INFORMATION

Cases of Poisoning Reported by Physicians

2007

BfR

Risiken erkennen – Gesundheit schützen

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Cases of Poisoning Reported by Physicians 2007

Centre for Documentation and Assessment of Poisonings at the Federal Institute for Risk Assessment – 14th Report (2007)

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1 Introduction

1.1 Legal basis and activities of the Centre
With the Chemicals Act (ChemG), legislation in the Federal Republic of Germany has provided a basis "to protect humans and the environment from harmful effects of dangerous substances and preparations, particularly to make them recognizable, to avert and to prevent the development of such effects" (according to § 1).

For a realistic assessment of risks for human health, importance has been increasingly given to the knowledge of data on human toxicology that can be obtained from the evaluation of cases of poisoning in humans. This is why legislation has introduced compulsory notification of poisonings by attending physicians from 1 August 1990, by the first amendment to the ChemG (§ 16e).

A physician who is consulted for treatment or evaluation of sequelae of diseases caused by chemical substances or products is obliged to submit essential data on poisonings to the Centre for Documentation and Assessment of Poisonings at the Federal Institute for Risk Assessment (BfR).

According to the Chemicals Act, reporting refers to illnesses or suspected poisonings that are associated with the following substances:

- Chemical substances and products used in the household, e.g. detergents and cleaning agents, hobby and DIY articles;
- Cosmetics;
- Pest control products;
- Plant protection products;
- Wood preservatives;
- Chemicals and products used at the workplace;
- Harmful chemical substances found in the environment, also after industrial accidents; and
- Plants/animals.

Within the meaning of the Chemicals Act, the term of poisoning designates all cases in which health impairment has occurred, including suspected cases of poisoning. Under the Act, also the poison information and treatment centres (Poison Control Centres, PCCs) were subjected to compulsory reporting of their knowledge (of general importance) gained in the context of their activities.

1.2 Processing of reports received
Reports received on health impairment associated with chemicals are subjected to an assessment procedure resulting in the rating of a possible causal relationship between the toxicant and the manifestations observed, as well as other conclusions. Such relationship may be classified as "possible", "probable", "confirmed", "absent" or "cannot be assessed". The rules applied in the assessment of individual cases have been described in detail in earlier annual reports.

The estimation of toxic risks in humans is based on differentiated analyses and evaluation of the data on cases. For these purposes, the data on cases in humans are continuously documented in the form of case data sets and case reports. Information on identified risks is passed on to the responsible ministries, manufacturers and industrial associations in the form of rapid communications or to the manufacturers in the form of annual summarizing reports by means of the product information system, PRINS (see Section 2.3). At the same time, the responsible manufacturers or distributors are requested to submit information on the measures envisaged by them to improve product safety.

The knowledge gained during this process is published by the BfR in its annual reports, Cases of Poisoning Reported by Physicians. These publications are available on request by writing

to Pressestelle, Bundesinstitut für Risikobewertung, Thielallee 88-92, 14195 Berlin, Germany, and they have also been published as electronic documents on the internet (www.bfr.bund.de).

In Fig. 1, these tasks and procedures are shown in graphical form.

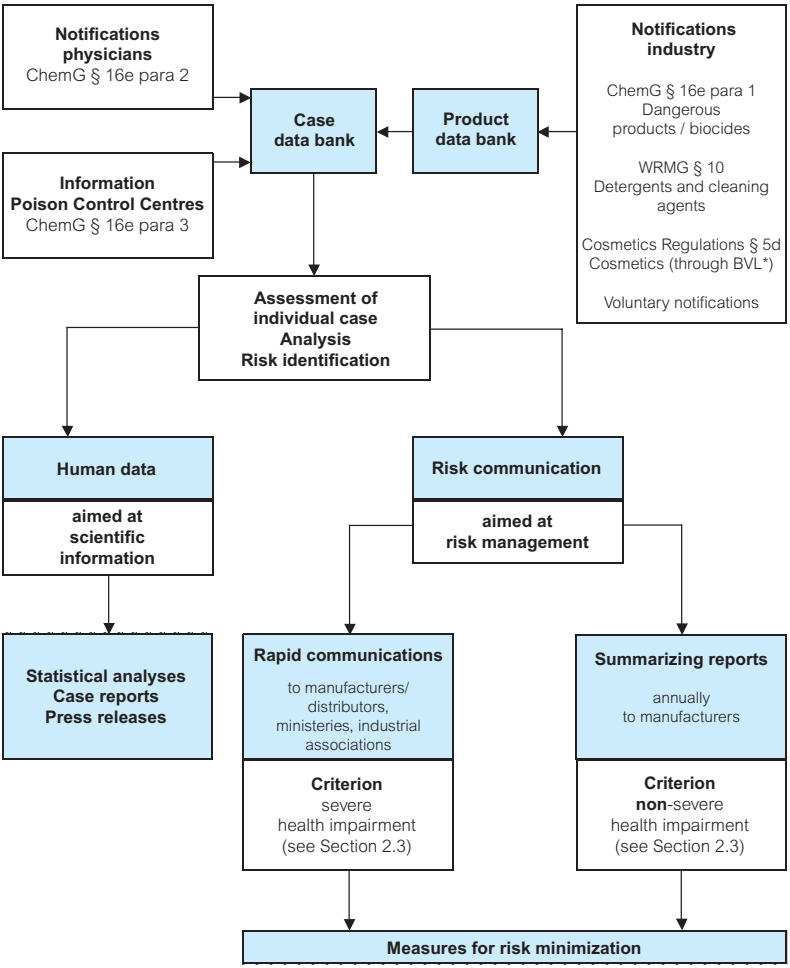


Fig. 1: Terms of reference of the Centre for Documentation and Assessment of Poisonings

*BVL: Bundesamt für Verbraucherschutz und Lebensmittelsicherheit – Federal Office for Consumer Protection and Food Safety

1.3 Product data bank (poison information data bank)

1.3.1 Figures

Until late December 2007, documents on 264 149 products were recorded in the poison information data bank maintained by the BfR, which can be accessed by the Poison control Centres (PCCs) in Germany, thus supporting their activities in providing consultation and treatment in cases of poisoning. Consequently, the number of notifications on products submitted to the Centre for Documentation and Assessment of Poisonings at the BfR increased by 35 731 in 2007. The structure of the data bank and the different types of product data sets have been described in detail in earlier reports.

1.3.2 Collaboration between the BfR, industry and Poison Control Centres

The major part of product data on dangerous preparations and biocidal products as well as of the voluntary reports by manufacturers, distributors and importers received by the BfR is still submitted on paper forms. The recording of cosmetics, which until June 2005 had been entered into the poison information data bank at the BfR predominantly directly in electronic form, is now carried out at the Federal Office for Consumer Protection and Food Safety (BVL), as a consequence of the subdivision of the former Federal Institute for Health Protection of Consumers and Veterinary Medicine (BgVV) into the two successor institutes, BfR and BVL. From the BVL, the data were returned to the BfR at monthly intervals and from there, transmitted to the PCCs together with the other product data in the well-established way. From 2008, the cosmetics data sets are directly distributed to the PCCs by the BVL.

Altogether, i.e. including the dangerous preparations and biocidal products notifiable under § 16e para 1 of the Chemicals Act as well as detergents and cleaning agents, 26 773 notifiable product data sets have been transmitted to the PCCs. Of these, 7 918 refer to dangerous preparations, 10 449, to biocides and 8 406, to detergents and cleaning agents.

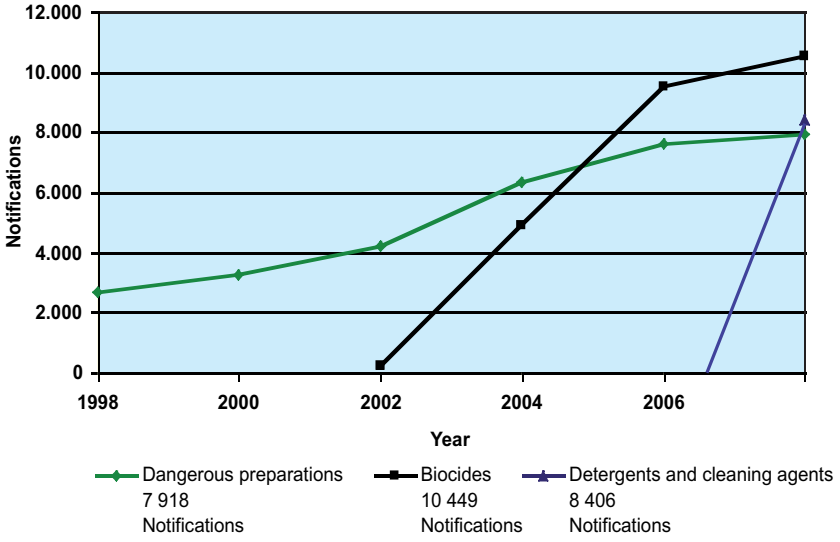


Fig. 2: Development of notifications legally required under § 16e para 1 of the Chemicals Act: Dangerous preparations, biocidal products (2002: entry into force of the regulations on biocides), as well as detergents and cleaning agents under the Detergents and Cleaning Agents Act (notifications since 5 May 2007)

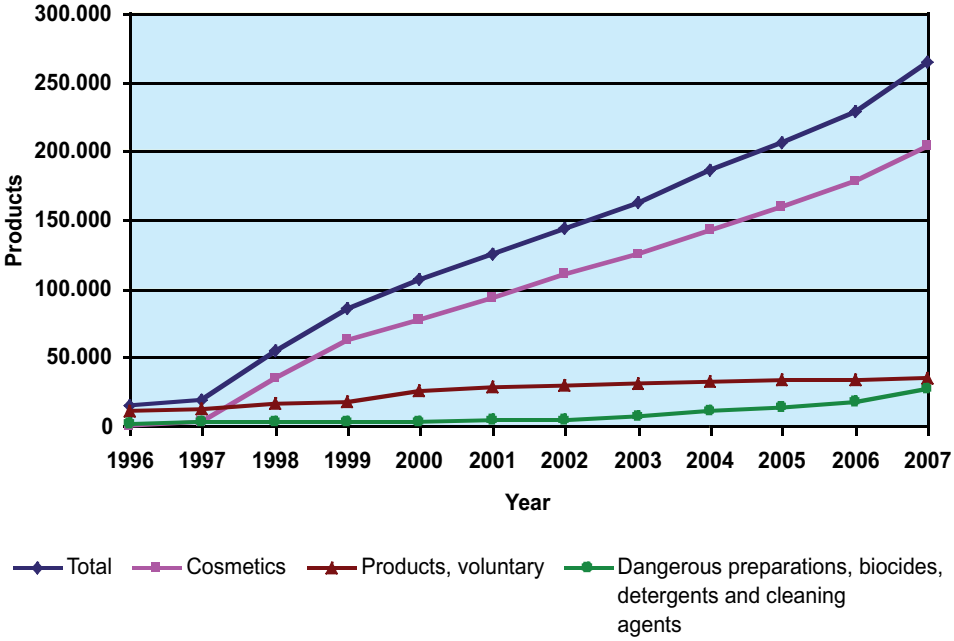


Fig. 3: Notifications on products received since 1996 and transmission of information to the German Poison Control Centres

1.3.3 The new Detergents and Cleaning Agents Act

On 5 May 2007, the new German Detergents and Cleaning Agents Act (Wasch- und Reinigungsmittelgesetz – WRMG) came into force. It has been harmonized with Regulation (EC) No. 648/2004 on detergents having been in effect since 8 October 2005, and replaces the old WRMG of 5 March 1987. As a consequence, the BfR has been assigned new tasks. In § 10, in conjunction with Annex VII C to the EU Detergents Regulation, the WRMG stipulates that manufacturers of detergents shall make available a data sheet to the BfR listing the name of the detergent, of the manufacturer and of the ingredients together with their corresponding weight percentage ranges. The data sheet shall be submitted in electronic form as determined by the BfR. For this purpose, a corresponding format has been defined in XML by the responsible unit. Among other tools, a ZIP file archive has been made available for product notifications under the WRMG. This archive also includes an Excel file allowing to record data and check them for plausibility to some extent. Finally, the WRMG notification is generated as an XML file and submitted to the BfR. For corresponding instructions, see the BfR website.

These data as well as those submitted under § 16e para 1 ChemG and those submitted on a voluntary basis are edited by the BfR for transmission to the PCCs to provide emergency advice on poisoning management. In addition, the BfR is obliged to submit to the Federal Environment Agency, also in electronic form, the name of the manufacturer and the trade name of the detergent and/or cleaning agent.

1.4 Standardization on the European level (CEN) for unequivocal product identification on labels (PI element)

More than six years after the BfR predecessor institute, the Federal Institute for Health Protection of Consumers and Veterinary Medicine – BgVV, had adopted the proposal of a BgVV commission for product identification by organizing an Initial Workshop (PCCs, industry, consumers' associations), a reasonable idea has been translated into a European standard (CEN standard EN 15178:2007). For emergency advice and in cases of adverse product effects, an easy and unmistakable identification of ingredients will be possible in the future by means of a product identification field provided in product labelling close to the bar code.

Fig. 4: Which is the correct product name? Problems to identify the name of a modern detergent

Tailor-made emergency advice in cases of poisoning and health evaluation of adverse product effects requires a precise knowledge of the formulation of the product involved. Up to the present, the formulation traditionally has been linked to the trade name and is recorded accordingly in the respective databases. However, the trade name rarely appears on packages in an unequivocal way. Therefore, both lay persons and specialists often find it difficult to identify the correct trade name, which in an emergency may be decisive for being able to provide advice. A targeted search on the package is complicated by the presence of company logos, corporate identity measures, certificates, instructions for use, additional information, warnings and advertising texts, references to daughter products, etc. In addition, many consumers become confused by a multilingual labelling of packages, which facilitates a cost-effective international marketing of products.

The original idea to distinguish the trade name by highlighting it in a contrasting colour or even by underlining could not be implemented for reasons of product design. Likewise, attempts to use the bar code (EAN code) for unequivocal product identification have remained unsuccessful because the bar code does not include a clear reference to the formulation of the product. It is used for pricing and marketing logistics purposes.

Beginning with a DIN standardization project on the national level and subsequently, also under a European CEN standardization project, a body of representatives of industry, government, politics and Poison Control Centres have developed a standard providing a solution for clear and easy product identification labelling, which came into effect in October 2007.

According to the new CEN standard, a product identification field has to be reserved on packages next to the bar code providing space for placing an unequivocal product identification element (PI element). The PI element begins with a standardized sign (the letter "i" in a circle), followed by a sequence of letters or numbers providing unequivocal reference to the formulation. Whenever possible, the address and contact data of the company responsible should be given below this PI element.

