ketone), the neurotoxicity of n-hexane increases exponentially, as has been demonstrated in animal experiments (*Altenkirch et al.,* 1982 a and b; *Altenkirch,* 1998).

Evaluation:

A long-term exposure of more than 50 ppm = 180 mg/m³ is considered as the "neurotoxic threshold value" for the causing of polyneuropathy as an occupational disease.

The current workplace limit value is 180 mg/m³ (50 ppm), and the corresponding BAT value 5 mg/l of urine, determined as 2,5-hexa-nedione plus 4,5-dihydroxy-2-hexanone (TRGS 900, 903).

2-Butanone (methyl ethyl ketone)

In high concentrations, of over 500 ppm = 1,500 mg/m³, the effect of 2-butanone is acutely narcotic (for an overview, see the evaluation for the current MAK maximum workplace concentration value [2000]) (*Greim* [ed.], 2006). A chronic effect upon the peripheral and central nervous system under exposure to 2-butanone alone has not been confirmed.

2-Butanone may however exacerbate the neurotoxic effect of n-hexane or methyl-n-butyl ketone (2-hexanone).

Evaluation:

500 ppm = 1,500 mg/m³ corresponds to the "neurotoxic threshold value" for narcotic effects.

The current workplace limit value is 600 mg/m³ (200 ppm), and the corresponding BAT biological tolerance value 5 mg 2-butanone/l of urine (TRGS, 900, 903).

2-Hexanone (methyl-n-butyl ketone)

In high concentrations, 2-hexanone has a narcotic effect. Following chronic exposure, toxic polyneuropathy is possible. The cause of the peripheral neurotoxic effect is the metabolite 2,5-hexanedione which is also produced during the oxidative metabolization of n-hexane.

In a plastics plant in the USA, several cases of polyneuropathy occurred after methyl isobutyl ketone (MIBK) was replaced by methyl-n-butyl ketone (MnBK) (*Allen et al.,* 1975; *Billmaier et al.,* 1974). Atmospheric measurements conducted by the responsible health ministry revealed figures of 9.2 ppm = 38 mg/m³ and 36.0 ppm = 150 mg/m³ MnBK around the printing machines. The concentrations stated for methyl ethyl ketone are 331 and 516 ppm = 1,380 and 2,150 mg/m³.

The presumed causal relationship was subsequently confirmed by animal experiments (*Mendell et al.,* 1974).

Evaluation:

Concentrations above the current workplace limit value of 21 mg/m³ (5 ppm) are regarded as the "neurotoxic threshold value". The corresponding BAT biological tolerance value is 5 mg/l of urine, determined as 2,5-hexanedione plus 4,5-dihydroxy-2-hexanone (TRGS 900, 903).

Note:

Where the common abbreviation MBK (methyl butyl ketone) is employed, further specification is always required of the particular isomer involved.

In contrast to methyl-n-butyl-ketone, a polyneuropathy-inducing effect is not known for the isomer methyl –iso-butyl ketone (MIBK, also 4-methyl-2-pentanone). Atmospheric MiBK concentrations of 100 ppm = 416 mg/m³ or more may trigger acute narcotic effects such as headaches and dizziness (refer to the rationale for the MAK maximum workplace concentration from 1996 [*Greim* (ed.), 2006]). The workplace limit value for 4-methyl-2-pentanone is (83 mg/m³) 20 ppm.

Methanol

Methanol is particularly toxic following oral uptake. Symptoms are primarily those of a central nervous system depression and, following several hours' latency, visual impairments, which may range from a reversible colour vision disorder to irreversible blindness. Besides the vision disorders, possible consequences of severe acute methanol intoxication particularly include extrapyramidal symptoms (Parkinson's syndrome) (refer to the rationale for the MAK maximum workplace concentration value, 1999) (*Greim* [ed.], 2006). The rationale for the MAK maximum workplace concentration value states that further studies are urgently needed for validation of an NOEC with regard to the neurotoxic effects in human beings.

A historical casuistic study reported that atmospheric methanol concentrations of 1,600 to 10,900 mg/m³ = 1,200 to 8,200 ppm caused temporary blindness (*Humperdinck*, 1941).

In an experimental study performed on volunteer subjects, methanol concentrations of 200 ppm = 270 mg/m³ for four hours did not lead to any visual disorders or to neurophysiological or neuropsychological changes (*Chuwers et al.,* 1995). In another standardized experiment involving exposure for four hours to 200 ppm = 270 mg/m³ methanol, a clear drop in the spectral performance in the theta band was observed in the EEG (*Muttray et al.,* 2001). The changes in the EEG suggest an activation of the noradrenergic system (*Dimpfel and Schober,* 2001).

Exposure to methanol concentrations of 365 to 3,080 ppm = 485 to 5,000 mg/m³ (average value 1,040 ppm = 1,380 mg/m³) led to symptoms such as blurred vision, head-

aches, dizziness and vomiting in the workers (*Frederik et al.*, 1984).

Kawai et al. (1991) reported visual disorders in a group of workers who had been exposed to 3,050 and 5,500 ppm = 2,290 and 4,140 mg/m³ methanol.

The scientific literature contains no indicators that methanol is capable of triggering polyneuropathy at workplace exposure levels (for an overview, see *Kavet and Nauss*, 1990).

Evaluation:

Repeated exposure to approximately 1,000 ppm = 1,330 mg/m³ methanol and higher is regarded as the "neurotoxic threshold value". The current workplace limit value is 270 mg/m³ (200 ppm), and the corresponding BAT value 30 mg methanol/l urine (TRGS 900, 903).

Ethanol

Whereas the acute effects of ethanol following oral uptake have been comprehensively studied, relatively little results exists for the respiratory exposure occurring at the workplace (for an overview, see the rationale for the current MAK maximum workplace concentration value [1998] (*Greim* [ed.], 2006)).

According to older reports, atmospheric ethanol concentrations of 1,000 to 2,500 ppm = 1,910 to 4,780 mg/ m³ led to minor intoxication phenomena, of 7,500 ppm = 14,325 mg/m³ to drowsiness and tiredness. During an experimental study on volunteers, no significant effects of psychological performance variables (such as reaction time, short-term memory) were observed at atmospheric concentrations of up to 1,000 ppm = 1,910 mg/m³ over a total of four hours (*Seeber et al.*, 1997). Alcoholic polyneuropathy generally occurs following many years of abuse with a daily alcohol intake of at least 100 g (*Scheid,* 1983). No data exist that polyneuropathy is caused under workplace exposure conditions.

Evaluation:

The "neurotoxic threshold value" for acute effects lies above 1,910 mg/m³ (1,000 ppm). The current workplace limit value is 960 mg/m³ (500 ppm); a BAT biological tolerance value has not been specified (TRGS 900).

2-Methoxyethanol (methyl glycol)

In a series of older case studies, the incidence of neurological and psychiatric symptoms such as tiredness, headaches, tremor and amnesia were described following occupational exposure to 2-methoxyethanol (for an overview, see the rationale for the MAK maximum workplace concentration value from 1983 [*Greim* (ed.), 2006]). The symptoms were found to be reversible following cessation of exposure; the recovery times extended in some cases from several weeks to months. Data on the level of exposure associated with the incidence of the health disorders can be found in *Zavon* (1963). The author states concentrations in the breathing air from 61 to approx. 4,000 ppm = 193 to approx. 12,600 mg/m³.