The standard covers all consumer products with the exception of human and veterinary medicinal products. In the sense of the standard, the manufacturer shall, on his own responsibility, use this field for giving unequivocal information based on the product formulation, using an identification element (I element). In doing so, he is free with regard to using corresponding codes or the trade name together with additional information that cannot be misunderstood.

However, uniform recommendations and requirements for all product categories as to the design of the identification element have been considered as meaningful and necessary. After careful consideration how to create a simple and unequivocal procedure, the BfR has proposed to maintain the principle of the reliable and well-established UBA numbers, which regrettably were abandoned due to the implementation of the European Detergents Regulation. The old UBA number consists of eight digits, with the first four digits to indicate the company code and the last four digits to accommodate the formulation code to be fixed by the manufacturer, importer, or distributor on their own responsibility.

Proposal made by the BfR

Based on the CEN standard, the BfR has proposed a uniform identification element starting with the i symbol followed by a 5-digit BfR company code, a 5-digit formulation code to be fixed by the manufacturer and a hazard symbol. It would be desirable if with the assistance of BfR recommendations and initiatives, the labelling of detergents and cleaning agents with the UBA number could be continued not only for detergents and cleaning agents but also for other consumer products in the interest of an improved product safety.

Therefore, the BfR advocates the implementation of the European standard, which in addition to a precise identification of the formulation in cases of emergency enquiries will also enable an exact identification of adverse health effects of products. The new CEN standard also offers obvious advantages for manufacturers, importers and distributors: Unlike the mere trade name, the identification element with its unmistakable reference to the formulation can minimize errors in the ordering system and thus, also save costs.

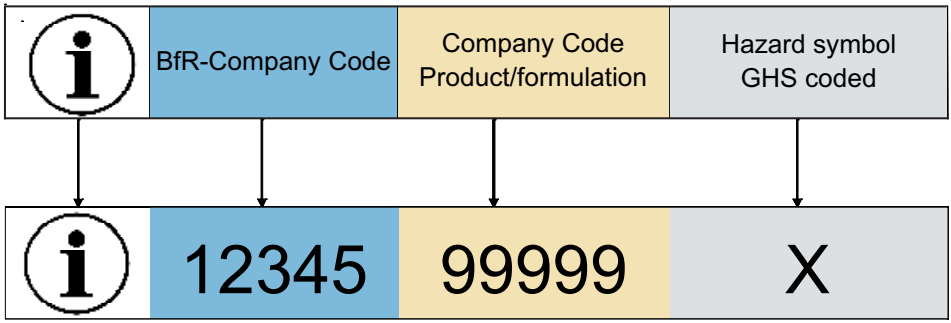


Fig. 5: BfR proposal for a uniform identification

2 Case reports by physicians

2.1 Evaluation of reports

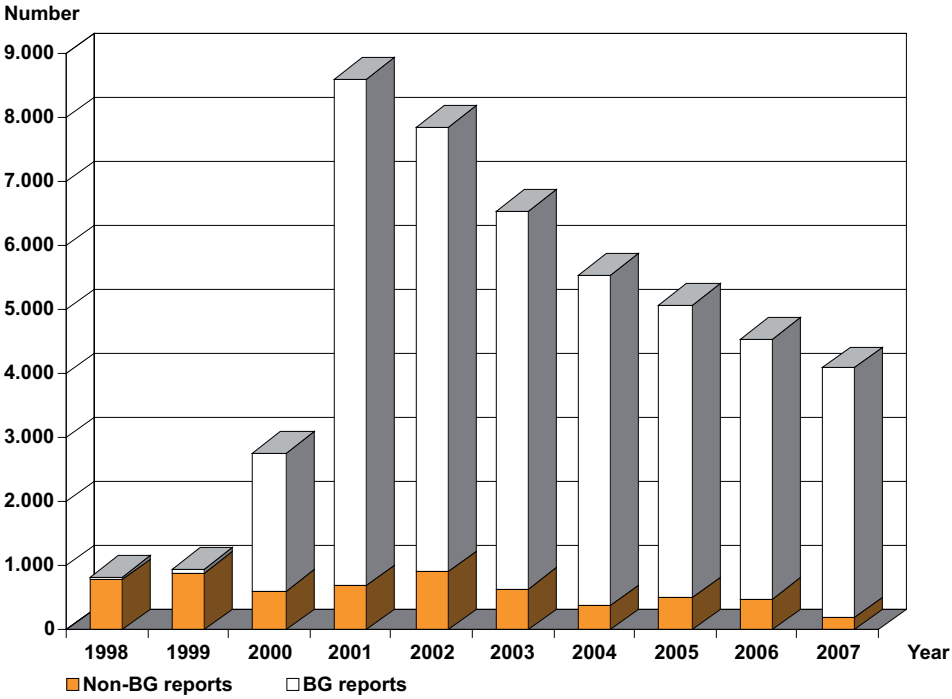


Fig. 6: Cases reported (BG reports 100 % = 3 895; non-BG reports 100 % = 198) BG: Berufsgenossenschaften – Institutions for statutory accident insurance and prevention for trade and industry in Germany

During the period from 1 August 1990, i.e. the beginning of the compulsory notification, to 31 December 2007, altogether 52 798 reports on cases of health impairment, poisoning or suspected cases of poisoning were received by the BfR. In 2007, i.e. the reporting year considered, 4 093 notifications were received (Fig. 6).

The increase in the number of notifications received in 2000 was due to an agreement with the Berufsgenossenschaften. According to this agreement, all cases of acute health impairment after contact with chemicals or chemical products are directly reported by the Berufsgenossenschaften to the BfR. Since 2001, a continuous decrease has been observed in the number of these reports. According to the BG-Institute for Occupational Safety and Health (Berufsgenossenschaftliches Institut für Arbeitsschutz – BIA), this decrease can be attributed to an actual reduction in the number of accidents, and not to changes in the reporting behaviour. This is caused by prophylactic campaigns informing about circumstances and prevention of accidents, an improved occupational safety and accident prevention due to more effective safety measures and changes in operational processes (in part also automation).

Also the share of reports received from hospitals and medical practitioners has decreased considerably. However, evaluations by the PCCs have shown that the share of health impairments after intake of or contact with chemical products, household chemicals, plant protection and pest control products and all other notifiable product groups has remained high and does not correspond to the number of notifications received by the BfR.

2.2 Reports on cases of poisoning in 2007

2.2.1 Origin

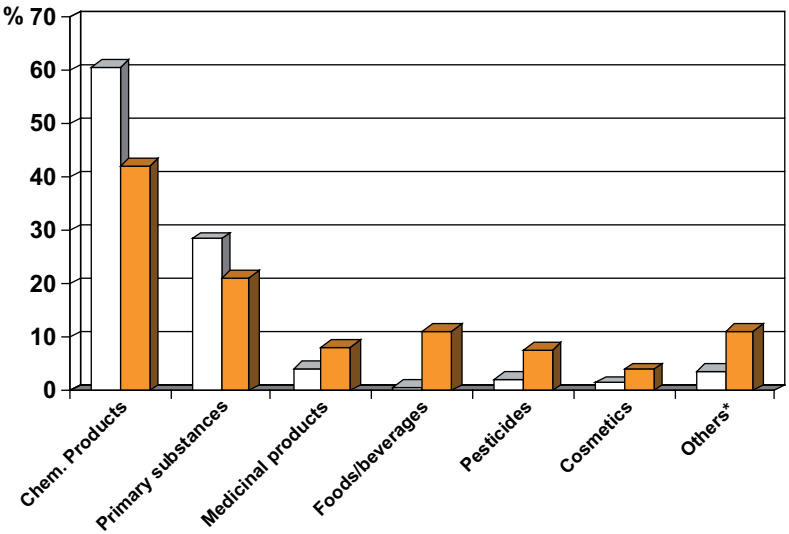
In 2007, 3 895 cases, i.e. 95.2 % of all cases notified, were reported by the Berufsgenossenschaften. The remaining 198 notifications (4.8 %) were essentially submitted by hospitals, medical practitioners and PCCs.

2.2.2 Spectrum of cases reported

Fig. 7 provides a synoptic view of the spectrum of product groups involved in the cases reported. Among the total of cases reported by the Berufsgenossenschaften, those of poisoning by chemical products and primary substances have remained in top position. All other product groups played a minor role, with shares of 4.3 % each, or less.

As expected, the spectrum of substances and products involved in cases of poisoning is different in the reports received from the Berufsgenossenschaften and in those received from hospitals and medical practitioners. Also among the latter, notifications related to chemical products ranked first in the reporting year. They are followed, at a clear distance, by the group of primary substances, similar to the BG reports. Next in the ranking are health complaints caused by foods and beverages, pesticides and medicinal products that were reported although these are not subject to compulsory notification.

For a detailed list of toxicants in tabular form see Annex. In this table, the cases reported in 2007 have been classified by product applica-



*Others: Plants, fungi, animals, veterinary medicines, agrochemicals, narcotic drugs, warfare/anti-riot agents, industrial accidents, miscellaneous

Fig. 7: Spectrum of cases reported (BG reports 100 % = 3 895 reports; non-BG reports 100 % = 198 reports)

	BG reports (100 % = 3 895 reports)		Non-BG reports (100 % = 198 reports)	
Chemical products	60.6 %	(2 359 Cases)	42.4 %	(84 Cases)
Primary substances	28.5 %	(1 110 Cases)	21.2 %	(42 Cases)
Medicinal products	4.3 %	(166 Cases)	8.1 %	(16 Cases)
Pesticides	2.4 %	(92 Cases)	7.6 %	(15 Cases)
Cosmetics/personal hygiene products	1.6 %	(64 Cases)	4.0 %	(8 Cases)
Foods and beverages	0.7 %	(27 Cases)	11.1 %	(22 Cases)
Agrochemicals	0.3 %	(10 Cases)	0 %	(0 Cases)
Industrial accidents	0.2 %	(6 Cases)	0 %	(0 Cases)
Veterinary medicinal products	0.1 %	(3 Cases)	0 %	(0 Cases)
Warfare/anti-riot agents	0.1 %	(2 Cases)	0 %	(0 Cases)
Plants	0.1 %	(3 Cases)	3.0 %	(6 Cases)
Animals	0 %	(1 Case)	0.5 %	(1 Case)
Narcotic drugs	0 %	(0 Cases)	1.0 %	(2 Cases)
Fungi	0 %	(1 Case)	6.1 %	(12 Cases)
Others	2.8 %	(111 Cases)	0.5 %	(1 Case)

Table 1: Spectrum of reports – synoptic view (repeat listing of toxicants per case possible)

tion groups (assignment of toxicants according to their intended use).

2.2.3 Circumstances of poisoning

The Berufsgenossenschaften almost exclusively reported cases of exposure to poisons in the context of occupational accidents (ca. 97 % of cases). The remaining 3 % of cases referred to accidents that had occurred during the common use of a product or because a chemical had been mistaken for another substance, or the circumstances of the accident were unknown.

Among the reports submitted by hospitals and medical practitioners, cases of accidental poisoning predominated (49.5 %), followed by exposure during common use (28.3 %). Exposure due to mistaking chemicals for other substances was the cause in 8.6 % of cases, suicidal actions were reported in 1.5 % of cases. Only 1 % of cases were associated with the abuse of substances. In the remaining cases, causes remained unknown.

2.2.4 Age structure and sex distribution

In 2007, the share of cases referring to adults among the total of cases reported was 98.4 %. The three accidents involving children occurred in schools and kindergartens, respectively.

The share of cases in adults predominated also among the reports received from hospitals and medical practitioners. However, the share of children in these cases was as high as 33 % (Table 3).

2.2.5 Degree of severity of health impairment

Also in 2007, the majority of cases reported referred to minor health impairment only, both among the cases reported by the Berufsgenossenschaften and among those reported by hospitals and medical practitioners. Moderate and severe health impairments were mostly reported by medical practitioners or physicians working in hospitals (Table 5).

The product groups involved most frequently with regard to the degree of severity of health effects

	BG reports (100 % = 3 895 reports)		Non-BG reports (100 % = 198 reports)	
Acute	99.9 %	(3 892 Cases)	83.8 %	(167 Cases)
Chronic	0.1 %	(2 Cases)	7.6 %	(15 Cases)
Unknown	0 %	(1 Case)	8.1 %	(16 Cases)

Table 2: Duration of exposure – synoptic view

	BG reports (100 % = 3 895 reports)		Non-BG reports (100 % = 198 reports)	
Children	0.1 %	(3 Cases)	32.8 %	(65 Cases)
Adults	99.9 %	(3 892 Cases)	67.2 %	(133 Cases)

Table 3: Age groups – synoptic view

	BG reports (100 % = 3 895 reports)		Non-BG reports (100 % = 198 reports)	
Male	59.2 %	(2 304 Cases)	51.0 %	(101 Cases)
Female	27.7 %	(1 079 Cases)	41.4 %	(82 Cases)
Unknown	13.1 %	(512 Cases)	7.6 %	(15 Cases)

Table 4: Sex distribution – synoptic view

	BG reports (100 % = 3 895 reports)		Non-BG reports (100 % = 198 reports)	
None	3.6 %	(139 Cases)	13.6 %	(27 Cases)
Minor	85.6 %	(3 334 Cases)	56.6 %	(112 Cases)
Moderate	6.6 %	(259 Cases)	13.6 %	(27 Cases)
Severe	0.2 %	(6 Cases)	10.1 %	(20 Cases)
Cannot be assessed	4.0 %	(157 Cases)	6.1 %	(12 Cases)

Table 5: Degree of severity of health impairment – synoptic view

have been listed in Table 6 for the cases reported by the Berufsgenossenschaften, and in Table 7, for the cases reported by hospitals and medical practitioners. Of course, the toxicants reported from occupational environments were different from those reported to have been involved in the private sphere, on account of e.g. the differences in the availability of certain product groups.

Exposure to substances from the group of building materials referred almost exclusively to lime, mortar, concrete and similar products forming calcium hydroxide under humid conditions, which may cause irritation or chemical burns. The group of "accumulators" summarizes reports on incidents such as the release of sulfuric acid from motor vehicle batteries due to an explosion.

Health impairment or cases of poisoning due to medicinal products are not subject to compulsory notification under the Chemicals Act. Nevertheless, cases of accidental contact, mostly referring to splashes of skin disinfectants affecting the eye, have been reported by the Berufsgenossenschaften.

	Health impairment		
Product group	Minor (3 334 Cases)	Moderate (259 Cases)	Severe (6 Cases)
Primary substances	907	101	3
Cleaning agents, total	636	63	1
Drain cleaners	*11*	*2*	*1*
All-purpose cleaners	*39*	*2*	
Oven and grill cleaners	*23*		
Descaling products	*13*		
Industrial cleaners	*56*	*11*	
Milking machine cleaners	*57*	*8*	
Metal cleaners	*20*	*1*	
Lavatory cleansers	*24*	*2*	
Disinfectants/sterilizers	332	13	
Medicinal products	149		
Waste gases	137	7	1
Paints and related materials	128	7	
Accumulators	76	4	
Building materials	99	19	
Pesticides	81	7	

Table 6: Product groups involved most frequently, by degree of severity of health impairment (BG reports)

	Health impairment		
Product group	Minor (112 Cases)	Moderate (27 Cases)	Severe (20 Cases)
Cleaning agents, total	15	4	4
Descaling products			*1*
Glass cleaners			*1*
Oven and grill cleansers	*2*		
Lavatory cleansers	*4*	*1*	*1*
Shoe and leather cleansers	*1*	*2*	*1*
Primary substances	28	5	4
Waste gases			1
Primers			1
Office materials, chemical	10	1	
Luminophors	6		
Lamp oil	3	1	
Pesticides, total	10	3	1
Insecticides	*3*	*2*	
Wood preservatives	*6*		
Foods and beverages	9	2	5
Alcoholic beverages			*1*
Fungi	5	2	3

	Health impairment		
Product group	Minor (112 Cases)	Moderate (27 Cases)	Severe (20 Cases)
Medicinal products	3	2	3
Textile, auxiliary products			2

Table 7: Product groups involved most frequently, by degree of severity of health impairment (non-BG reports)

2.2.6 Outcome of cases

For the notifications submitted by the Berufsgenossenschaften, the outcome has remained unknown in ca. 41 % of cases. The reason for this is that in the majority of cases, the report submitted corresponds to that by the "Durchgangsarzt" ("transition doctor" appointed by the Berufsgenossenschaft). As a rule, the reporting form is completed after the patient's first presentation. Therefore, such report does not contain any information on the course of the patient's illness. In selected cases, enquiries were made to obtain information on the course of illness. In the majority of cases on which information was available, patients had recovered completely.

Of the notifications submitted by hospitals and medical practitioners, patients recovered completely in 147 cases (74.2 %). In 32 cases 16.2 %), the outcome was unknown; in eleven cases (5.5 %), late sequelae could not be excluded or partial recovery was reported. The remaining eight cases (4.1 %) had lethal outcomes.

Altogether, nine deaths were reported to the BfR (by BGs, hospitals and medical practitioners) in 2007. Below, some of these lethal cases have been listed in a summarizing view:

- For unknown reasons, a 31-year-old patient had ingested 400 mL of a 25 % vinegar concentrate. In the course of this case, the patient developed haemolysis and massive renal damage. He eventually died from cardiovascular failure.
- Four cases were reported to the BfR by forensic institutes. The causes of these deaths have remained unclear. In one of these cases, several food supplements were found in the immediate vicinity of the corpse. In the other three cases, carbon monoxide and hydrocyanic acid, respectively, were detected at post-mortem examinations.
- A lethal case due to rust remover spray has been described in detail in the corresponding case report (Section 3.2.3.5).
- One patient had taken metformin, an antidiabetic, together with an unknown quantity of alcohol and ramipril as a continuous medication. He developed a severe health disturbance and eventually died from multiple organ failure.
- A particularly tragic case was the death of a child after ingestion of a lethal dose of common salt.
- The last death that occurred in 2007 was due to an occupational accident that took a tragic course. The patient had inhaled chlorine gas and as a consequence, developed pulmonary oedema. In spite of intensive therapy he died from multiple organ failure.

2.3 The product information system, PRINS

The notifications by physicians in cases of poisoning legally required under the Chemicals Act (§ 16e para 2) are regularly evaluated to protect consumers from health risks posed by chemicals and chemical products. Since 1994, the reporting physicians, the responsible ministries and the scientific community have been informed by annual reports on analyses of these notifications and the corresponding results. In the context of these notifications, the term, poisoning, is used to designate any health impairment associated with chemicals, including for example also allergies.

Since 1998, manufacturers and distributors of chemical products such as household chemicals and DIY products, cosmetics, plant protection and pest control products and corresponding products for commercial use have been informed about selected cases of health impairment associated with their products that have become known to the BfR through case reports. For this purpose, a formal procedure (PRINS) was established. In the event of reported health impairments, rapid communications are provided for in these cases, depending on the urgency of measures to be taken. By such approach, industry is enabled to immediately fulfil their obligations with regard to product safety. All other reports are summarized and sent to the recipients at annual intervals.

2.3.1 Rapid communications

If reports on severe health risks are received by the BfR or a preparation is suspected of possibly involving a risk, the BfR will provide for immediate information of the manufacturer/distributor of the chemical product involved as well as the competent industrial association/federal trade association and the Federal Office for Consumer Protection. In addition, an immediate report is submitted to the three competent ministries, i.e. the Federal Ministry of Food, Agriculture and Consumer Protection (BMELV), the Federal Ministry for the Environment, Nature Conservation and Nuclear Safety (BMU), and the Federal Ministry of Health (BMG). Suicides and improper use are excluded from rapid communications.

Between 1 January 1998 and 31 December 2007, 26 rapid communications were prepared and communicated. A synoptic view of the last five years is given in Table 8.

In the reporting year of 2007, one rapid communication was distributed. It referred to a case of poisoning in a 46-year-old female who had developed toxic lung oedema after the use and inhalation of an impregnation spray for tents. Owing to the fact that effective therapeutic measures were initiated without delay, manifestations receded rapidly, and the patient could be discharged after two days. The case has been described in detail in Section 3.2.3.1.

For explanations of individual cases up to 2006, reference is made to the previous annual reports.

Year	Product	Toxicologically relevant substance	Person exposed	Outcome	Proposal by BfR (P) and results (R)
2002	Lavatory cleanser	Surfactant	Elderly male	Chemical burns	P: Information
2002	Mild detergent	Surfactant	Elderly male	Death	P: Information
2003	Cleanser	Surfactant	Elderly male	Respiratory insufficiency	P: Information
2003	Food supplement	Proteins	Adult male	Severe allergy	P: Information
2003	Fumigant	Sulfuryl difluoride	Adult male	Death	P: Information
2003	Drain cleaner	Potassium hydroxide solution	Child	Severe chemical burns	P: Information
2003	Disinfectant	Peracetic acid	Adult male	Respiratory insufficiency	P: Information
2004	Garden torch	Paraffins, colourless	Infant	Respiratory insufficiency, death	P: Information R: Accepted

Year	Product	Toxicologically relevant substance	Person exposed	Outcome	Proposal by BfR (P) and results (R)
2004	Oil lamp	Paraffins, colourless	Infant	Respiratory insufficiency, death	P: Information R: Accepted
2005	Detergents	Surfactant	Elderly male	Death	None
2005	Dishwasher cleanser for industrial use	Potassium hydroxide	Elderly female	Severe chemical burns	None
2005	Breadseed poppy	Morphine	Infant	Respiratory insufficiency	P: Guideline values/ maximum levels, control, measures to reduce opiate levels R: Accepted
2006	Detergents	Surfactant	Elderly female	Death	None
2007	Impregnation spray for tents	Cannot be assessed	Adult female	Lung oedema	P: Investigation

Table 8: Rapid communications 1 January 2002–31 December 2007

2.3.2. Summary reports

Information on reports referring to cases of non-severe health impairment caused by chemical products in occupational or private environments are transmitted to the responsible manufacturers/distributors in a summarized form in the year following the incidents. Since 2003, also suicides and attempted suicides have been included in the summary reports, irrespective of the degree of severity of poisoning. Rarely, also reports of severe cases are submitted to manufacturers in the form of a summary report if the data available were insufficient for a rapid communication.

Summary reports provide information in tabular form which, depending on the data available from the case reports, includes the following elements:

- Product name;
- Date of receipt by the BfR of the report on the case of poisoning;
- Case number;
- Anonymized patient data such as sex and age group;
- Aetiology of the poisoning case (e.g. accidental or common use, abuse or mistake);
- Site of exposure (workplace or private sphere);
- Duration of exposure (acute or chronic);
- Degree of severity of health impairment as assessed by the BfR.

Cases reported to the BfR will only result in a report being sent to the manufacturers if a causal relationship between the health impairment experienced and the product mentioned is considered at least as possible after evaluation by the BfR. Information is also submitted on cases reported for which the degree of severity and/or the causal relationship cannot be assessed. Also in these cases, it is intended to draw the manufacturer's attention to risks that may arise from his product.

By means of the BfR summary reports, manufacturers and distributors will gain knowledge on possible risks associated with the handling of their products. In single cases, they will not be satisfied by such summarized information

and seek contact with the BfR in writing or by telephone in order to obtain more detailed information on a specific case of poisoning.

After evaluation of the total of 4 093 reports on cases of poisoning received by the BfR in 2007, 325 of these resulted in summary reports to the corresponding manufacturers. These cases referred to 301 different products from 140 different manufacturers.

The table below (Table 9) provides a synoptic view of product application groups (minimum three listings) to which the summary reports on

First level		Second level		Third level	
Agrochemicals	7				
Chemical products	269	Paints and related materials	4	Primers	3
		Building materials, auxiliary products	5		
		Office materials, chemical	5		
		Disinfectants/ sterilizers	73		
		Glues	5		
		Metallurgy, auxiliary products	3		
		Lubricants	3		
		Cleaning products	127	All-purpose cleaners	5
				Oven and grill cleaners	4
				Descaling products	3
				Industrial cleaners	30
				Milking machine cleaners	20
				Lavatory cleansers	17
				Shoe and leather cleaners	4
		Water treatment products	7		
Primary substances	4				
Cosmetics/personal hygiene products	14	Oral care/dental products	4		
		Skin care products	8	Creams/ointments/ lotions	3
Pesticides	31	Herbicides	12		
		Insecticides	14	Pyrethroids	4
				Phosphoric esters	7
		Fungicides	4		

Table 9: Product groups frequently involved in 2007 summary reports

frequently listed products can be assigned. As in the previous years, the majority of reports referred to chemical products (altogether 269). Strikingly high numbers have been recorded for disinfectants (73 cases) and cleaning agents (127 cases). Attention has to be drawn to the high number of cases involving milking machine cleaners, which has even increased compared with the previous year (from 11 to 20 cases). The 325 cases leading to summary reports to manufacturers referred to health impairments characterized by the following degrees of severity:

Degree of severity of health impairment	No. of cases
Minor	266
Moderate	32
Severe	5
Cannot be assessed	22

Table 10: Degrees of severity of cases in summary reports 2007

Table 11 below shows the number of products in the individual product groups that were involved in moderate health impairments (32 products). It may be concluded that an involvement in cases of moderate health impairment was seen for ca. 10 % of the total of 301 products listed in summary reports to manufacturers.

In 22 of the total number of 325 cases of poisoning where summary reports had to be sent to manufacturers, the degree of severity could not be assessed despite further investigations made.

Five cases were reported to the respective manufacturers by way of summary reports although they referred to severe health impairment: In accordance with the decision to include cases of attempted suicide, one case involving ingestion of a disinfectant was reported. Another case reported referred to ingestion of a cleaning agent by mistake. In three cases, there was delayed

First level		Second level		Third level	
Chemical products	22	Fire lighting products	1		
		Building materials, auxiliary products	1		
		Disinfectants/ sterilizers	3		
		Lubricants	1		
		Cleaning products	13	Dishwasher cleaners	1
				Industrial cleaners	3
				Milking machine cleaners	1
				Soot remover	1
				Lavatory cleansers	2
				Shoe and leather cleaners	2
				Others	3
		Others	3		
Primary substances	1				
Cosmetics / personal hygiene products	4	Skin care products	2	Creams/ointments/ lotions	2

First level		Second level		Third level	
		Hair care products	1	Hair dyes/colorants	1
		Oral care/dental products	1		
Pesticides	5	Insecticides	2	Phosphoric esters	1
		Herbicides	2		
		Fungicides	1		

Table 11: Product groups involved in cases of moderate health impairment listed in summary reports in 2007

reporting of accidents to the BfR i.e. in the subsequent year only, while the manufacturers had already been informed about possible health risks involved in the product in the context of rapid communications, for example in the case series in 2006 when health impairments had been caused by “nano sealing sprays”.

The BfR also performs cumulative data analyses of case reports. If trends become apparent, the manufacturers of the products concerned are informed. Manufacturers are requested by the BfR to, in turn, communicate comparable data and trends that may serve to improve product safety.

3 Selected toxicological problems

3.1 Container fumigation using methyl bromide

Health risks associated with the fumigation of containers have been increasingly discussed in previous years. The attention of the public regarding this problem was shown for example in an article by the German magazine, Der Spiegel. This article named in particular three substances being used for container fumigation: Chloropicrin (a type of Green Cross gas), 1,2-dichloroethane and methyl bromide.

Evaluation of data has shown that in the context of physicians' reports on cases of poisoning under § 16e Chemicals Act, the BfR received reports on 22 cases involving the above substances during the period between 1 August 1990, i.e. the beginning of compulsory notification, and 31 December 2007.

Chloropicrin	0 cases
1,2-dichloroethane	8 cases
Methyl bromide	14 cases

- Chloropicrin (trichloronitromethane or nitrochloroform) is a chemical warfare agent causing pulmonary effects. Like phosgene, it became known under the German name of Grünkreuz (Green Cross) and was one of the components of Green Cross gas shells. No cases caused by this substance have been reported.
- Reports on 1,2-dichloroethane (ethylene dichloride) referred to accidents in the chemical industry or agriculture where patients had direct contact with low quantities of this substance.
- The highest number of cases reported by the end of 2007 was associated with methyl bromide, also referred to as bromomethane. In all of these cases, health disorders were rated as minor ones. Symptoms reported included above all irritations of the mucous membranes of the upper respiratory tract and of the eyes such as dryness of mouth, tickling throat, cough, lachrymation. Also headache, dizziness and malaise as well as skin rash and pruritus were frequently reported.
- Sulfuryl difluoride, a substance recommended as an alternative to methyl bromide, was involved in eight cases reported to the BfR. In these cases, health disorders were observed during fumigation operations, but they were not associated with fumigation of containers.

In September 2007, the Joint Poison Control Centre (Gemeinsames Giftinformationszentrum) of the Federal Länder of Mecklenburg-Western Pomerania, Saxony, Saxony-Anhalt and Thuringia located in the city of Erfurt informed the BfR about cases of poisoning with methyl bromide and in this context reported two cases whose details are presented in the following (case reports).

Alerted by this problem, the BfR initiated a survey among PCCs in Germany (nine centres), Switzerland, Austria and France in late December 2007. PCCs were asked whether they had received any enquiries regarding the fumigation of containers since the year 2000 and whether an increasing trend could be seen in the numbers of such enquiries. The active substances referred to in this survey included chloropicrin, 1,2-dichloroethane, methyl bromide and sulfuryl difluoride. In addition, information was requested with regard to manifestations and degrees of severity of corresponding cases of poisoning. Six out of twelve Poison Control Centres addressed responded to the letter sent by the BfR:

- The Bonn PCC had not received any enquiries on the substances concerned.
- The Berlin PCC had recorded two cases in 2003, one in 2006 and two again in 2007.
- The Joint PCC in Erfurt, who had already submitted reports on two cases to the BfR

before (see above), reported another case on the occasion of the survey.