The exposure data should however be interpreted with consideration for the fact that 2-methoxyethanol can be absorbed easily through the skin.

The scientific literature contains no indicators that 2-methoxyethanol causes polyneuropathy following workplace exposure.

Evaluation:

Sufficient exposure data do not exist to permit estimation of a "neurotoxic threshold value". Provided the MAK maximum workplace concentration value is observed, neurotoxic effects upon the CNS can be excluded.

The current workplace limit value is 16 mg/m³ (5 ppm); a BAT value has not been defined (TRGS 900).

Benzene

Information on the acute neurotoxicity of benzene is found in the older literature, according to which acute intoxication occurred leading to narcotic effects and unconsciousness at relatively high concentrations of several "100 to 1,000 ppm = 325 to 3,250 mg/m³" (cited from the rationale for the MAK maximum workplace concentration value for 1971 [*Greim* (ed.), 2006]). The Chinese literature on this subject states that exposure levels of 50 to 150 ppm = 160 to 490 mg/m³ led to drowsiness and headaches; unconsciousness and fatal intoxication occurred following exposure to approximately 1,500 ppm = 4,880 mg/m³ to 20,000 ppm = 65,000 mg/m³ (cited from *Irons and Gross,* 2002).

The scientific literature contains no concrete indicators that benzene causes polyneuropathy under workplace exposure conditions (for an overview, see *Irons and Gross,* 2002).

Compared to the acute effect upon the central nervous system, hemotoxic and geno-toxic effects may be observed at substantially lower concentrations. At the prevailing exposure, i.e. with observance of the former technical guidance concentrations of 1 ppm/2.5 ppm = 3 mg/m³/8 mg/m³, acute neurotoxic effects can be excluded.

Evaluation:

Since sufficient valid data are not available, deduction of a "neurotoxic threshold value" is not possible. Observance of the formally valid technical guidance concentrations provides reliable protection against neurotoxic effects.

Toluene

Comprehensive scientific literature is available concerning the toxicity of toluene in humans which was evaluated in 1993 in the rationale for the MAK maximum workplace concentration value (*Greim* [ed.], 2006).

At high concentrations, toluene vapours cause acute headaches, dizziness, nausea, and even somnolence and loss of consciousness.

Numerous epidemiological and casuistic reports are available concerning chronic exposure. It can be concluded that no

specific clinical picture exists, particularly for the neurotoxic effects following chronic toluene intoxication.

The primary symptoms are vague subjective complaints such as tiredness, lethargy, loss of appetite, nausea, headaches, nervousness and insomnia. It is important to note that no scientific indicators exist for a peripheral neurotoxic effect of toluene. With the exception of isolated casuistic studies, the numerous epidemiological studies employing sensitive study methods for the peripheral nervous system report no accumulation of polyneuropathic symptoms or diseases (for an overview, see *Triebig,* 1998). Recent findings show that the polyneuropathy diagnosed in substance abusers are attributable to the n-hexane contained in the solvent mixtures.

In animal experiments, reduced nerve conduction velocities were reported at 200 ppm = 770 mg/m³ and 1,000 ppm = 3,830 mg/m³; these normalized again following cessation of exposure, however. Polyneuropathy did not arise in the animal experiments, however (refer to the rationale for the MAK maximum workplace concentration value for 1985 [*Greim* (ed.), 2006]).

Neuropsychological methods were used to investigate the incidence of subjective disorders and cognitive changes in a number of exposure studies conducted on volunteer subjects (*Andersen et al.,* 1983; *Echeverria et al.,* 1989; *Olson et al.,* 1985; *Iregren et al.,* 1986; *Baelum et al.,* 1985; *Dick et al.,* 1984; *Winneke,* 1982). The studies consistently report that several hours' exposure to up to 100 ppm = 380 mg/m³ caused subjective complaints such as headaches and tiredness; relevant cognitive impairments were however not observed.

The results of epidemiological studies, particularly of printers exposed to toluene, have yielded information on impairments to performance associated with exposures of around 88 ppm = 337 mg/m³ (*Kempe et al.,* 1980; *Foo et al.,* 1990; Iregren, 1982; *Ørbæk and Nise,* 1989).

A multi-centre study conducted recently in the German rotogravure industry found no clear adverse effects, including in the central nervous system, among printers subject to many years' exposure (*Gericke et al.,* 2001; *Neubert et al.,* 2001). A 5-year longitudinal study in the German rotogravure industry involving four repeat examinations yielded no evidence of cognitive, sensory (hearing, colour discrimination, balance) or other health effects or of subjective symptoms clearly attributable to toluene (*Seeber et al.,* 2002; *Zupanic et al.,* 2002). Exposure levels in this study were in the order of prevailing values of on average 25.7 ± 20.1 ppm = 98.4 ± 77.0 mg/m³ over the five years observed, whereas past exposure of on average 59 ppm = 226 mg/m³ was measured over 21 years in a group subject to "high" and "long" exposure.

Chouanière et al. (2002) studied printers who had been chronically exposed to toluene concentrations of up to 27 ppm = 103 mg/m³. Neurotoxic symptoms did not

correlate significantly with the instantaneous exposure. No relationship was observed between the cumulative exposure and the psychometric test results or the neurotoxic symptoms.

Evaluation:

Concentrations of 80 ppm = 306 mg/m³ or higher are regarded as the "neurotoxic threshold value" for chronic effects in the central nervous system. This value corresponds to approximately 1.5 mg of toluene per liter of blood, the blood samples being taken at the end of the shift or exposure.

The current workplace limit value is 190 mg/m³ (50 ml/m³), and the corresponding BAT biological tolerance value is 1 mg of toluene/l of blood (TRGS 900, 903).

Xylenes (all isomers)

Comprehensive scientific literature exists concerning the toxicity in humans and in particular the neurotoxicity of the three xylene isomers which under workplace conditions generally occur as mixtures (see the rationales for the MAK maximum workplace concentration and BAT biological tolerance values [1983, 1984, 1986, 1998, 2001] (*Greim* [ed.], 2006)).

Xylene vapours have an acute narcotic effect; as a function of their concentration, they cause uncharacteristic symptoms such as headaches, drowsiness and concentration disorders.

Studies under controlled exposure conditions have shown that atmospheric concentrations of between 90 and 460 ppm = 400 and 2,030 mg/m³ may lead to balance disorders, extension of reaction times, and subjective disorders (*Gamberale et al.*, 1978; *Savolainen et al.*, 1980). Respiratory exposure to approximately 80 ppm = 350 mg/m³ xylene did not lead to a measurable change in cognitive performance (*Olson et al.*, 1985). *Laine et al.* (1993) exposed volunteer subjects to 200 ppm = 880 mg/m³ xylene and measured a number of neurophysiological parameters (body sway, reaction times). The effects were only minor in their pronouncement, and could not be differentiated clearly from the physiological variation in the parameters.

Physical activity has a considerable influence upon the internal xylene exposure. Even during light physical work, blood levels in the region of 200 to 300 ppm = 880 to 1,320 mg/m³ may be attained under rest conditions at atmospheric concentrations of 100 ppm = 440 mg/m³ xylene (*Laine et al.*, 1993).

The results of epidemiological cross-sectional studies in which more pronounced symptoms were reported are not conclusive, owing to the inadequate consideration given to confounders (*Chen et al.*, 1994; *Uchida et al.*, 1993).

The experience with human subjects and the results of animal testing consistently confirm that xylene does not cause polyneuropathy under typical workplace exposure conditions.

Evaluation:

A xylene concentration of 100 ppm (440/m³) is proposed as the "neurotoxic threshold value". This value takes account of the physical activity in the workplace situation.

The current workplace limit value is 440 mg/m³ (100 ppm), and the corresponding BAT biological tolerance value 1.5 mg of xylene/l of blood or 2,000 mg of methyl hippuric acid/l of urine (TRGS 900, 903).

Styrene

Comprehensive scientific literature exists on the acute and chronic neurotoxicity of styrene (refer to the rationales for the MAK maximum workplace concentration and BAT biological tolerance values [1983, 1987, 1998] (*Greim* [ed.], 2006)).

In the context of a literature survey, *Dick* (1988) evaluated the results of neuropsychological studies and concluded that at styrene concentrations of up to 50 ppm = 210 mg/m³, no relevant psychomotor effects need be anticipated.

In their critical literature study, *Rebert and Hall* (1994) concluded that owing to differences between the test methods, obtaining a coherent picture of acute styrene effects poses difficulties. If the neuropsychological test methods are considered, it can be concluded that styrene concentrations of 100 ppm = 430 mg/m³ and possibly of 200 ppm = 860 mg/m³ must be exceeded before measurable effects are caused (*Rebert and Hall,* 1994).

The available results concerning the effect of styrene upon the peripheral nervous system are inconsistent. Whereas some studies reported neurophysiological abnormalities, other authors observed no changes in the nerve conduction velocities (*Cherry and Gautrin,* 1990; *Lilis et al.,* 1978; *Murata et al.,* 1991; *Rosén et al.,* 1978; *Seppäläinen and Härkönen,* 1976; *Triebig et al.,* 1985). In this context, the result of a longitudinal study is relevant in which no evidence was found of an exposure-effect relationship with regard to nerve conduction velocities (*Triebig et al.,* 1985).

Several studies reported an elevated risk of sub-clinical colour vision disorders following chronic styrene exposure (*Campagna,* 1995; *Chia et al.,* 1994; *Eguchi et al.,* 1995; *Fallas et al.,* 1992; *Gobba et al.,* 1991; *Iregren et al.,* 2005; *Mergler et al.,* 1996; *Triebig et al.,* 2001). Even if allowance is made for the deficiencies of particular studies, the results permit confirmation of a correlation between chronic styrene exposure, measured for example with the aid of an exposure index, and the indicator for acquired colour-vision disorder in the form of the Colour-Confusion Index (CCI) (*Muttray et al.,* 1993). The exposure level at which changes can be confirmed clearly is not certain at this time. The studies conducted by *Kishi et al.* (2001) and *Iregren et al.* (2005) indicate that an impairment in colour vision is possible even at atmospheric concentrations of less than 20 to 30 mg/m³ = 5 to 7 ppm.

A metaanalytic evaluation of ten studies revealed major variation in the magnitude of colour-vision disorder and, contrary to expectations, no common negative effect following exposure to styrene (*Paramei et al.,* 2004). As causes of the inhomogeneity, the authors discuss a number of confounders, including the lighting situation, gender influences, alcohol consumption and smoking.

Several studies address the issue of the reversibility of colour-vision disorders, but differ in their results (*Gobba and Cavalleri,* 2000; *Mergler et al.,* 1996; *Castillo et al.,* 2001; *Triebig et al.,* 2001). Whereas *Triebig et al.* (2001) report a statistically significant improvement in the CCI following a four-week interruption to exposure (holiday), the other studies found weak or no change.

Evaluation:

A concentration of 50 ppm (210 mg/m³) is regarded as the "neurotoxic threshold value" for effects upon the central nervous system. Colour-vision disorders were not considered in this context, since their significance cannot be assessed conclusively at the present time.

The current workplace limit value is 86 mg/m³ (20 ml/m³), the corresponding BAT biological tolerance value 600 mg amygdalic acid and phenyl glyoxylic acid/g creatinine in the urine (TRGS 900, 903).

Dichloromethane (methylene chloride)

Dichloromethane (DCM) has an acute depressive effect upon the central nervous system as a function of the amount of exposure. It was used in the past as an inhalation anaesthetic. The neurotoxicity of dichloromethane is determined by the incidence of carbon monoxide produced during metabolization.

The MAK maximum workplace concentration value for dichloromethane of 100 ppm = 350 mg/m³ was defined in 1981 on the grounds that the carbon monoxide-haemoglobin level must be maintained below 5%. In 2000, the MAK maximum workplace concentration value was suspended owing to the proven genotoxic action (Category 3 A).

In experimental studies, toxic effects upon the CNS, such as impaired attention and a drop in the flicker fusion frequency, were demonstrated at atmospheric concentrations of 300 to 800 ppm = 1,060 to 2,820 mg/m³ (*Winneke and Fodor,* 1970).

Gamberale et al. (1975) observed no influence upon mental performance following 30-minute exposure to 22, 400, 800 and 1,000 ppm = 78, 1,410, 2,820, 3,530 mg/m³ DCM.

In another study, changes in CNS performance were detected only above 1,000 ppm = 3,530 mg/m³ (*Stewart,* 1972).

Lash et al. (1991) studied a cohort of 1,758 mechanics previously exposed to DCM. When potential confounders were considered, no significant differences in mental performance were found in comparison with a control group. Atmospheric measurements at the former workplaces revealed average concentrations of 100 to 200 ppm = 350 to 700 mg/m³, with a maximum value of 800 ppm = 2,820 mg/m³. No concrete indicators exist that DCM causes polyneuropathy in human beings (*Kunath and Irmer,* 1979).

Evaluation:

300 ppm (1,060 mg/m³) is proposed as the "neurotoxic threshold value".

Trichloroethylene

Comprehensive scientific literature is available on the evaluation of the toxicity in humans, particularly the neurotoxicity, of trichloroethylene (refer to the rationale for the MAK maximum workplace concentration and BAT biological tolerance values [1976, 1980, 1997, 2000, 2001] (*Greim* [ed.], 2006)).

Acute neurotoxicity, i.e. narcotic effects occur above 200 ppm. Trichloroethylene is addictive and can result in mental dependence (sniffing syndrome). In field studies, particularly that by *Grandjean et al.* (1955), symptoms of a "psychoorganic syndrome" were observed at average atmospheric concentrations of 100 ppm = 540 mg/m³.

Attention is drawn to the alcohol intolerance following chronic exposure to trichloroethylene.

Konietzko et al. (1975) reported significant impairments to psychomotor performance in workers with chronic exposure to trichloroethylene at levels of approximately 50 ppm to 100 ppm = 270 bis 540 mg/m³.

No impairment in mental performance was detected in voluntary subjects exposed to an average of 100 ppm = 540 mg/m³ trichloroethylene for six hours per day on five successive days (*Triebig et al.,* 1976).