- The Freiburg PCC submitted information on eight cases of poisoning: two in 2002, one in 2005, three in 2006 and two in 2007. These cases referred to five poisoning incidents that had affected a total of 32 persons.
- The Swiss PCC had recorded eight enquiries on this problem: Six cases had already occurred in 1999 (involving methyl bromide and phosphine), one case in 2003 and one enquiry (no poisoning) had been received in 2006.
- The Northern Germany PCC located in Göttingen reported 79 exposure incidents and 36 precautionary enquiries (share of container fumigation operations unclear): Phosphine: 40 exposure incidents and ten precautionary enquiries; hydrogen cyanide: 20 exposure incidents and 17 precautionary enquiries; methyl bromide: 13 exposure incidents and two precautionary enquiries, 1,2-dichloroethane: six exposure incidents and no precautionary enquiry, sulfuryl difluoride: no exposure incident and seven precautionary enquiries, and chloropicrin: neither exposure incidents nor enquiries.
- The poison emergency telephone service in Munich verbally reported another 32 cases that had occurred in September 2007 at a trade fair when machine parts from India were unpacked (another case associated with this accident is presented below as an example). All of the patients affected showed only mild symptoms but were admitted to hospital for observation. They could all be discharged in a symptom-free condition on the following day. Essentially, measurement of bromide adducts in the patients showed normal values. No methyl bromide could be detected in the wood samples kept for reference. However, it has to be taken into account that a considerable period of time had passed between the onset of health complaints and sampling so that outgassing of the active substance was possible.

Fig. 8: Measurement before clearance

In general, it has to be assumed that the frequency of cases of poisoning associated with fumigation of containers is highly underestimated in the corresponding records, for the following reasons:

- Allocation of toxicants is impossible because many containers are unlabelled. For example, health impairment due to “an unknown gas” is reported without stating the name of the poison involved. Such reports cannot be assigned to any defined exposure in follow-up enquiries by the BfR or Poison Control Centres.
- Attending physicians are lacking sufficient information about this problem. Therefore, it may be missed when establishing the patient’s medical history. Health complaints are not associated with an exposure to fumigants and instead, assigned to a different clinical picture.
- There is no good reporting behaviour shown by medical practitioners and hospital physicians. Reasons for this may be seen in the lack of remuneration of reports, overburdening by acute problems, or ignorance of § 16e of the Chemicals Act.
- Employees are not aware of the problem. Since they lack information about fumigation and the risks involved, they would not associate their health complaints with exposure to fumigants. They would not see a doctor, so that no report will be submitted on these cases.

The BfR will continue to discuss this issue and make efforts to inform the public in appropriate ways.

Notes

Methyl bromide, or bromomethane, is a colourless and odourless gas. It cannot be perceived by a warning odour if the maximum admissible concentration at the workplace is exceeded. This is why frequently, an odorous substance is added to ensure a certain signalling or warning effect. Due to its toxicity, it has been used for pest control, particularly for container fumigation, to control wood pests e.g. in building materials, and for soil disinfestation. Methyl bromide has a depleting effect on the ozone layer. Therefore, its use was limited in the Montreal Protocol on Substances that Deplete the Ozone Layer. Since 1 September 2006, it has been banned as a fumigant in Germany.

In order to prevent the introduction of pests, the International Plant Protection Convention (IPPC), a multilateral convention under the auspices of the UN Food and Agriculture Organization (FAO), has adopted ISPM 15 (International Standards for Phytosanitary Measures), entitled Guidelines for Regulating Wood Packaging Material in International Trade. These guidelines require that wood packaging material should be treated with methyl bromide or heat. Meanwhile, wood used in overseas exports from Germany is exclusively treated with heat. Nevertheless, containers used for imports from non-European countries, particularly from Asia, still have to be assumed to have undergone fumigation with methyl bromide. The provisions of the International Maritime Organisation (IMO) requiring such containers to be labelled as having been fumigated are frequently not complied with in practice. Persons opening or unloading import containers or unpacking goods transported in such containers may therefore unknowingly become exposed to methyl bromide.

Case reports

Chronic inhalational exposure to methyl bromide at the workplace associated with container fumigation operations

The female patient had frequently been exposed to fumigants originating from imported containers in her working environment. Therefore, a long-term contact with the substance has to be assumed. Methyl bromide was stated to have been the fumigant applied. The patient had not been informed about occupational safety measures. Since the last contact with the substance on a Friday she had been complaining of pronounced hoarseness and a burning sensation on all her mucous membranes, including the genital area. Because these complaints did not recede, she sought medical advice at the emergency unit of a hospital on the following Monday.

Manifestations/course

In the hospital, hoarseness persisted and the patient stated to suffer from a burning pain on her skin. The hospital staff consulted a PCC, which recommended to perform dermatological, neurological and ophthalmological diagnosis. It was intended to contact the company physician in order to provide for appropriate occupational safety measures. The BfR lacks information about the further course of this case.

Evaluation of the case described

Based on the temporal relationship between the exposure and the appearance of symptoms and in the absence of other causes, a low-grade poisoning by methyl bromide has been considered as probable.

Inhalational exposure to methyl bromide at the workplace associated with container fumigation operations

A 35-year-old worker had been unpacking containers in a closed fair hall over a full

working day. The containers had been loaded with machine parts in wooden boxes from India. According to information given by the forwarding company, they had been fumigated with methyl bromide to prevent pest infestation. To comply with a given deadline, the recommended waiting period for ventilation had been ignored. Several workers had perceived an unpleasant odour when unpacking the goods and complained of minor symptoms such as headache, sore throat and generalized itching of the skin.

After work, the patient complained of dizziness and myoclonic twitches in his thighs. Due to a common cold infection he had been suffering from cough already prior to the exposure. Three days later, the patient sought medical advice in a hospital in his home town because he associated his health complaints with the container fumigation. He had informed himself about possible signs and symptoms of poisoning with methyl bromide in the press and on the internet.

Manifestations/course
The hospital consulted a Poison Control Centre. A thorough physical examination and ECG were recommended. The patient was referred to outpatient treatment. The BfR lacks information about the further course of this case.

Evaluation of the case described
Based on the temporal relationship between the exposure and the appearance of symptoms and in the absence of other causes, low-grade poisoning by methyl bromide can be assumed as possible. In addition and already prior to the exposure, the patient had been suffering from an infection of the upper respiratory tract with cough.

Inhalational exposure to methyl bromide at the workplace associated with container fumigation operations
In March 2007, a 44-year-old worker unloaded wood products from a fumigated container and was exposed to the gas for about three hours. The container had been fumigated with methyl bromide and had not been ventilated sufficiently prior to unloading. After work, the patient suffered from a tickle in his throat and dizziness and sought medical treatment.

Manifestations/course
On admission, auscultatory findings of the lungs were non-significant and circulatory parameters were in the normal range as well. Lung X-ray findings were normal for the patient's age. The hospital consulted a Poison Control Centre, which recommended inpatient observation. The patient was administered a corticoid spray in order to prevent toxic lung oedema. In addition, infusion therapy was performed for fluid replacement.

Evaluation of the case described
Based on the temporal relationship between exposure and appearance of typical manifestations and in the absence of other causes, a low-grade poisoning by methyl bromide has to be rated as probable.

Notes regarding the three cases presented above:
Methyl bromide is highly toxic and can be absorbed by inhalation or by the dermal route (contact poison). It causes irritation to the skin, the eyes and the respiratory tract. Local effects on the eyes include reddening, pain, blurred vision with temporary visual disturbance and conjunctivitis.

Dermal effects include erythema, pain, chemical burns, a burning sensation, scab formation and blistering.

Inhalation will cause nausea, vomiting, abdominal pain, cephalgia, dizziness, tiredness, disorientation, hallucinations, speech disorders, weakness, impaired coordination, muscular spasms, dyspnoea, and in the worst case, pulmonary oedema. Exposure to high concentrations may result in disturbances and loss of consciousness with a lethal outcome. In most cases, there will be a latency period before the onset of manifestations. Repeated or long-term exposure may result in damage to lungs, liver, heart and central nervous system.

After contact with the substance, the patient should be removed from the contaminated environment using a self-contained breathing apparatus. Decontamination should be performed, including a change of clothing and showering or rinsing of the affected sites with water. In order to prevent toxic pulmonary oedema, patients showing pulmonary manifestations should be administered glucocorticoids as soon as possible, either by means of a CFC-free metered-dose inhaler (e.g. Budesonide) with aerosol holding chamber or by i.v. injection of high doses (preferably methylprednisolone), if massive exposure is assumed to have taken place. In severe cases, oxygen supply and artificial respiration may be required. Onward therapy will be oriented by the existing symptomatology. In any case, clinical observation should follow.

When handling this substance, safety goggles and cold-resistant protective gloves should be worn as a protective measure. Under the German Technische Regeln für Gefahrstoffe (TRGS 512 – Technical Rules for Hazardous Substances, Fumigation), a suitable breathing protection, i.e. the use of a full protective mask with a sufficient filter is required for fumigation operations.

3.2 Selected cases by route of exposure

3.2.1 Dermal exposure

Notes regarding the skin diseases presented below

Below, a number of individual cases of **contact eczema** are described. The following advance information is given for a better understanding of all of these case reports.

Contact eczema or contact dermatitis are terms used to designate acute or chronic superficial inflammatory skin diseases.

Such diseases are referred to as **non-allergic contact eczema** if caused by acute or cumulative toxic, physical or chemical exposure. This includes, for example, the *acute-toxic contact dermatitis* resulting from exposure to UV radiation (solar dermatitis), acids or alkalis. *Cumulative toxic contact eczemas* include, for example, diaper rash in children. Otherwise, only in adults this type of eczema is caused by cumulative toxic stimulation. Reddening and swelling of the skin are observed at exposed body sites.

In contrast, **allergic contact eczema** is caused by an acquired cell-mediated allergy to defined contact substances. Hence, allergic contact eczema is a special form of an allergy classified as a delayed-type hypersensitivity reaction. It is the classic representative of type IV reactions according to the Gell and Coombs' classification and in the majority of cases is observed among adolescents and adults.

It can be assumed that hypersensitivity rates among the population are continuously on the increase. Nickel and fragrances are among the substances frequently associated with sensitization. In the majority of cases, sensitization is triggered by incomplete antigens referred to as haptens. These are predominantly fat-soluble substances with a low molecular mass. They bind to proteins in the epidermis, thus trans-

forming to complete antigens. Complete antigens activate Langerhans' cells, which in turn produce cytokines. This is followed by transformation into lymphocytes and their multiplication. These will infiltrate the smallest blood vessels of the skin and act as memory cells. Sensitization will take about 8 to 21 days and in most cases, will take an asymptomatic course. Only after a second contact, antigen-specific memory cells will become transformed into effector cells which in turn, will cause the release of several messenger substances. More inflammatory cells will be recruited followed by interference with the epidermal barrier function and an excessive inflammatory reaction of the skin. Contact with substances having caused an existing cell-mediated allergy will result in erythema, oedema and papulovesicles, sometimes also in weeping erosions, scab formation and secondary effects from scratching at the contact sites.

Diagnosis is based on the patient's history, eczematous skin changes and typical localization. If a defined substance is suspected of having caused the contact allergy, a standardized commercial patch test (epicutaneous test) is performed. For this test, the allergen is applied to the skin by means of a taped pad and left there for 48 hours; the reaction is read 48 and 72 hours later. Formation of an infiltrate is interpreted as a positive reaction to the test.

The most important measure of treatment is elimination or avoidance of the toxicant or the allergen. Hyposensitization as performed to treat inhalation allergy has not yet become established in such cases. Therefore, treatment of the eczema will depend on the manifestations present. Corticosteroids are the medication of choice for initial topical therapy. After inflammatory manifestations have subsided, a nurturing and stabilizing treatment of the skin will follow. Weeping skin areas will be treated with moist compresses and water-based ointments, chronically dry skin changes with oil-based creams.

Sensitization will often persist for more than ten years even if the allergen is carefully avoided. Renewed exposure will result in symptoms returning. This is why in a prognostic view, a definite cure is considered as rather improbable.

3.2.1.1 Allergic contact eczema

Allergic contact eczema after use of an anti-wrinkle product

A 51-year-old physician had used a cosmetic product over a period of approximately one year in order to treat the facial lines around his eyes. For this purpose, he had applied the product to his upper and lower eyelids twice

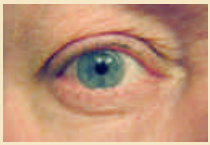


Fig. 9: Right eye prior to use of the anti-wrinkle product

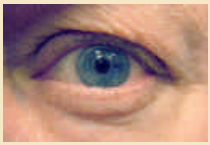


Fig. 10: Left eye prior to use of the anti-wrinkle product

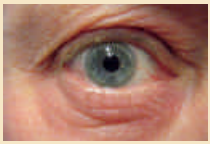


Fig. 11: Allergic contact eczema after use of the anti-wrinkle product – right eye

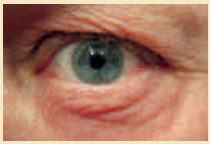


Fig. 12: Allergic contact eczema after use of the anti-wrinkle product – left eye

a day (except for occasional single-day interruptions) slightly rubbing it in as described in the instructions for use. Eleven months after the first use, he noticed itching, burning and reddening of the treated skin areas. These manifestations deteriorated, and an increase rather than a reduction of wrinkles was observed. In addition, the patient developed desquamation (shedding of the horny outer layers of the skin associated with scale formation). Therefore, he discontinued the treat-

ment three days later. The patient's medical history did not mention any other diseases, nor had he taken any medicines or used dermal products, ointments or other cosmetics.

Manifestations/course
The physician treated himself with 0.5 % hydrocortisone preparations as a topical therapy and with prednisolone tablets as a systemic therapy at doses of 15 mg daily administered over a period of three days. Under this therapy, the symptomatology showed a considerable improvement so that treatment could be discontinued. Subsequently, the patient had almost no complaints and in the further course, he became symptom-free.

Notes
In the above case, it has to be assumed that the patient suffered from an allergic contact eczema. The typical symptoms developed on repeated contact and after a sensitization period. The patient became symptom-free as a result of allergen avoidance and an appropriate treatment with steroids.

Evaluation of the case described
Based on the information given on the temporal relationship between contact with the allergen and the appearance of manifestations, and in the absence of other causes, a causal relationship has been rated as probable in the case described.

3.2.1.2 Non-allergic contact eczema

Severe inflammatory reaction with scar formation after use of a tattoo remover
A 28-year-old patient had a tattoo removal performed. This was to be achieved by intradermal injection of a substance which has remained unknown to the BfR. The media (press and TV) had promoted this method as the most up-to-date and harmless procedure for tattoo removal. The active substance was not revealed. Allegedly, this treatment was carried out in Germany by only one tattoo removal consultant who for this purpose imported the substance from the United Kingdom.