A number of case descriptions have reported the incidence of neuropathy of cranial nerves (trigeminal nerve, facial nerve) following high exposure to trichloroethylene (*Buxton and Hayward,* 1976; *Feldman et al.,* 1970; *Mitchel and Parsons-Smith,* 1969). Decomposition products of the trichloroethylene (such as dichloroacetylene) and stabilizers of the industrial product were discussed as the cause (*Henschler et al.,* 1970). A virus infection (herpes simplex) is also a possible differential diagnosis for the symptoms of the disease (*Cavanagh and Buxton,* 1989).

Field studies of employees with chronic exposure to trichloroethylene revealed no indication of impairment of the peripheral nervous system under the exposure conditions stated (atmospheric concentration up to 70 ppm = 380 mg/m³) (*Triebig et al.,* 1978 and 1982). The measured motor and sensory nerve conduction velocities did not exhibit any dose-effect relationship.

In a group of 31 printers with several years' exposure of trichloroethylene, only minor effects, if any, were observed upon the motor and sensory nerve conduction velocities (*Ruijten et al.,* 1991). A relationship with the cumulative duration of exposure was not reported in a group of 30 workers who were examined owing to solvent-induced encephalopathy. None were found to be suffering from polyneuropathy caused by exposure to trichloroethylene (*Albers et al.,* 1999).

Evaluation:

A concentration of 50 ppm (270 mg/m³) is proposed for the "neurotoxic threshold value" for effects upon the central nervous system.

The scientific literature contains no validated evidence that trichloroethylene is capable of causing polyneuropathy.

1,1,1-Trichloroethane

1,1,1-Trichloroethane has a depressive effect upon the central nervous system.

A current rationale for the MAK maximum workplace concentration value from 2001 is available in this context (*Greim* [ed.], 2006).

Acute exposure to 1,1,1-trichloroethane above approximately 5,000 = 27,700 mg/m³ ppm causes deep narcosis. Conversely, concentrations of 200 ppm or 250 ppm = 1,100 mg/m³ or 1,400 mg/m³ are not associated with narcotic effects.

In the course of several experimental studies, extended reaction times were observed upwards of 175 ppm/400 ppm = 970 mg/m³/2,220 mg/m³ (*Gamberale and Hultengren,* 1973; *Laine et al.,* 1996; *Mackay et al.,* 1987; *Savolainen et al.,* 1981). *Muttray et al.* (2000) reported EEG changes and increased tiredness in an exposure study involving a 1,1,1-trichloroethane concentration of 200 ppm = 1,100 mg/m³ over four hours. Other authors, albeit employing different methods, observed no EEG changes at these exposure levels (*Laine et al.,* 1996).

With one exception, no consistent findings are available which substantiate a peripheral neurotoxic effect. The reduced amplitudes in the sural nerve described by *House et al.* (1994) are difficult to assess in terms of their significance and etiology. The woman who complained of paresthesia in the feet had occupational contact with 1,1,1-trichloroethane which contained 1% to 5% dimethyl ether. The measured motor and sensory nerve conduction velocities were normal. Repeat examinations revealed an improvement in the sensory amplitudes. The level of exposure was not indicted by the authors (*House et al.,* 1994).

Schaumburg (2000) does not list 1,1,1-trichloroethane as a substance with peripheral neurotoxic action.

Evaluation:

A concentration of 200 ppm (1,100 mg/m³) is proposed as the "neurotoxic threshold

value" for an acute effect upon the CNS. The current workplace limit value is 1,100 mg/m³ (200 ml/m³), and the corresponding BAT value 550 µg trichloroethane/l of blood (TRGS 900, 903).

Tetrachloroethylene (perchloroethylene)

The toxicity/neurotoxicity of tetrachloroethylene in humans is described in detail in the scientific rationales for the MAK maximum workplace concentration and BAT biological tolerance values from the years 1961, 1982 and 1997 (*Greim* [ed.], 2006).

In an experimental study, the test subjects complained of drowsiness, nausea, dizziness and headaches after seven hours' exposure to 100 ppm = 690 mg/m³. The *Romberg* test is described as abnormal (*Stewart et al.,* 1970).

In 26 employees in dry-cleaning businesses (exposure to 21 ppm for an average of 6.4 years), no significant differences were observed in 17 out of 22 symptoms in comparison with control persons. Psychomotor tests revealed no deficits in the exposed persons (*Lauwerys et al.,* 1983).

A study of 101 employees in dry-cleaning shops revealed differences in numerous neuropsychological variables compared to a control group; in the comparison between employees with low (12 ppm = 83 mg/m³) and high (53 ppm = 365 mg/m³) exposure, however, no significant dose-effect relationship was observed (*Seeber,* 1989).

Significant impairments in performance with increasing cumulative exposure were observed in 65 dry-cleaners divided into three groups of differing exposure (11 ppm, 23 ppm, 41 ppm = 76, 160, 280 mg/m³). The same could not be demonstrated for the current exposure; the symptoms stated did not differ significantly (*Echeverria et al.,* 1995).

The results of a controlled trial with exposure to 10 and 50 ppm = 69 and 345 mg/m³ were inconsistent (*Altmann et al.,* 1990 and 1992). Whereas vigilance, eye and hand co-ordination and simple reaction times were significantly poorer at higher exposure, the same was not observed for the psychomotor speed or in the learning and memory tests.

In conclusion, it may be said that in several studies, the employees exposed to tetrachloroethylene complained about more symptoms. Significant impairments in neuropsychological performance could not be demonstrated consistently. Since statistically significant dose/concentration-effect relationships were not demonstrated in any of the studies, a concluding evaluation for atmospheric concentrations below 50 ppm = 345 mg/ m³ was not possible (*Greim* [ed.], 2006).

With the exception of casuistic reports, the scientific literature contains no concrete indications that tetrachloroethylene gives rise to polyneuropathy in humans under workplace conditions. The ten cases of intoxication described by *Lob* (1957) – in two cases, the author assumes permanent damage of

the vegetative centres and of the central and peripheral nervous system – cannot be a ssessed further owing to the limited diagnostic and etiopathogenetic confirmation.

Evaluation:

A concentration of 50 ppm (345 mg/m³) is proposed for the "neurotoxic threshold value" for the central nervous system.

6.3 Estimation of neurotoxic threshold values for exposure to organic solvent mixtures

6.3.1 Objective

At this point, threshold values for neurotoxic effects resulting from exposure to organic solvents will be evaluated in the context of a literature survey.

A differentiation is necessary between:

A: Acute effects, which occur during or at the end of a working shift

B: Chronic effects, which may be observed following many years' exposure

To evaluate a threshold value, the "neurotoxicity endpoint" must first be defined. With reference to the different levels of severity of toxic encephalopathy, the following endpoints may be considered:

1. Typical subjective disorders with no objectively demonstrable loss of important CNS functions (cognition, psychomotor functions) (system level)

2. Typical subjective disorders and demonstrable loss of important CNS functions, without neurological dysfunctions (ataxia, tremor, neuropathy) (function level)

3. Neurological and psychiatric diagnosis according to ICD/DMS with a considerable criterion for the condition (disease level)

Sufficient data for further evaluation are available only for the endpoints stated under Points 1 and 2.

Older epidemiological studies describe an elevated morbidity for neuropsychiatric diseases. This yielded important information with regard to occupations under risk (*Axelson et al.,* 1976; *Lindström et al.,* 1984; *Olsen and Sabroe,* 1980; *van Vliet et al.,* 1989; *Riise and Moen,* 1990; *Mikkelsen,* 1980; *Gregersen et al.,* 1987; *Guberan et al.,* 1989; *Brackbill et al.,* 1990). These studies are however not suitable for the estimation of neurotoxic threshold values, since the necessary quantitative data on the solvent exposure are missing.

It was therefore necessary to conduct a literature survey in order to identify studies in which the substance exposure was adequately documented. The studies under consideration must satisfy modern scientific quality criteria. This particularly

applies to selection criteria, confounding and bias.

The diagnosis of "polyneuropathy" is of lesser relevance for the solvent mixtures considered here. Some studies have made isolated reference to changes in the area of the peripheral nervous system, such as retarded nerve conduction velocities (*Seppäläinen et al.,* 1985; *Ruijten et al.,* 1994). These could not however be confirmed in other studies. At this time, the available data cannot therefore be considered consistent (*Ørbæk et al.,*1985; *Triebig* [ed.], 1986 and 1989; *Nasterlack et al.,* 1997). Exposure data, on the basis of which possible "threshold values" for the peripheral nervous system could be discussed, are also generally lacking.

In the context of evaluation of solvent mixtures, interactions between the individual components are possible which concern both toxicokinetic and toxicodynamic aspects (*Alessio et al.,* 1994; *Ballantyne,* 1985). The interactions of interest in this context can be classified as follows:

A Additive: the overall effect is the sum of the individual effects

B Synergistic: the overall effect is greater than the sum of the individual effects

C Potentiating: the effect of a less toxic substance is increased by the presence of another substance

D Antagonistic: the overall effect is lower than the sum of the individual effects

E Independent: no interaction occurs between the discrete substances

With few exceptions (such as n-hexane and methyl ethyl ketone), the action of the solvent components is primarily assumed to be additive. With complex solvent mixtures, however, synergistic neurotoxic effects must be anticipated (*Alessio et al.,* 1994). The existing data do not suffice as a basis for the substantiation of concrete conclusions, however.

6.3.2 Method

In a literature survey conducted in a number of databases (MEDLINE, TOXLINE, SOZMED, Current Contents) and with reference to more recent literature surveys, approximately 100 publications were identified for the period from 1980 to the end of 2002 under the keywords neurotoxicity, central nervous system, organic solvent mixtures and occupational exposure (*Gamble,* 2000; *Ritchie et al.,* 2001; *Spurgeon,* 2001).
The selection process included following criteria:

- Chemical definition of the solvent mixture with indication of the main components
- Indication of the solvent concentrations in the air at the workplaces studied and/or evaluation with reference to the atmospheric limit values in force at the time of the study (MAK, TLV etc.)

- Retrospective assessment of the solvent exposure based upon work histories, classification of the task, historical measurement data, etc.
- Use of standardized neuropsychological test methods or questionnaires of symptoms
- Inclusion of an adequate control group (cross-sectional study) (exception: longitudinal study)
- Clear indication of the time of examination, e.g. before, during or after the shift
- Consideration of relevant confounders (e.g. age, academic/vocational training, premorbid intelligence quotient, alcohol consumption, medication intake)

Due to the heterogeneity of solvent mixtures, a comparison is only possible on the basis of so called evaluation and exposure indices.

The Current Exposure Index (CEI) is employed for estimation of the solvent exposure at time of examination. This index is calculated from the air concentrations of the discrete substances according to the summation formula as stated for example in the technical rules TRGS 900 or TRGS 403 or by the American Conference of Governmental Industrial Hygienists (ACGIH).

The CEI is calculated as follows:

$$CEI = \frac{C1}{LV_1} + \frac{C_2}{LV_2} + \frac{C_n}{LV_n}$$

C_1 = atmospheric concentration of substance 1

LV_1 = limit value (TRGS 900) of substance 1

The sum index for mixtures is defined at this point by formation of the Current Exposure Index (CEI) in accordance with the technical rules TRGS 900/TRGS 403. Neurotoxic threshold values may be used in place of the limit value if available for all substance in the summation. If however, as is the case for the majority of neurotoxic substances (beyond those stated in the scientific rationale), no threshold values exist, only limit values can be used. Threshold and limit values should not be mixed, as comparability of the CEI between different mixtures is not otherwise possible.

For quantification of the chronic exposure, a Chronic Exposure Index (CREI) is frequently formed; this can be calculated as the product of the Current Exposure Index (CEI) and the duration of the exposure in years. The CREI may be employed for example for estimation of exposure-effect relationships.

An alternative procedure is the formation of groups exhibiting different chronic exposures based upon exceeding or otherwise of the CEI and the duration of exposure, for example dichotomized by less than ten years and more than ten years. A number of aspects/constraints must be considered during estimation of the chronic exposure.

Firstly, the solvent mixtures vary widely in their composition; as a result, a consistent exposure situation cannot be assumed.

Secondly, past exposure must be estimated, since objective measurement data are not available.

Thirdly and finally, the level of solvent exposure has been reduced in the past at many workplaces.

A recently published literature study on this subject found that the atmospheric concentration of hydrocarbon solvents during various tasks, for example those performed by painters, lacquerers, floor-layers and printers, fell on average by a factor of four between 1960 and 1998 (*Caldwell et al.,* 2000). In addition, analysis of the data revealed that since 1980, the atmospheric concentrations have been around 40% below the limit values.

A study at painters' workplaces in the Netherlands came to a similar conclusion (*Burstyn and Kromhout,* 2002). The authors report that toluene measurements performed between 1980 and 1999 show the concentration to have fallen by a factor of 11. This is essentially the result of paints containing solvents being replaced by water-based products. Comparable observations have been made with styrene exposure during the lamination and puttying of reaction resins. For measurements of metabolites of the styrene in the urine (amygdalic acid as the degradation product), reductions to 50% of the initial value were shown over a period of 20 years (*Welp et al.,* 1996; *Gong et al.,* 2002). In the printing industry, too, in rotogravure printing involving toluene exposure, reductions in exposure to approximately 20% of the original value have been observed over the last 25 years in France, Denmark and Germany (*Chouanière et al.,* 2002; *Eller et al.,* 1999; *Seeber et al.,* 2004).

In view of this fact, a risk exists of former exposure being underestimated and thus of the chronic neurotoxicity being overestimated if only the current exposure data are used for its evaluation.

Despite the complex interrelationship between the products of interest here, the number of quantitatively relevant discrete substances is generally limited to a few essential components. Studies conducted in a number of countries show the following solvents to be those most commonly found in paints, thinners, adhesives and cleaning agents (*Seedorff and Olsen,* 1990; *Ikeda,* 1992; *Anger,* 1987):

- Aromatic hydrocarbons: toluene and xylene
- Alcohols: ethanol, propanol and 1,2-ethanediol
- Esters: butyl acetate and ethyl acetate
- Ketones: acetone, methyl ethyl ketone and methyl isobutyl ketone
- Mineral turpentines

The most frequently encountered solvents, are neurotoxic to humans according to the scientific rationale of the occupational disease No. 1317 in the context of the occupational disease legislation. For a subset of the solvents listed (propanol, butyl acetate, ethyl acetate, acetone and 1,2-ethanediol) and a series of other solvents not listed here owing to their low de-facto relevance, neurotoxic effects are assumed in the rationale for the MAK maximum workplace concentration values and by *Konietzko et al.* (2000) which, however, are less relevant in terms of their proven neurotoxic effect at the current state of knowledge. If the substances with proven neurotoxic action as identified as validated in the scientific rationale for occupational disease No. 1317 (see Section II.1., Table 1, and the listing in Section III.3.2.1) are considered accordingly, these substances account for around 30% to 90% of the sum concentration. Of particular de-facto importance in this context are toluene, xylenes, and 2-butanone (= methyl ethyl ketone).