Manifestations/course
In the context of the removal attempt, the patient developed severe inflammatory reactions of the skin followed by a formation of raised scars. Dark shades of the former tattoo were still visible under the skin. The patient presented to a laser centre for further removal treatment. His skin above the former tattoo

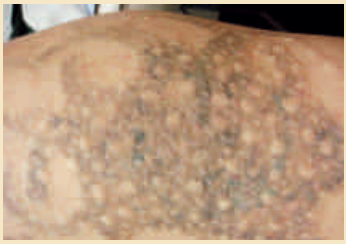


Fig. 13

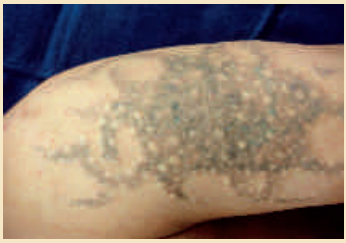


Fig. 14

Fig. 15

Fig. 13, Fig. 14, Fig. 15: Severe inflammatory reaction with scar formation after use of a tattoo remover

exhibited numerous scars which probably cannot be removed. The BfR lacks information about the further course of this case.

Evaluation of the case described
Based on the information given on the temporal relationship between administration of the substance and the appearance of manifestations, and in the absence of other causes, a causal relationship with the tattoo removal has been rated as probable.

Severe inflammatory reaction with scar formation after use of a permanent make-up remover
A 55-year-old patient, who was a cosmetician herself, had a permanent make-up of her eyebrows performed eight years ago. Because she was discontent with it, she had it removed by a permanent make-up designer. The tattoo and permanent make-up remover she had bought for this purpose was administered by subcutaneous injection, in compliance with the instructions for use. According to the information provided by the manufacturer, the product contained certain fruit acids intended to remove the permanent make-up. The ingredients of this remover product are unknown to the BfR.

After the treatment, the patient developed a massive purulent inflammation in the region of the eyebrows. She complained of swelling, itching, burning, severe headache and severely inflamed eyes. She tried to soothe her symptoms by means of local ice packs, as it was recommended by the seller of the product, and then she consulted a dermatology practitioner.

Manifestations/course
The dermatologist's findings included severely inflamed and weeping skin changes in the region of the patient's eyebrows. A toxic contact dermatitis caused by the remover was diagnosed. Treatment consisted in topical application of a cream containing antibiotics and cortisone. Two weeks later, the areas affected still exhibited massive keratinization and scab formation with additional superinfection in part. In addition, a slight swelling of the eyelids was observed. Even two months after the attempted removal, the patient was still experiencing pain. Two flesh-coloured itchy scars formed in the region of the eyebrows. It has remained unclear whether this condition can be cured. The resulting disfigurement means a considerable mental strain and a high degree of suffering for the patient.

Evaluation of the case described
Based on the information given on the temporal relationship between administration of the substance and the appearance of manifestations, and in the absence of other causes, a causal relationship has been rated as probable in the above case.

Notes referring to both cases (tattoo and permanent make-up remover)
As suggested by the purpose of the product stated, the ingredients of the tattoo and permanent make-up removers might contain aggressive substances causing skin damage (non-allergic contact eczema). Both cases described may be classified under this category.

If a preparation is injected, treatment under non-sterile conditions may as well result in a transmission of pathogenic microorganisms. This will increase the risk of infection.

It has remained unclear whether in the above cases the presence of an aggressive ingredient of the removal preparation resulted in acute-toxic dermatitis, or the skin damage has to be attributed to an infection due to non-sterile conditions.

3.2.1.3 Non-classifiable contact eczema

Contact eczema after the application of herbicides

A 41-year-old patient had applied two spray chemicals at his workplace. One of these contained the active substance amidosulfuron, a sulfonylurea, the other herbicide contained ioxynil and sodium hydroxide, the latter in a corrosive concentration. During this work, his arms and hands were uncovered. In the afternoon of the same day, he developed vesicles on both his hands and arms similar to those associated with sun allergy. During the night, the patient's condition deteriorated, he complained of severe pain. In addition, he developed blood blisters on the exposed body parts (both arms and hands). He consulted a doctor. It has remained unknown whether the patient had had contact with the two substances involved before the incident. No statements can be made regarding the patient's medical history nor that of his family.

Manifestations/course

The attending dermatologist treated the patient with cortisone. No more information has been available concerning the further course, in particular, it has remained unknown whether epicutaneous testing was performed.

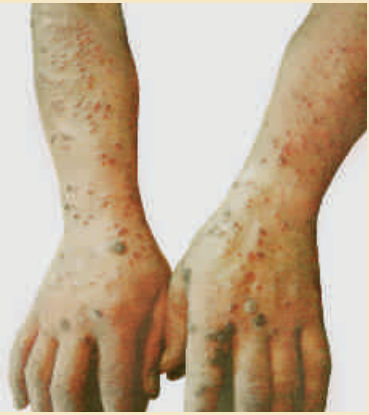


Fig. 16: Contact eczema after the application of herbicides

Notes

The information available to the BfR was insufficient to elucidate whether in the above case, the patient suffered from contact eczema caused by acute exposure to toxic chemicals (ingredient sodium hydroxide) or from a contact allergy in the sense of a type IV reaction according to the Gell and Coombs' classification (cortisone treatment).

Evaluation of the case described

Based on the information given on the temporal relationship between the contact with the products and the appearance of manifestations, and in the absence of other causes, a causal relationship has been rated as probable in the above case.

3.2.1.4 Special forms

Meadow grass dermatitis due to hogweed contact

As part of his job in the waste management industry, a 25-year-old metalworker had contact with hogweed during mowing operations. It has remained unknown to the BfR whether the plant involved was the common hogweed (*Heracleum sphondylium*) or the giant hogweed (*Heracleum mantegazzianum*). The patient developed dermal symptoms and therefore consulted a doctor.

Manifestations/course

The "Durchgangsarzt" diagnosed contact dermatitis due to hogweed. After a course of outpatient treatment, the patient recovered. No more details were available on this case.

Fig. 17: Giant Hogweed (Heracleum mantegazzianum), toxic

Notes
Both the giant hogweed (*Heracleum mantegazzianum*) and the common hogweed (*Heracleum sphondylium*) belong to the genus Heracleum.

The common hogweed is frequently found on meadows and along roadsides and forest edges in central Europe. Its typical characteristics include flat umbels of mostly five white, greenish or reddish blossoms. The fruit is flat and mostly of elliptic form, with a length of 6–10 mm, and its lateral ridges are prolonged to form broad wings. It is a herbaceous plant of 0.5–1.5 m height with bristly-hairy stalks becoming puffy sheaths near the stem.

The giant hogweed is often found along roadsides and forest edges, on moist rich soils and on fertilized meadows in Europe. The plant may reach a height of more than 3.5 m and has thick stalks of ca. 10 cm in diameter with purple blotches. Its leaves are deeply incised and three-lobed, single leaves are five-lobed and pointed. The impressive white flowers are flat umbels reaching up to 50 cm in diameter.

All parts of plants belonging to the genus Heracleum are toxic. The responsible substances are referred to as furocoumarins. In common hogweed, these plant ingredients are mainly found in the unripe fruits, in giant hogweed, particularly in the sap. On contact with the skin and simultaneous or subsequent exposure to sunlight, furocoumarins cause a phototoxic reaction resulting in meadow grass dermatitis. Initial manifestations include itching, burning and erythema with oedema. About 10–48 hours later, a clearly circumscribed dermatitis will develop on the skin areas affected, it is associated with itching, reddening and blistering. These skin changes take a long time to heal (one to two weeks). They may remain visible up to one year and leave scar-like hyperpigmentation. Acute toxicity of furocoumarins is low in the absence of light. Therefore, exposed persons should absolutely avoid exposure to sunlight. Treatment will depend on the symptoms experienced and may include e.g. topical administration of anti-swelling and antiphlogistic agents. Once the blisters have dried up, most persons affected will no longer suffer from complaints. In cases of ingestion, fluid should be given for dilution.

In the case described above, it can be assumed that the contact dermatitis diagnosed was meadow grass dermatitis.

Evaluation of the case described
Based on the information given on the temporal relationship between the contact with the plant and the appearance of manifestations typical of contact dermatitis, and in the absence of other causes, a causal relationship has been rated as probable in the case described.

Allergic exanthema after contact with insects
A 34-year-old forester had occupational contact with insects which, according to the information submitted, also included the oak processionary moth. The patient developed dermal symptoms and therefore consulted a doctor.

Fig. 18 and Fig. 19: Oak processionary moth (Thaumetopoea processionea)

Manifestations/course

The patient was diagnosed with allergic exanthema after contact with insects, probably the oak processionary moth. He was administered an unspecified infusion treatment. Following this treatment, his symptomatology improved. No more details about the course have become available to the BfR.

Notes

The oak processionary moth (*Thaumetopoea processionea*) has been named after the habit of its larvae (caterpillars) to form processions at night when crawling from their nests to the crowns of oaks to feed on the foliage. It is native to central Europe and thrives in a warm and dry climate. A growing occurrence of the species has been observed since the mid-1990ies. A particularly steep increase in the population density of the moth tending towards mass reproduction was found to occur after the extremely hot and dry summer of the year 2003. Kindergartens and schools had to be shut down temporarily due to caterpillar infestation in their vicinity. Control of the spreading has been particularly difficult because some methods of mechanic elimination have proved to be problematic. For example, removal of the webs by means of water jets may promote swirling of the toxic caterpillar hairs. A method that has proved to be successful is spraying of the larval nests with a binder. Afterwards, the nests are collected and disposed of in closed plastic bags in a waste incineration plant. Operators performing this work should wear full protective suits and respiratory protection.

A particular health risk for humans is posed by the hairs of older caterpillars. These urticating hairs possess barbs and therefore may remain stuck in the skin. They break readily, releasing the urticating toxin, thaumetopoein, which may cause allergic skin reactions. Dermal contact will immediately result in unpleasant itching followed by skin rash. In addition to inflammatory skin reactions, also wheals or persistent nodules may develop macroscopically resembling insect bites. Exposure of the eyes will result in eye irritation, on inhalation there will be irritation of the upper respiratory tract, which in predisposed subjects may result in dyspnoea. In very rare cases, also general manifestations such as dizziness, drowsiness and fever may occur.

After contact with caterpillar hairs in the absence of protective clothing, a thorough showering and laundering of clothes are recommended. Onward therapy will be oriented by the existing symptomatology.

Caterpillar hairs accumulate particularly in underwood and ground cover and adhere to clothes and shoes. They preserve their activity over a long period and remain dangerous for approximately one year. Thus, they may cause reactions again and again.

It has to be assumed that in the case described above, the forester had worked without wearing protective clothing. Contact with the urticating

hairs caused the release of thaumetopoein resulting in the manifestations described above.

Evaluation of the case described
Based on the information given on the temporal relationship between contact with the caterpillars and the appearance of manifestations, and in the absence of other causes, a causal relationship has been rated as probable in the case described.

3.2.2 Oral exposure

3.2.2.1 Water intoxication

Severe hypotonic hyperhydration from drinking ca. 4 L of tap water following accidental ingestion of a descaling agent
A 57-year-old patient had accidentally ingested a sip of a descaling agent containing amidosulfonic acid. Therefore, she decided to drink about 4 L of tap water subsequently. This large quantity was confirmed by her husband. By doing so, she intended to prevent health damage possibly caused by the descaling product. Shortly afterwards, nausea set in and she experienced two episodes of vomiting. Because the accident occurred during the Christmas holidays, she consulted the medical emergency service. In order to exclude a chemical burn due to the descaling product, the patient was admitted to hospital by the physician on duty. In the ambulance, the patient began to suffer from increasing mental clouding and developed recurrent generalized convulsions.

The patient's medical history revealed regular alcohol consumption. She had stated to consume one or two glasses of wine per day.

Manifestations/course
After admission to the intensive care unit, the patient suffered again a convulsive seizure which was associated with a persistent drop in oxygen saturation requiring intubation and artificial respiration. Clinical and radiological findings revealed pulmonary oedema. Already after a short period of time, the patient showed sufficient gas exchange and respiration and could be extubated. Clinical chemistry revealed massive metabolic acidosis, mild leukocytosis of 11.6 10^3 /L, CRP increase of 48 mg/L and a mild increase in liver enzymes. Problems arose from a severe disturbance of the water and electrolyte balance that had been the cause of the central manifestations including the convulsive seizures. Laboratory measurements found sodium levels of 112.6 mmol/L, a decrease in osmolality to 265 mosmol/kg H_2O, a reduced red blood cell count of 3.4 10^{12} /L and a reduced haematocrit of 33 %. These findings indicated severe water intoxication. Since the condition was still at an early stage, it was decided to perform haemofiltration. A few hours after the incident it could be assumed that a final redistribution had not yet taken place in the body. The treatment was aimed at the restoration of the physiological volume homoeostasis. After successful haemofiltration, the alert patient could be transferred to a normal ward, with normal reflexes and a compensated acid-base balance. At that time, also spontaneous respiration had been restored. No more convulsive seizures were observed. The patient's cardiovascular condition had been stable throughout the inpatient treatment.

The BfR has not received any information about the further course of this case. It is assumed that the patient recovered and was discharged from hospital after appropriate observation and follow-up examinations.

Notes
Descalers contain acids. Depending on the concentration, they may cause chemical burns.

Fig. 20: Descaling product

Manifestations of chemical burns include nausea, vomiting, hypersalivation, pain (in the oral cavity, retrosternal) resulting in refusal to eat particularly in children, and signs of burns in the oral and pharyngeal regions. The latter may be absent in cases of fluid ingestion because fluids will quickly pass the oral cavity prior to causing visible lesions.

Symptomatic patients should always see a doctor to exclude chemical burns.

In any case, drinking of a quickly available fluid such as tap water is recommended as an immediate measure. This is done to flush the oesophagus. The ingredients of tea, tap water and mineral water do not correspond to what the body needs. If ingestion of too high amounts of these fluids is not accompanied by the consumption of other foods, this will result in sodium chloride deficiency, also referred to as hyponatraemia. There will be a state of salt-to-water imbalance in the body.

Symptoms include dizziness, nausea and vomiting. In extremely severe cases, drinking of large amounts of water may result in water intoxication with hyponatraemia if the intake of minerals and common salt is insufficient. Low sodium levels may lead to disorientation and severe organ damage such as cerebral dysfunction (cerebral oedema) and thus, to a lethal outcome. Therefore, it is recommended not to consume large amounts of water at once. If nevertheless, large quantities of water were consumed without the simultaneous supply of any other food, electrolyte control should be performed. Findings of imbalance require intensive medical monitoring including careful assessment of the water and electrolyte balance and a cautious and slow electrolyte replacement.