Mineral turpentines and special boiling-point gasolines are complex hydrocarbon mixtures which are refined/distilled from crude oil. They are defined in terms of their boiling-point range (*Elstner et al.,* 1998).

6.3.3 Results and discussion

6.3.4 Acute neurotoxic effects

Only the studies conducted by *Olson* (1982), *Muijser et al.* (1996) and *Dietz et al.* (1999) may be employed for the evaluation of acute neurotoxic effects. These studies fulfill the essential criteria for the method, i.e. the study was performed at the end of a working shift.

The cross-sectional study, *Olson* (1982) studied 47 workers of a paint production, nine of whom were cleaners with higher exposure. For the latter group, a CEI of 2.94 is stated; for the remaining 38 persons, the CEI is 0.35. The symptoms recorded by means of the Q 16 questionnaire are significantly higher among the cleaners than those for a control group (5.9 vs. 2.1). For the group of the other employees, the difference is not significant (4.8 vs. 3.9).

In the psychomotor tests, a significantly longer reaction time in the cleaners group is reported. The same difference cannot be confirmed for workers with lower exposure. In a field study, *Muijser et al.* (1996) conducted a psychometric study (NES test battery) of a total of 89 floor-layers before and after the working shift. Based upon the reported average shift values and the maximum values for toluene, cyclohexane, ethyl acetate and n-heptane, an average CEI of 0.7 is calculated, with a maximum of 2.2. Comparison of the psychometric findings obtained at the end of the working shift revealed no significant differences suggesting an acute effect of the solvents.

Dietz et al. (1999) reported the results of a longitudinal study among painters, lacquerers and printers. The average CEI was 0.27 (± 0.44). The neuropsychological findings (reaction times, information processing speed, memory span) recorded at the end of

the shift showed no differences as a function of the exposure from those at the beginning of the shift. An analysis of correlation yields no relationship between the acute solvent exposure and the neuropsychological findings.

From these findings the following conclusions can be drawn:

I. At Current Exposure Index (CEI) of 0.5 to 1.0, acute symptoms may occur. Objectively measurable impairments of important CNS functions (psychomotor functions, cognition) are unlikely.

II. Acute symptoms may generally be observed at an CEI above 1.0. Slight dysfunctions of CNS are possible.

6.3.5 Chronic neurotoxic effects

The main results of twelve studies published between 1985 and 1999 are summarized in Table 30. The studies exclusively concerned active employees with chronic exposure to solvents. The workers were predominantly painters and employees in the paint production.

Table 30:
Overview of the results of the studies indicating sufficient data on exposure and effects

Author	Exposed persons	Average duration of exposure (years)
Cherry et al. (1985)	44 spray painters	12
Ørbæk et al. (1985)	50 paint producers	15 (5-46)
Bolla et al. (1990) *Bleecker et al.* (1991)	187 paint producers	15 ± 7
Ng et al. (1990)	78 printers, lacquerers, paint producers	9 (1-41)
Spurgeon et al. (1994)	110 paint producers	–
Lundberg et al. (1995)	135 painters	5-36
Nasterlack et al. (1997)	401 painters	26 (10-46)
Tsai et al. (1997)	325 paint producers	7 ± 8
Lee et al. (1998)	40 women in footwear manufacture	–
Myers et al. (1999)	228 paint producers	14 ± 7
Dietz et al. (1999)	127 painters, lacquerers, printers	15 ± 12

Criteria for the inclusion of studies are:

- A sufficiently long period without exposure (at least eight hours) before examination, to exclude acute effects
- Results of solvent concentration in the air at the present workplaces, and the exposure indices (CEI and CREI) deduced from them

Most studies report significant differences compared to an adequate control group for both the symptom and function levels.

Exceptions are the studies by *Spurgeon et al.* (1994) and *Myers et al.* (1999), in which no statistically significant differences for the two target variables are reported. Relevant in comparison with the other studies however is that the solvent exposure levels were below the atmospheric limit values.

With a few exceptions, it can be concluded from the studies that differences on the functional level were associated with an CEI which includes/exceeds the value of 1.0.

The studies by *Bolla et al.* (1990) and by *Bleecker et al.* (1991), in which the same cohort was studied, do not permit clear interpretation owing to the deviations in their results. It may be concluded that although exposure-effect-relationships were identified for neuropsychological variables, no typical symptoms of a clinical picture

CEI	CREI	Significant differences		Exposure-effect-relationships
		Symptoms	Functions	
0.67 (0.24-1.1)	7.8 (2.8-12.9)	Yes	Yes	No
0.1-4.5	16 (1-68)	Yes	Yes	Yes
‹ LV	–	No	Yes	Yes
0.39 9% ‹ 1.0	3.7	Yes	No	No
‹ LV	–	No	No	No
1	4.6-36.5	Yes	No	Yes
0.1-0.6	0.3-14.8	Yes	No	Yes
0-7.6	0-66	–	No	Yes
0.5-2.4	–	–	Yes	Yes
0-1.0	0-32	No	No	No
0.27 ± 0.44	3.9	–	–	Yes

associated with solvent exposure were found. The neuropsychological changes were also interpreted as "subclinical" (*Bleecker et al.,* 1991).

For evaluation of chronic neurotoxic effects, it can be stated that neurological symptoms of the kind which may be present in the medium and severe forms of toxic encephalopathy are not reported in the studies.

Based upon their study of 40 female footwear production workers in Korea who were subject to solvent exposure, *Lee et al.* (1998) conclude that the "chronic exposure index" is more valid for estimation of the hazard than is for example the duration of employment. In this study, neuropsychological changes were associated with an exposure duration of more than ten years.

This estimation is consistent with earlier empirical epidemiological experiences in that periods of less than ten years may be considered only in exceptional cases to be a cause of solvent-induced chronic encephalopathy (disease level).

A significantly increased risk for neuropsychiatric diseases has been identified for workers who were exposed to organic solvents for an average of 20 to 30 years (*Axelson et al.,* 1976; *Flodin et al.,* 1984; *Lindström et al.,* 1984; *Rasmussen et al.,* 1993).

In addition to the studies listed in Table 30, further publications require brief discussion.

Daniell et al. (1999) examined 69 painters who on average had been in retirement for five years. In comparison with a control group (joiners), painters with high cumulative solvent exposure showed differences in terms of their visuomotor speed, motor abilities, and to a small degree in their attention and memory performance. The chronic exposure was evaluated according to the working hours, work techniques and the use of protective measures. This is however not identical to the "Chronic Exposure Index" employed here.

Nilson et al. (2002) conducted a longitudinal study of floor-layers, who were examined after an interval of 18 years. In comparison with a control group, no significant changes (general intelligence, visuomotor abilities, attention) were detected for the group of floor-layers. If, however, consideration is given to a subgroup with higher exposure as estimated from the quantities of adhesives used, neuropsychological changes were observed for attention and for visual memory.

Attention is also drawn to the result of a longitudinal study conducted on active solvent exposed workers (*Dietz et al.,* 1999). The occupational medical and neuropsychological study of 127 workers before the shift revealed no exposure-effect relationship with regard to the subjective complaints (Q 16 modified). For the neuropsychological variables (current intelligence quotient, information processing speed, memory span, trailmaking test, reaction times), significant correlations were observed

between the Chronic Exposure Index (average = 3.9) and certain variables. It is important to note that the neuropsychological findings are within the normal reference values. A measurable influence of the solvent exposure upon cognitive performance cannot be verified.

The results of the study by *Dietz et al.* (1999) are consistent with the assumption that in general, high solvent exposures over a longer period are required before impairments to cognitive performance may occur.

Finally, the results of the study by *Muijser et al.* (1996) should be mentioned. The authors conducted a psychometric study (NES test battery) of 77 floor-layers and 71 control persons before the working shift. After controlling for known confounders, they found a significant difference in memory functions. Since the floor-layers performed better than the control persons, however, a solvent effect can be excluded. The authors conclude that the study found no indicators of persistent neuropsychological deficits.

However, it has to be mentioned that a Chronic Exposure Index cannot be stated, nor can it be calculated, since the duration of eposure is not indicated.

In the discussion of empirical observations to date, the fact must be considered that as yet, a consistent pattern of neuropsychological findings has not been observed and that only limited indicators exist that workers with longer and higher solvent exposure exhibit more neuropsychological changes than persons subject to lower exposure. The wide range of neuropsychological methods and questionnaires makes it difficult to compare the results of different studies directly.

6.3.6 Conclusions

Due to the heterogeneity of the studies and the lack of exposure data, the evaluation of neurotoxic threshold values for organic solvent mixtures is difficult and associated with considerable uncertainty.

It is therefore important to note that the conclusions given below are valid only at group level. There is no scientific rationale for direct application to individual cases during evaluations of causality. In this case a synoptic evaluation is necessary with consideration of the occupational exposures, risks in the non-insured scope, and individual circumstances.

For acute neurotoxic effects the following thresholds are recommended:

Below 0.5:
Symptoms unlikely, no dysfunctions

0.5 to 1.0:
Symptoms possible to probable,
dysfunctions unlikely

Over 1.0:
Symptoms frequent, dysfunctions possible

For the “Chronic Exposure Index”, the following conclusion is drawn:

The incidence of dysfunctions (and symptoms) is generally associated with solvent exposure over many years which can be estimated at a Chronic Exposure Index of 10 or higher. Assuming an exposure period of 10 years, this would mean that the exposure level as calculated by the summation formula would be around 1.0.

For calculation of the CEI and CREI, all organic solvents stated by the authors were considered, and not only listed substances in the context of occupational disease No. 1317. This generally leads to higher values, and may result in underestimation of the hazard if only the listed substances are considered.

Expression of thanks

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6.4 Code of practice for occupational disease No. 1317

(Announcement by the BMGS, BArbBl. 2005, No. 3, p. 49)

Polyneuropathy or encephalopathy caused by organic solvents, or solvent mixtures

I. Incidence and sources of hazards

Toxic polyneuropathy or encephalopathy may be caused by exposure to neurotoxic organic solvents. At the present state of knowledge, proven neurotoxic solvents are:

- Aliphatic hydrocarbons: n-hexane, n-heptane
- Ketones: 2-butanone, 2-hexanone
- Alcohols: methanol, ethanol, 2-methoxyethanol
- Aromatic hydrocarbons: benzene, toluene, xylene, styrene
- Chlorinated aliphatic hydrocarbons: dichloromethane, 1,1,1-trichloroethane, trichloroethylene, tetrachloroethylene

These neurotoxic solvents may be employed in numerous products, either as single substance or in mixtures with other solvents [13]:

- For cleaning and removal in the metal, textile and plastics industries
- As solvents for paints, lacquers, adhesives, wood-treatment agents, rubber solutions, and for stripping
- As initial or intermediate products for numerous chemical reactions, or as dissolving intermediaries

Organic solvents are generally highly volatile, i.e. they evaporate rapidly even at low temperatures. Under unfavourable ventilation conditions, elevated concentrations may therefore arise in the breathing air. Direct contact with the skin may increase uptake of the solvent.

Elevated risks exist during the following tasks:

Stripping, sealing, application of adhesives or lacquers over large areas, and application of polyester resins over large areas

Occupations at particular risk are:

Floor-layers, parquet layers, laminators; in some cases tank cleaners, acidproof installation fitters

II. Pathology

Owing to their volatility, organic solvents are primarily taken up via the lungs, but are also absorbed to some extent through skin. Following uptake, they are distributed throughout the organism, particularly in the nervous system. They are then partly exhaled again unchanged, and partly metabolized and excreted via the kidneys. The elimination half-lives vary for the individual solvents between a few hours and up to two days [1].

All organic solvents may lead, through short-term action upon the membranes of the nerve cells, to brief prenarcotic symptoms and even to narcosis. The effective long-term action of neurotoxic solvents, ultimately resulting in polyneuropathy or encephalopathy, is however based upon their biotransformation to neurotoxic metabolites. The targets of these metabolites in the nerve cells differ and are not yet fully explained. As a neurotoxic metabolite of n-hexane and butyl methyl ketone, 2,5-hexanedione impairs axonal transport, for example. The consequences are in the first instance function disorders (paresthesia, loss of sensitivity), followed in the further progress by morphological changes with primarily axonal damage. Histological damage occurs in the form of large paranodal axonal swellings, and accumulations of neurofilaments and glycogen granules. Non-occupational neurotoxic factors (such as alcohol, medication or diseases such as diabetes mellitus) may influence this progress.

III. Clinical picture and diagnosis

Polyneuropathy

Typical of neurotoxic polyneuropathy are symmetric distal, sensory, motor or sensory-motor deficits primarily in the arms and legs, in a stocking-glove distribution. An important aspect for the case history is that the sensory disorders increase from distal to proximal and that the parasthesia frequently increase during night. Objectively, distal symmetrical sensory disorders can be detected through disturbances of sensitivity, such as vibration, position, esthesia, algesia, and two-point discrimination, according to the intensity of the disease.

In the further progress of the condition, reflex attenuation or areflexia, disturbances of the autonomic nerve supply, reduction of the sensory and motor nerve conduction velocities, distal latencies, and patterns of neurogenic damage can be detected in the EMG.

The form taken by the motor changes may range from minor motor weaknesses to com-

plete muscle paralysis with muscle atrophy. The muscular system in the hand and foot region is primarily affected.

In severe cases, however, complete tetraplegia and involvement of the respiratory musculature may occur [1, 5, 12]. Conversely, trichloroethylene-induced polyneuropathy is characterized by loss of sensitivity and reflex or sensory-motor failure in the distribution area of the trigeminal nerve in the face. Involvement of the oculomotor nerve and the abducent nerve also occurs. Peripheral polyneuropathy has also been described following exposure to trichloroethylene [6; 7].

The development of solvent-induced polyneuropathy generally coincides closely with the incidence of occupational solvent exposure. Isolated cases of the disease's progress have however been reported in which deterioration in mobility occurs two to three months after cessation of the hazardous activity [4], with the result that clinical diagnosis of polyneuropathy may not be possible until after a corresponding period.