In the case described above, the symptoms experienced by the patient indicated that she needed to see a physician in order to exclude possible chemical burns. As recommended, she drank a rapidly available fluid as a first measure, however, without consuming anything else in addition. Presumably, the quantity of 4 L she consumed was too high and probably not excreted in full later on. The lack of a simultaneous supply of minerals together with insufficient excretion of the excessive amounts of water resulted in water intoxication. As a consequence, the patient suffered a disturbance of her water and electrolyte balance. The high water retention can probably be attributed to an increased release of the antidiuretic hormone (ADH) under conditions of nausea. Nausea or vomiting stimulate the release of ADH, which reduces fluid excretion in order to protect the body from fluid loss.

The mild increase in liver enzymes may be attributed to regular alcohol consumption. There were no indications of alcohol withdrawal symptoms. The metabolic acidosis observed was most probably caused by the derailed metabolic situation. The absorptive effect of the descaler was considered as less probable.

Quantities of about 100 mL would be insufficient to cause such an effect. Higher amounts are only ingested with suicidal intent. A suicide attempt was however excluded on account of the medical history in the case described above.

Evaluation of the case described
Based on the temporal relationship between the drinking of large amounts of water and the appearance of typical symptoms, a causal relationship has been rated as possible in the above case. Nevertheless, such pronounced cases have been observed extremely rarely in practice.

3.2.2.2 Accidental intake of cleaning agent

Cleaning agent mistaken for orange juice by elderly patient
A 69-year-old patient had accidentally ingested a sip of a cleaning agent. Due to the product's colour and a package design resembling that of a food product, it was mistaken by him for orange juice. In addition, the label showed a picture of oranges and the word "Orange" appeared in the product name.

The patient saw a doctor because of a burning sensation in his mouth and throat. No cough was observed.

Manifestations/course
The attending physician consulted a Poison Control Centre to assess the risk and initiate appropriate treatment. Because the cleaner contained a surfactant, the patient was administered an agent to prevent foam formation. In addition, he was recommended to drink fluid. Physical examination findings were non-significant, and admission to hospital was not required.

Notes
An enquiry at the Berlin poison emergency telephone service revealed that the product concerned had been involved in only one case of poisoning so far.

In addition to surfactants, the cleaner involved contains a relatively high share of synthetic essential oils.

Essential oils have been used as a common cold remedy in medicine, as indoor air fresheners or conditioners in the household, for aromatherapy, in stain removers or other cleaning agents, in cosmetics, and also in industry, for example as a fat solvent.

As far as is known, they are readily absorbed from the gastrointestinal tract, the lungs and the skin and mucous membranes. No exact toxicological data have been published recently. Lethal doses stated in the past were 50–500 mg/kg body weight. It has to be taken into account that the toxicity of the individual essential oils varies. Special caution should be exercised when using camphor, eucalyptus, thyme and peppermint oil (menthol). These essential oils are considered as particularly problematic. Camphor is extremely toxic, ingestion even of small amounts may cause convulsions. Synthetic oils are considered as harmless rather than dangerous. Otherwise, minor symptoms may occur already after ingestion of a few droplets irrespective of the dose. Severe symp-

Fig. 21: This cleaning agent can easily be mistaken for a beverage

toms have to be expected only after ingestion of large amounts but due to the irritating effect on the mucous membranes, intake of large quantities is rather improbable. There are, however, numerous essential oils whose taste is similar to that of fruit juice. All manifestations will occur within the first two hours after ingestion. Irritation of the mucous membranes will result in gastrointestinal complaints, absorption may be followed by CNS manifestations similar to those of alcohol intoxication such as ataxia, sedation, unrest, tremor and a lack of distance. In rare cases, severe symptoms such as unconsciousness and convulsive seizures may occur.

Therapy will depend on the symptoms observed. In cases where the amounts ingested do not exceed a sip, administration of fluid and observation at home for two hours are sufficient.

Surfactants (anionic and non-ionic) are rather safe in terms of health. In addition to the irritating effect on mucous membranes, foam formation is the predominant problem. Manifestations may also include vomiting, abdominal pain, flatulence and diarrhoea. In rare cases, vomiting or formation of considerable amounts of foam in the mouth involve an aspiration risk. Aspiration may have taken place if persistent cough and respiratory complaints are observed. For healthy children and adults, ingredients containing surfactants do not pose a particular risk. For elderly persons, however, shower gels, bubble baths, shampoos, all-purpose cleansers, liquid detergents etc. may be life-threatening. They are more prone to foam aspiration, which may result in severe pulmonary manifestations. In the context of the reports entitled Cases of Poisoning Reported by Physicians, a total of 23 cases have come to the knowledge of the BfR since 1990 where the ingestion of large amounts of household cleaners and disinfectants resulted in severe manifestations. A lethal outcome was recorded in 17 cases. All of these cases referred to disoriented elderly persons. There has certainly been a considerable number of undetected and unreported cases.

Another risk group is that of infants particularly in their oral phase because coloured fluids may be considered by them as attractive “toys” and are explored by putting them into the mouth. As a rule, these children will develop only minor gastrointestinal symptoms. Treatment will consist in the administration of an anti-foaming agent, which, however, has to be procured or prescribed before it can be used.

Elimination of the risk of accidental ingestion due to mistake, e.g. by different designs of package and choice of colours for such products, could spare patients unpleasant complaints and medical consultations and avoid unnecessary treatment costs. A positive example to be mentioned is the ban on coloured lamp oils. Such measures could reduce the risk involved for elderly individuals who otherwise might mistake certain substances for foods, thus preventing cases of severe poisoning and a lethal outcome.

Evaluation of the case described
Based on the information given on the temporal relationship between the ingestion and the appearance of manifestations, and in the absence of other causes, a causal relationship has been rated as probable in the above case.

3.2.2.3 Carbon grease remover

Severe chemical burns in a young child after ingestion of a carbon grease remover containing sodium hydroxide
A 4-year-old child accidentally drank one or two sips of a carbon grease remover containing sodium hydroxide. The product had been filled into a lemonade bottle and could therefore be mistaken for a beverage. The child was immediately given water to drink by her mother. Subsequently, the child vomited sever-

al times, and the emergency medical service was called. When the emergency physician arrived, vomiting had stopped. Oral lavage with isotonic saline was performed repeatedly, and the child transported to a hospital.

Manifestations/course
During admission to the paediatric hospital, the child vomited again. During medical examinations, she was found to be in a reduced general condition. Symptoms of chemical burns included swelling of the lower lip and oral mucosa. Except for stress-related tachycardia (130/min), no abnormality was detected with regard to the status of other organs. Laboratory parameters routinely examined showed normal levels except for a leukocytosis of 19 200/µl. Radiology performed one day after admittance revealed an infiltrate in the right upper lobe of the lung.

On the next morning, gastroscopy was performed under endotracheal anaesthesia. The examination revealed pronounced changes of the hypopharynx, epiglottis and larynx with oedematous swelling. The oesophagus exhibited second-degree, mostly circular, chemical burns with fibrinous deposits, and the gastric cardia was covered with altered blood (haematin). Due to these pronounced findings, the child received parenteral nutrition, and a central venous catheter (CVC) was implanted for this purpose. According to the scheme for treatment of chemical burns, she was administered systemic steroids and put on antibiotic cover with cefotaxime. In addition, she was administered omeprazol. During the first night, the patient was monitored at the intensive care unit and analgosedated with midazolam and piritramide.

This therapy was continued after transfer to a normal ward. Paracetamol and if required, metamizole were now administered for pain

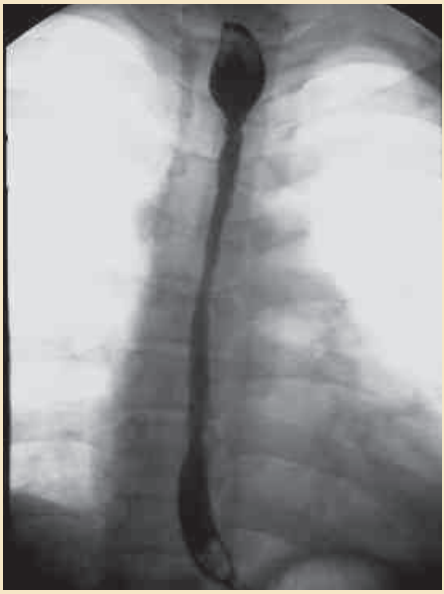


Fig. 22: X-ray picture of extended oesophageal stenosis

prophylaxis. During the following days, the patient still complained of pronounced difficulty to swallow. Local findings improved slowly, and steroid doses could be gradually reduced. On the sixth day, the patient's condition had stabilized so that the girl was allowed to drink in small sips, followed by a liquid diet given from the seventh day. On the ninth day, the CVC could be removed, and partial parenteral nutrition was performed over a peripheral access. The latter as well as the administration of steroids and antibiotics were discontinued on the following day. Solid food could be gradually reintroduced. Local findings made by non-invasive examination were satisfactory at that time.

Follow-up gastroscopy performed almost two weeks after the incident revealed stenosis passable for a 6mm device. Therefore, gastroscopy was repeated several times and

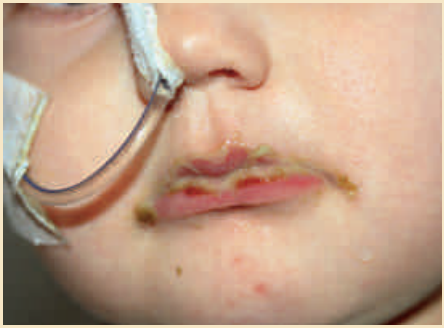


Fig. 23: Chemical burn of mucous membranes with lesions in the oral region

bougienage performed. The first bougienage lead to lesions of the mucous membrane which again required temporary abstinence from food. Subsequently, food was gradually reintroduced without problems. Afterwards, repeated gastroscopy and bougienage were performed and the child was discharged in the meantime with appropriate food to be given at home. Extended oesophageal stenosis required implantation of a stent.

About six months after the poisoning accident, the child had to be admitted to hospital again because of difficulties to ingest even liquid foods and increasing difficulty to swallow, which suggested dislocation of the stent. This was confirmed by gastroscopy and in addition, another stenosis was found, located cranial to the stent. After initial bougienage, attempts were made to relocate the stent. However, these attempts remained unsuccessful since the stent was non-relocatable. Another attempt was made a few days later followed by the decision to remove the stent. Due to the resulting severe irritation of the oesophagus, a new stent was not yet implanted. Five days later, the clinical course was complicated due to a perforation of the oesophagus which occurred during an attempt to implant a new stent.

The child was transferred to the paediatric surgery ward for onward treatment. On admission to this ward, the girl's circulation was stable but she was very restless and complained of severe upper abdominal pain. She was transferred to the intensive care unit. During tracheoscopy and oesophagoscopy, a gastric tube using a guide wire, as well as a suction drain tube for saliva drainage were inserted. In order to prevent mediastinitis resulting from pneumomediastinum, the patient was administered triple antibiotic treatment. There were no clinical signs of infection observed at any time of the treatment. An initial increase in CRP was followed by a clear decrease in the further course. Food abstinence was required and parenteral nutrition given. As a result of this therapy, the patient's general condition improved. After long-term parenteral nutrition via a CVC, continuation of relief through gastric tube and continuous saliva draining, the patient's clinical condition improved. An initial skin emphysema on the left coastal arch had disappeared. Antibiotic therapy could be discontinued as inflammatory parameters remained in the normal range. When X-ray of the gastrointestinal tract showed that the oesophageal leakage had disappeared, the suction drain tube was removed and gradual reintroduction of food started. No hypersalivation or vomiting occurred in the further course so that a gradual change to high-caloric enteral feeding and a likewise gradual reduction of parenteral feeding could be performed. Eventually, total enteral feeding of the child was possible, also oral fluid intake did no longer cause any problems and the patient could be discharged home.

Repeated follow-up oesophagoscopy including bougienage is envisaged the results of which have not yet been established. It re-

mains to be seen how the further gradual reintroduction of food and the eventual change to solid foods will develop.

Notes

Chemical burns are caused by exposure to acids, alkalies or other chemicals having corrosive or colliquative effects. Body areas particularly at risk include the mucosae of the upper gastrointestinal tract, mainly the oesophagus, after oral ingestion of a corrosive substance. Based on the clinical course, there are essentially two types of chemical burns.

- Acids will cause immediate precipitation of proteins resulting in coagulation necrosis, which will prevent further deep action and thus protect the underlying tissue. Sulfuric acid causes dehydration and strong heating of the tissue and thus may cause damage to all layers of the skin, mucous membranes and the eyes. Similarly, deep action is produced by hydrofluoric and nitric acids. Therefore, the extent of the damage can be assessed only after a certain latency period.
- Exposure to alkalies will result in colliquative necrosis. Due to cell lysis, the chemical will rapidly penetrate the outer layers of the skin. Among alkaline burns those caused by lime are prominent. Exposure to unslaked lime (calcium oxide, also referred to as quicklime or burnt lime) will result in the formation of calcium hydroxide on the mucous membranes and in the eyes (lacrimal fluid). This is accompanied by heat formation, which may cause additional damage to the skin, the mucosa and the eyes.

After exposure to low concentrations of corrosive substances, a clear differentiation of clinical manifestations is often impossible. Both acid and alkaline substances will cause no more than various degrees of irritation of the skin or mucosa because the underlying tissue is affected to a minor degree only.

Oesophageal burns are classified by three degrees of severity:

- First-degree burns are characterized by superficial lesions of the mucosa with erythema and oedema and without epithelial damage. In most cases they will heal without sequelae.
- Second-degree burns are associated with minor erosions, ulcerations and fibrin exudation. They reach the submucosa which shows tissue necrosis. Their healing process will include reactive granulation followed by scar formation.
- Third-degree burns are characterized by deep ulceration reaching into the muscularis mucosae and being associated with bacterial penetration into the perioesophageal tissue and perforation followed by mediastinitis. This will result in the formation of stenosing scars impairing food intake.

Most corrosive poisons act very quickly. Therefore, immediate action is of essential importance. Less rapid action is developed by dry substances in granular form because these can act only after having become dissolved. After oral ingestion, the first measure to be taken by the person affected is to spit out the corrosive substance. Particularly in the case of children and after ingestion of solid corrosive substances such as granular dishwasher cleaners, the patient's mouth should be wiped out with a damp cloth as soon as possible. To make use of the dilution effect, the patient should be prompted to immediately drink water or another (non-alcoholic, non-carbonated) fluid quickly available such as tea or juice. If some of the granules are stuck e.g. in one of the oesophageal sphincters, drinking of large amounts of fluid may also be effective some minutes later: the oesophagus becomes flushed. Any administration of milk in cases of poisoning is of no practical benefit; rather, it is contraindicated. Since poisons are either fat-soluble or water-soluble, milk will constitute an ideal transport medium, and the toxicants will be absorbed with particular readiness. In children, milk will often have an

additional emetic effect so that the corrosive substance passes the oesophagus twice, thus causing double damage. Therefore, vomiting must never be induced. Also for a so-called neutralization, milk is of minor importance because its buffering capacity is minimal. Drinking of milk is only recommended in exceptional cases such as after accidental ingestion of fluorides, tetracyclines or iron since the poison types formed as a result are less readily absorbed. Also gastric lavage is not recommended. However, it may be indicated to remove the corrosive substance ingested through a feeding tube if in addition, there is a risk of poisoning by absorption (e.g. hydrofluoric acid, formic acid).