Solvent-induced polyneuropathy frequently improves following cessation of the hazardous activity; however, it is also not uncommon for it to remain constant or deteriorate clinically following cessation of the hazardous activity [1; 4; 5; 11; 12; 14].

Persistence or deterioration of the condition following cessation of the hazardous activity does not exclude solvents as the cause.

For the purpose of differential diagnosis, alcoholic or diabetic polyneuropathy should first be considered. Solvents can largely be ruled out as the cause of asymmetric, multifocal, purely motor or autonomic neuropathies.

Toxic encephalopathy

Toxic encephalopathy is apparent primarily in the form of diffuse disorders of brain function, impaired concentration and memory, impaired attention, disturbances of thinking, personality changes (often with low motivation, irritability and affective disorders).

The following levels of severity are distinguished in the clinical progress [15]:

- Degree of severity I:
  Exhaustion, fatigability, poor concentration, weak memory, general reduction in motivation

- Degree of severity II A:
  Pronounced and sustained personality changes, increasingly poor concentration and memory, changes in mood with elements of depression, affective lability; impaired performance demonstrated by psychological tests

- Degree of severity II B:
  In addition to the mental disorders listed under II A, minor neurological findings such as tremor, ataxia and other co-ordination disorders are confirmed

- Degree of severity III:
  Dementia with pronounced intelligence and memory defects, evidence in cranial computer tomography of cerebral atrophic change; degree of severity III is observed with severe exogenous (alcohols) and endogenous intoxications; encephalopathy with cerebral atrophy has also been described following chronic exposure to solvents [2; 9].

Toxic encephalopathy generally occurs before the end of exposure. Several studies however indicate an increase in the subjective complaints and deterioration in the results of psychological test and neurological study results years after cessation of the hazardous activity [2; 7; 10; 11]. From this, it follows that solvent-induced encephalopathy may also be diagnosed clinically for the first time several years after cessation of the hazardous activity.

Solvent-induced encephalopathy may improve, remain constant or deteriorate following cessation of the hazardous activity [2; 3; 7; 10; 11].

Persistence or deterioration of the condition following cessation of the hazardous activity does not exclude solvents as the cause.

The diagnosis is based upon the case history and the psychopathological findings. Important indicators in the case history are alcohol intolerance and frequent prenarcotic symptoms directly associated with the solvent exposure (drowsiness, feeling drunken, tiredness, nausea, vomiting, but also states of euphoria). The psychopathological findings must be objectified by psychological test methods which take the patient's age into account. These test methods must examine the following: the premorbid intelligence, attention and memory performance, psychomotor performance, personality changes, and subjective velocity disorders.

Neurophysiological examinations (EEG, evoked potentials, nerve conduction study) and imaging methods (computer tomography, nuclear magnetic resonance tomography) generally yield normal findings in cases of solvent-induced encephalopathy. They are however relevant for differential diagnosis purposes. Elevated values observed during biomonitoring (solvents or their metabolites in the blood or urine) may support the diagnosis.

Multi-infarct dementia, Alzheimer's disease and alcohol-induced encephalopathy must be excluded in the first instance by differential diagnosis. The entire differential diagnosis of exogenous and endogenous toxic encephalopathy, traumatic psychosyndromes, affective psychoses and neurotic development must also be considered.

IV. Further information

Further manifestations of disease beyond polyneuropathy and encephalopathy which may arise as a result of occupational exposure to solvents in isolation or mixtures do not fall within the scope of this occupational disease number. Such manifestations include, for example, epileptic attacks caused

by benzene, Parkinson's disease caused by methanol, and hallucinatory psychoses caused by toluene, dichloromethane and tetrachloroethylene. Compensation may be made for these conditions under the occupational disease numbers of the corresponding substances.

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Index of abbreviations/units

AEP	=	acoustically evoked potential
AL	=	analytical limit of detection
BArbBl	=	Federal Labour Gazette (Bundesarbeitsblatt)
BAT value	=	biological tolerance value (Biologischer Arbeitsstofftoleranzwert, BAT-Wert)
BAuA	=	German Federal Institute for Occupational Health and Safety (Bundesanstalt für Arbeitsschutz und Arbeitsmedizin)
BG	=	institution for statutory accident insurance and prevention (Berufsgenossenschaft)
BGBl	=	Federal Law Gazette (Bundesgesetzblatt)
BGIA	=	BGIA – Institute for Occupational Safety and Health of the German Social Accident Insurance (BGIA – Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung; formerly BIA)
BGMG	=	measurement system for exposure assessment of the German Accident Insurance Institutions (Messsystem der UV-Träger zur Gefährdungsermittlung)
BImSchG	=	German Federal Immission Control Act (Bundes-Immissionsschutzgesetz)
BImSchV	=	Ordinance for the Implementation of the German Federal Immission Control Act (Verordnung zur Durchführung des Bundes-Immissionsschutzgesetzes)
BKV	=	German regulation on occupational diseases (Berufskrankheiten-Verordnung)

BMA	=	German Federal Ministry of Health and Social Affairs (Bundesministerium für Arbeit und Sozialordnung, former title)
BMGS	=	German Federal Ministry of Health and Social Affairs (Bundesministerium für Gesundheit und Soziale Sicherung)
CAS	=	Chemical Abstracts Service
CCT	=	cranial computed tomography
CFC	=	chlorofluorocarbon
CNS	=	central nervous system
DFG	=	German Research Foundation (Deutsche Forschungsgemeinschaft)
DIN	=	German Institute for Standardization (Deutsches Institut für Normung)
EEG	=	electroencephalogram
EN	=	European standard
g	=	gramme
GefStoffV	=	German Hazardous Substances Ordinance (Gefahrstoffverordnung)
GRP	=	glassfibre reinforced plastic
HC	=	hydrocarbon
hPa	=	hectopascal
HVBG	=	Federation of Institutions for Statutory Accident Insurance and Prevention (Hauptverband der gewerblichen Berufsgenossenschaften, now DGUV)
LV	=	limit value

MAK	=	maximum workplace concentration (maximale Arbeitsplatzkonzentration)
MEGA	=	measurement data on the exposure to hazardous substances at the workplace
mg/m³	=	(atmospheric concentration in) milligramme per cubic metre
ml/l	=	(concentration in) millilitres per litre
ml/m³	=	(atmospheric concentration in) millilitres per cubic metre
MRT	=	magnetic resonance tomography
MSDS	=	material safety data sheet
µg/m³	=	(atmospheric concentration in) microgrammes per cubic metre
NOEC	=	no observed effect concentration
PER	=	perchloroethylene (tetrachloroethylene)
PET	=	positron emission tomography
ppm	=	parts per million
PS	=	polystyrene
RON	=	octane number
SBP	=	special boiling-point products
SEP	=	somatosensory evoked potential
SPECT	=	single photon emission computed tomography
TRGS	=	technical rules for hazardous substances (Technische Regel für Gefahrstoffe)
TRK	=	technical exposure limit (Technische Richtkonzentration)

VCI	=	Association of the German Chemical Industry (Verband der Chemischen Industrie)
VEP	=	visually evoked potential
ZVG	=	centrally assigned substance number of the GESTIS system (Zentrale Vergabe Nummer)

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