All cases of confirmed ingestion of a corrosive substance will require treatment. In cases of suspected ingestion, a chemical burn is suggested by at least one of the following manifestations observed within the first 24 hours after the incident:

- Signs of burns in the oral and pharyngeal regions
- Hypersalivation
- Retching
- Vomiting
- Retrosternal or epigastric pain and refusal to eat (in children, an indirect manifestation of pain).

It has to be taken into account that although sings of burn may be absent in the mouth after ingestion of a corrosive fluid due to the rapid passage and short duration of exposure, considerable chemical burns may be present in the oesophagus. Patients who are initially symptom-free after suspected ingestion do not undergo treatment. However, they should see a physician for control and observation.

Immediate measures to be taken still on the scene of the accident may include pain relief, circulatory assistance, and intubation or tracheotomy. Systemic administration of 3 mg/kg body weight prednisolone should be performed to prevent glottic oedema. Oesophagoscopy should be performed later when this can be done on a routine basis (as a rule, on the following morning) and should be carried out by an experienced team. This will ensure that the extent of damage suffered is correctly identified. Inspection is performed until the first sign of burn becomes visible. The stomach has to be inspected only after ingestion of strong acids, soldering fluid or potassium permanganate crystals in order to exclude lesions of the stomach wall or to remove remaining crystals to prevent them from penetrating into deeper regions. If findings are negative, the patient can be discharged without any further measures. Also first-degree chemical burns do not require any treatment or follow-up examination. In cases of second-degree chemical burns, administration of prednisolone at a dose of 1 mg/kg body weight is recommended until healing has been verified by endoscopy. In animal studies, prednisolone has reduced abnormal growth of fibroblasts. Therefore, it was assumed to be able to prevent the formation of oesophageal strictures in humans. However, this assumption has not been confirmed in follow-up examinations of patients after chemical burns. In cases of third-degree burns, steroid therapy is discontinued. Such lesions may require surgical intervention. In cases of severe chemical burns where a high risk of stricture formation is involved or oesophageal stenosis has developed after healing, treatment may consist in (early) bougienage, insertion of a permanent gastric tube, or percutaneous endoscopic gastrostomy (PEG).

Onward therapy will be oriented by the symptoms. It may include administration of antibiotics to control mediastinitis and secondary infections associated with gastric ulcers, of proton pump inhibitors to reduce the production of gastric acid, and dietetic measures to ensure food intake (liquid or mushy diet or parenteral nutrition depending on findings). After ingestion of large quantities of acids, possible effects from absorption such as acidosis, haemolysis or renal

failure have to be taken into account. Finally, follow-up endoscopy is required, with the appropriate time of such examination depending on the extent and severity of the initial findings. Contrast X-ray examinations should be performed not earlier than three to four weeks later, in cases where apparent stenosis in the oesophagus or in the pyloric region has to be confirmed or excluded.

Evaluation of the case described
Based on the information given on the temporal relationship between exposure and the occurrence of the manifestations observed, and in the absence of other causes, a causal relationship has been rated as probable.

3.2.3 Inhalation exposure

3.2.3.1 Impregnation spray for tents

Severe inhalation poisoning with pulmonary oedema after exposure to impregnation spray for tents
Together with her husband, the patient had treated an awning with impregnation spray in the open air. She was situated at a distance of one or two meters from the spraying action performed by her husband. Shortly afterwards, the patient began to suffer from dyspnoea, shivers, a feeling of cold and weakness. For this reason, she sought assistance at the emergency unit of a hospital.

Manifestations/course
Examinations on admission and ECG revealed tachycardia with heart rates of about 100/min, and moist rales on lung auscultation. Radiological findings revealed pulmonary oedema. Blood gas levels taken on the day of discharge and lung function (date of examination unknown) were normal. Treatment of the patient included inhalatory and systemic administration of corticoids (initially i.v., later orally). In addition, she was administered diuretics. As a result of this therapy, her symptomatology improved rapidly. Pulmonary congestion as initially seen was no longer found to be present in the further course. After two days of inpatient treatment, the patient could be discharged and referred to outpatient treatment. She was recommended to consult a pulmonologist for follow-up examinations.

Notes
In the above case, the spray may have been used excessively. Also ventilation and wind direction, respectively, would have to be taken into account. This is the only explanation why the patient's husband did not experience any symptoms. Probably, he was less exposed. The patient became symptom-free within a short period of time owing to an effective therapy which had been initiated without delay.

A rapid communication on this case was distributed.

Evaluation of the case described
Based on the information given on the temporal relationship between the exposure and the occurrence of manifestations, and in the absence of other causes, a causal relationship has been rated as probable.

Severe inhalation poisoning with pulmonary oedema after exposure to impregnation spray for tents (product identical with that of the previous case)
A 35-year-old female patient had treated two igloo tents with an impregnation spray in the open air. The product used was identical with that involved in the case described above. The patient had also sprayed one of the tents along the seams from inside with the tent door remaining open. One hour after exposure she complained of dry cough during the slightest physical effort.

The attending physician consulted a Poison Control Centre seven hours after the patient's exposure to the product. At that time, his findings included minimal pulmonary spasms, tachypnoea and diffuse bilateral rales. The patient was administered corticoids and betamimetics by inhalation and was admitted to hospital.

In the patient's history, bronchial asthma not requiring treatment had been known for three years. It should be added that the patient was a smoker with a daily consumption of one package of cigarettes.

Manifestations/course
On admission, the patient was in a reduced condition in a status asthmaticus. Findings included orthopnoea and tachypnoea as well as tachycardia of about 100/min. On auscultation, consonating medium rales and slight wheezes and rhonchi were heard over the entire chest. X-ray examination revealed the presence of pulmonary oedema. Conspicuous findings made by clinical chemistry included leukocytosis of max. 27 200/µL, an increase in ESR and in CRP to 58.85 mg/dL. The other laboratory parameters routinely measured such as electrolytes, renal retention values, hepatic parameters and coagulation were within normal ranges. The patient was administered salbutamol by inhalation, a single dose of 40 mg furosemide and 2 g corticosteroids (i.v.). As a result of this therapy, the pulmonary complaints soon receded completely, the pulmonary oedema improved promptly and the heart rate returned to normal. Follow-up X-ray findings were non-significant so that after three days of inpatient treatment, the patient, who was in an improved general condition, could be discharged and referred to her family doctor for onward attendance. She was recommended to avoid physical strain for two weeks and to continue therapy with corticosteroids, a proton pump inhibitor for gastric ulcer prophylaxis and an antibiotic.

Notes
Impregnating agents are used in the household to restore the water and dirt repelling properties of textiles and leather products and for sanitary facilities to act as a sealing coat for surfaces. The agent is a liquid available in pump spray or convenient aerosol cans providing for an even distribution. These are pressure-tight cans containing the impregnating agent consisting of propellants, solvents and the active substance. Propellants used include propane, butane, and air. Typical solvents used include petrol or short-chain alcohols, and in a few products, xylene. Active substances used include silicones (polysiloxanes), fluorocarbon and melamine resins, beeswax or wool fat. The impregnating liquid has a low toxicity. Also in the form of pump sprays, impregnating or sealant sprays have been considered as safe in terms of health. In contrast, problems have been associated with aerosol sprays. In Germany, attention was directed to the pulmonary toxicity of impregnation sprays already in 1981. Because of their inherent health risk, several sprays for the impregnation of leather were withdrawn from the market. In addition, numerous modifications of the respective formulations by the manufacturers contributed to a reduction in the number of cases of poisoning showing relevant manifestations. In 2002, another rise was recorded in the number of reports concerning impaired airway functions associated with impregnation sprays for leather and textiles in the Netherlands and in Switzerland. A last case series was reported in spring 2006. Within a short period of time, Poison Control Centres in the German federal Länder reported a great number of cases with severe health disorders. Persons affected complained of cough and shortness of breath and in several cases, developed lung oedema. The causes of these manifestations have not yet been elucidated.

The use of sprays in small and insufficiently ventilated rooms may result in conjunctival irritation, dyspnoea or in rare cases, narcosis-like manifestations due to the solvents contained. Based on systematic animal studies in birds, a key role has been attributed to fluorocarbon resins and/or reactive polysiloxanes in combination with solvents. In addition, improper use such as spraying for extended periods or failure to shake the contents sufficiently etc. should also be taken into account. However, it is mainly the physical properties such as the droplet size of the sprays that decide on whether and which toxic effects are caused in the respiratory tract. Obviously, the persons affected had inhaled components of the atomized sprays that had remained in the indoor air as fine aerosols. Due to the small droplet size, these components may have reached the alveolar region causing accumulation of fluid, which resulted in an impairment of the oxygen and moisture exchange, respectively. The small droplet size is only achieved if the liquid applied contains a propellant and is applied by means of a correspondingly small nozzle in the spray head. If, in contrast, the same liquid is applied by means of a pump mechanism, the droplets are larger than 100 micrometres and therefore, cannot penetrate into the alveolar tissue. This is probably the reason why products applied to surfaces by means of pump spray bottles have not caused any problems so far. Hence, toxic effects may only occur if the product itself, i.e. the entire substance mixture of the formulation is inhaled as a fine spray mist characterized by a correspondingly small droplet size.

Patients developing symptoms are provided with a fresh air supply as a first measure. There should be an early inhalation therapy using topical steroids and the patient should present to a hospital, to exclude a presence of lung infiltrates. Onward therapy will be oriented by the existing symptomatology.

In the above case, the spray might have been used improperly. The product had not been used in the open air only but also inside the tent with insufficient ventilation. Therefore, no rapid communication was distributed. The patient's history of pulmonary disease and nicotine abuse have certainly to be taken into account as risk factors in addition. The patient became symptom-free within a short period of time owing to an effective therapy which had been initiated without delay.

Evaluation of the case described
Based on the information given on the temporal relationship between exposure and the occurrence of the manifestations, and in the absence of other causes, a causal relationship has been rated as probable.

3.2.3.2 Glyphosate

Severe dyspnoea after spraying of a pesticide – Lung damage histologically confirmed
In May 2007, a 59-year-old farmer had applied a pesticide on a wooded area measuring 5000 m^2 for three hours in the morning. The weather was very warm with temperatures of about 25 °C. Altogether, a total quantity of three litres of glyphosate herbicide diluted at the proper ratio were applied by means of a knapsack sprayer. The farmer did not wear any respiratory protection. After having finished this work, he experienced first health complaints. Due to increasing dyspnoea, he had to be admitted to hospital and monitored at the intensive care unit. After twelve days of inpatient treatment, the patient was discharged in an improved condition and referred to his family doctor for onward attendance.

Manifestations/course
First symptoms developed about seven hours after the pesticide had been sprayed. Initially, the patient complained of aching muscles in his chest, then he developed rapidly increas-

ing shortness of breath, initially only under conditions of exercise, later on also at rest, with neither expectoration nor cough. Simultaneously, his body temperature rose to ca. 38 °C. On account of this symptomatology, the patient was admitted to hospital on the following evening and initially monitored at the intensive care unit.

On admission, findings included slight dyspnoea at rest with minor coarse and moist rales bilaterally, a temperature of 38 °C, a slightly reduced general condition and a normal nutritional status. X-ray revealed a diffuse infiltration in the area of the right lateral lower lung field on the day of admission. In the left paracardiac region, a peribronchial thickening was seen corresponding to a peribronchial infiltration. Already on the following day, this infiltration was no longer seen. Clinical chemistry revealed a minor increase in inflammatory parameters. On admission to the hospital, blood gas analysis revealed largely normal values: PCO2: 23.5 mmHg; PO2: 83.3 mmHg; oxygen saturation: 97.1 %. ECG findings were non-significant. In this context, a history of cardiac valve surgery (mitral valve replacement) in January 2006 should be noted. Nevertheless, a cardiac aetiology of the symptoms experienced could be excluded.

Also during the following days, auscultatory lung findings remained normal. Due to prevailing diffuse infiltration, a special pulmonary examination was performed (spiral CT scan). This revealed an extensive ground-glass infiltration in the left upper lobe. Because of these pathological findings, the patient was transferred to the pulmonological department of another hospital for diagnostic work-up after five days.

Lung biopsy was performed by means of bronchoscopy. The pathological/histological opinion revealed changes characteristic of acute alveolitis and accompanying cellular bronchitis with intra-alveolar foam cell reaction – inflammation of the alveoli and smallest bronchi. The opinion emphasized that the histomorphological picture was well compatible with lung damage induced by an irritant gas and was not that of a conventional bacterial infection.

The patient was put on antibiotic cover for seven days and simultaneously administered i.v. steroids at high initial doses, which were gradually reduced to 50 mg on the day of his discharge, and in general, were well tolerated. Follow-up CT revealed an obvious reversal of the ground-glass lung changes previously described. Lung function testing revealed largely normal values.

Six months after the incident, the patient still complained of moderate breathing difficulties under conditions of exercise. He had continued with outpatient treatment by a pulmonologist which included follow-up examinations at quarterly intervals. According to the patient, chest X-ray findings continued to improve, however, changes were still found.

Notes

The main component of the pesticide used is a glyphosate salt in aqueous solution. The wetting agent contained is a tallow alkylamine salt (tallow amine). The biological action of the glyphosate consists in the blocking of a certain enzyme needed by plants for the synthesis of aromatic amino acids (phenylalanine, tryptophan, tyrosine). Animals lack this enzyme. Therefore, they cannot perform de novo synthesis of these amino acids and also, they are insensitive to this herbicide.

In humans, signs of poisoning have so far only been described after oral exposure to pesti-

cides containing glyphosate. However, very low quantities are sufficient to cause life-threatening health disorders. The clinical picture will be characterized by mucosal lesions of the gastrointestinal tract and diffuse lung damage and may even include non-cardiac pulmonary oedema, cardiovascular failure and prerenal failure. So far, severe signs of poisoning after inhalation of pesticides containing glyphosate had been unknown.

In the period between 1990 and 2007, the BfR received reports on a total of 60 cases of health impairment after exposure to pesticides containing glyphosate. Even after inhalation (20 cases), there had been only minor breathing disorders. Dermal exposure (25 cases) resulted in health disorders classified as moderate in four cases. Symptoms included for example blistering as characteristic of an allergic skin reaction. When stating the route of exposure, multiple mentioning was possible. Eye irritation was described in 22 cases. Eight cases were characterized by the oral route of exposure, but only one of these was associated with life-threatening signs of poisoning as in the case described above. A 33-year-old mentally ill male had ingested 200 mL of a pesticide containing glyphosate with suicidal intent.

With regard to the persistent extreme breathing difficulties with histologically confirmed toxic inflammatory reaction of the lungs experienced by the patient in the case described above, the mechanism of exposure is of importance: The patient had inhaled the atomized spray under conditions of a high outside temperature and minor air movement over several hours (knapsack sprayer, closed woodland area). According to the safety data sheet valid at that time, the product was classified as dangerous for the environment and irritant. Also, a warning was issued that contact might result in the risk of serious damage to the eyes. The risk of damage to the airways had not been expressly mentioned in the warnings up to that time. First aid measures in the event of accidental inhalation consisted in the suggestion to “get fresh air” as the only immediate measure. The safety data sheet recommended skin and eye protection but stated that no respiratory protection was required.

Fig. 24: Knapsack sprayer with protective mask for the application of pesticides

Since according to the knowledge gained so far, the active substance, glyphosate, has only a low toxicity, it has been assumed that the complete formulation, i.e. in particular the combination of the contained surface active wetting agent, tallow amine (surfactant) with the active substance, glyphosate, was the cause of the toxic effect observed. Wetting agents generally enhance the uptake of active substances into the plant tissue. The same mechanism could explain a possible toxic effect in humans after considerable inhalational exposure to this pesticide.

Evaluation of the cases reported to the BfR, particularly of this recent case, has shown that a more explicit warning is required with regard to severe lung damage due to exposure to the atomized spray of this type of pesticides. Responsible bodies have already pointed out the possibly toxicity-enhancing effect of tallow amines in combination with glyphosate. For reasons of preventive health care, the BfR therefore

deems it necessary to label all pesticides containing glyphosate and tallow amines with the corresponding safety advice in addition, warning about possible health risks for the respiratory system. The responsible government authority has already been informed by the BfR and has been asked to provide for a corresponding additional labelling of all pesticides concerned.

Evaluation of the case described
Based on the information given on the temporal relationship between the inhalational exposure to the pesticide and the appearance of signs of severe dyspnoea with histologically confirmed lung damage, and in the absence of other causes, a causal relationship has been assumed to exist in the case described.

3.2.3.3 Bromine

Inhalational exposure to bromine at the workplace

In a pharmacy, an initially unknown chemical leaked out, which quickly evaporated. The fluid emitted brown pungent vapours. Three members of the pharmacy staff inhaled these vapours for a short period of time. Subsequently, all of them complained about irritation of the airways. The fire brigade was called and the patients presented at a toxicological outpatient clinic. Based on the history and above all, on the characteristic brown colour and the pungent odour, leaked bromine could be identified as the causative substance.

Fig. 25: Bromine

Case No 1:

Manifestations/course
The first patient complained of dizziness, a tickle in her throat and slight burning in her nose and throat. Physical examination did not result in any significant findings. No spastic rales were heard on auscultation of the chest, also oxygen saturation was normal (97 %). A slightly elevated bromide level (57 mg/L) was detected in the serum (therapeutic levels up to 50 mg/L). Clinical chemistry revealed mild leukocytosis (10 360 /µL). In addition, an increase in cholestatic liver enzymes was noticed as a secondary finding. This patient had presented herself at the same clinic already three years before. At that time, the gamma GT level was slightly higher than the normal value. Diagnostic work-up was recommended.

Based on the fact that serum levels were only slightly elevated, massive bromine contamination could be excluded.

The patient left the clinic contrary to medical advice. Since bromine is an irritant gas with an moderate latency period, a follow-up visit on the next day was proposed to perform lung function testing. The peak flow value measured on this occasion was 490 L/min, thus corresponding to the normal value.

Evaluation of the case described
The increase in cholestatic liver enzymes in the patient was not consistent with the clinical picture of poisoning. Therefore, it cannot be attributed to the bromine exposure and requires further diagnostic work-up. Based on the temporal relationship between exposure and appearance of symptoms (except for the pathological liver parameters) as well as the slight increase in the serum bromine level, a mild bromine poisoning has to be rated as confirmed.

Case No 2:

Manifestations/course

The second patient complained of a sore throat and a tickle in her throat after exposure to the vapours. Physical examination on admission did not result in any significant findings. In particular, no spastic rales were heard on auscultation of the chest. Also oxygen saturation was within the normal range (97 %). No elevated bromide level could be detected in the serum. The value measured was 4.7 mg/L, i.e. a level corresponding to a physiological one (therapeutic levels up to 50 mg/L) and thus excluding massive bromine exposure. Clinical chemistry did not reveal any significant findings, except for a slight increase in TSH levels. This finding was unrelated to the exposure and had to be attributed to iodine deficiency. Probably, the patient was to be given iodine supplementation.

Since bromine is an irritant gas with a moderate latency period, a follow-up visit on the next day was proposed to perform lung function testing. The peak flow value obtained on this occasion was 420 L/min, which still corresponded to a normal value.

Evaluation of the case described

Based on the temporal relationship between the exposure and the appearance of symptoms as well as the detection of bromine in the serum, a mild bromine poisoning could be confirmed.

Case No 3:

Manifestations/course

The third female patient also experienced a sore and tickling throat. The physical examination performed on admission did not reveal any significant findings except for reddened conjunctivae. In particular, no spastic rales were heard on auscultation of the chest. Oxygen saturation was within the normal range (95 %). No elevated bromide level could be detected in the serum. The value measured was 25 mg/L, i.e. a level corresponding to a physiological one (therapeutic levels up to 50 mg/L) and thus excluding massive bromine exposure. Clinical chemistry revealed a slight retention of substances usually eliminated in the urine (creatinine: 1.4 mg/L, normal up to 1.3 mg/L; blood urea nitrogen: 20 mg/L, normal up to 18 mg/L), which was probably unrelated to the incident. Follow-up examination after sufficient fluid intake was recommended. This was to include also CK, showing an increase to 322 U/L (normal value up to 174 U/L) possibly due to physical activity.

Since bromine is an irritant gas with a moderate latency period, a follow-up visit on the next day was proposed to perform lung function testing. The peak flow value obtained on this occasion was 600 L/min, corresponding to the normal range.

Evaluation of the case described

Based on the temporal relationship between the exposure and the appearance of symptoms as well as the detection of bromine in the serum, a mild bromine poisoning has to be rated as confirmed.

Notes regarding all three cases

Bromine is a halogen and was isolated for the first time from marine algae in 1826. Technological production started in 1860. Due to its pungent odour, it was named after the Greek word “bromos“, meaning the stench characteristic of he-goats. It is of high reactivity. Bromine is a dark-brown and heavy liquid forming dark reddish-brown and pungent vapours on contact with air, which are five times heavier than the latter and therefore, will accumulate on the ground. It is used as a disinfectant and a medicine (narcotics, sedatives and soporifics, anticonvulsants), and it has a variety of other uses.

It has to be stored in containers made from glass, lead, monel (a copper/nickel alloy) or nickel because coatings, rubber and plastic materials are attacked.

The substance may be absorbed by the oral or inhalational route. Oral or inhalational exposure will cause cough, dyspnoea, headache, dizziness, chemical burns, abdominal cramps, circulatory disorders and collapse. Inhalation of the irritant gas having a moderate water solubility may result in toxic pulmonary oedema, after a latency period. Due to the substance's caustic effects, direct contact of the skin may cause badly healing wounds and produce reddening of and pain in the eyes.

Exposed persons should quickly leave the gas-contaminated area. Other measures include immobilization and if required, sedation and protection against a loss of body heat. Patients suffering from symptoms such as cough should see a doctor and undergo inpatient observation to account for the latency period. In order to prevent lung oedema, glucocorticoids should be administered as soon as possible, either by means of a CFC-free metered-dose inhaler (e.g. Budesonide) with aerosol holding chamber or by i.v. injection of high doses (preferably methylprednisolone), if a massive exposure is assumed to have taken place. Onward therapy will be oriented by the symptoms.

From the dangerous substances reported to the BfR, bromine is the toxic agent involved most frequently in school accidents (> 20 %). Altogether, 106 reports of cases involving bromine have been submitted to the BfR so far. Typically, such poisoning accidents resulted in series of cases because commonly, many persons (entire school classes) were affected. In the school accidents, the cause was always a glass bottle which fell down and broke on the floor. As mentioned above, glass containers are needed for storage because unbreakable plastic containers would be attacked by the substance. Possibly, this was also the cause of the accidents involving the cases described. However, it should also be discussed whether safety regulations had been complied with. It has remained unknown to the BfR whether the patients had worked under a ventilation hood.

The majority of persons affected in cases reported to the BfR (67 %) experienced mild symptoms as described above. Typically, breathing difficulty (ca. 70 %) predominated, followed by nausea and headache (almost 50 %). The majority of patients was observed as inpatients in a hospital setting, and all of them, except for one patient who had no manifestations, saw a doctor. Owing to quick and effective therapeutic measures, severe poisoning resulting in pulmonary oedema or irreversible health damage could be prevented.

Evacuation measures and medical care required after such incidents involve high expenditure on labour and other costs. Storage of the chemical in unbreakable containers (e.g. monel) could probably help to prevent such accidents in the future.

3.2.3.4 Cannabis and lead

Chronic lead poisoning after smoking/abuse of contaminated cannabis
A 23-year-old student of mathematics had smoked between one and two grams of cannabis daily. He had obtained the drug always from the same source in a city in Saxony. He had noticed black smut adhering to the cannabis. Earlier, he had been supplied with cannabis with sugar-like smut. For the first time in October 2007, he experienced symptoms of lead poisoning characterized by severe colicky abdominal pain. Having read a newspaper article about cases of lead poisoning due to contaminated cannabis in Saxony, the student associated his complaints with the same cause. On his initiative, his blood lead level

was determined in November after prior diagnostic efforts had not resulted in any findings. Analysis revealed a grossly elevated lead level of 1 850 µg/L (average blood lead level in children 50–70 µg/L). Findings also revealed the presence of anaemia. When asked, he denied having experienced headache, mental changes observed by himself or others, and any impairment of mental ability. No history of physical or mental illness was known. He was admitted to the toxicological department of a special hospital for treatment.

Manifestations/course
Examinations performed on admission of the very slim patient, who weighed only 57 kg and had a body height of 175 cm (BMI 18.6), recorded a strikingly pale skin. No lead hem (Burtonian line) was found. Findings included unsteadiness in the finger-to-nose test, normal gross strength, propioceptive reflexes equal on both sides and no tremor. In addition to persisting strong abdominal colic, further symptoms of lead poisoning were found such as arterial hypertension and short-term orthostatic dysregulation probably caused by volume deficiency. His heart rate was elevated (101/min). Clinical chemistry revealed leukocytosis of 21 100/µL (follow-up examination 15 200/µL) with normal CRP and anaemia with a Hb of 7.9 g/dL (follow-up examination 8.3 g/dL) with low mean corpuscular haemoglobin levels. Other pathological findings worth mentioning included an increase in gamma-GT of 69 U/L, increasing to 93 U/L (normal up to 28 U/L), GOT of 99 U/L (normal up to 35 U/L) and GPT of 319 U/L, on follow-up examination 282 U/L (normal up to 30 U/L). By means of toxicological analysis, cannabinoids could be detected in the urine. Blood lead levels had remained high, with a maximum of 1 562 µg/L on admission. In addition, severe lead poisoning was confirmed by an increase in the urine levels of delta-aminolaevulinic acid (160 mg/24 h, normal up to 49 mg/24 h), porphobilinogen (22.27 mg/24 h, normal up to 7.5 mg/24 h) and a very strong increase in total porphyrin levels in the urine to more than twenty times the normal value (3767 µg/24 h, normal up to 145 µg/24 h). Additional diagnostic procedures included sonography of the upper abdomen, which did not reveal any pathological findings except for a pre-existing pyelectasis. ECG findings were non-significant. Results of electromyography (EMG) performed on the day of discharge and of the measurement of nerve conduction velocity were not yet available when the discharge summary was written. Due to the confirmed lead intoxication, antidote therapy with a chelating agent was required. This was very problematic because the medicinal product approved for this indication in Germany, namely DMPS, was not available. Therefore, a chelating agent tried and tested in the USA in cases of lead poisoning, namely DMSA, was obtained from an international pharmacy, and treatment of the patient with this agent was initiated (see below). The duration of the first course of treatment was 19 days. Because the therapy could be continued on an outpatient basis, the patient was discharged after six days of inpatient treatment.

It was recommended to perform follow-up measurements of blood lead levels after the first course of treatment lasting for 19 days and to discontinue treatment for 14 days. After this period of time, the blood lead level was to be measured again and if levels still exceeded 400–600 µg/L, another course of treatment with a chelating agent was to be administered.

Notes
In late July 2007, an increased incidence of cases of lead poisoning of initially unclear origin was observed in Saxony and Thuringia. The

persons affected were exclusively young adults who in their majority were known to consume narcotic drugs. An association with lead-contaminated narcotic drugs was therefore suggested, which could be confirmed later. Twenty cases similar to that described above have become known from Saxony. In addition to the responsible ministries, also the BfR was informed about this problem by the Erfurt Poison Control Centre. So far, known sources of chronic lead exposure had included lead-containing cosmetics or natural remedies, particularly of Asian origin. In contrast to what has been seen in the USA, chronic poisoning due to exposure to lead-based paint chips or peels from deteriorated surfaces does not play any role in Germany.

The absorption rate after inhalation of lead (dust) or its compounds is as high as 30–85 %. Subsequent distribution will take place in a three-compartment system: A share of 95 % of the lead is bound to red blood cells and the remaining part, to plasma proteins. After distribution, lead will initially accumulate in the parenchymatous organs such as the liver, the kidneys and the brain. Afterwards, approximately 95 % of the lead is firmly bound in the hydroxylapatite crystals of the bones. Lead is non-toxic in bone, however, it is released into the other compartments as part of the bone metabolism. Therefore, only little information about a history of lead exposure can be derived from blood lead levels.

For example, the average blood lead level in German children aged six to seven years is 55–70 µg/L. Lead is of no physiological importance. No safe lower limit level has been defined so far. From ca. 100 µg/L, growth and hearing disturbances associated with a reduced intelligence quotient, an increase in erythrocyte protoporphyrin levels and an inhibition of delta-aminolaevulinic acid dehydratase have been described. Levels exceeding 200 µg/L will reduce nerve conduction velocity, disrupt vitamin D metabolism and inhibit haemoglobin synthesis. Levels between 500 and 1 000 µg/L are known to potentially cause encephalopathy and nephropathy, higher levels may lead to death.

The mechanism of action proper has not yet been completely elucidated, only the effect on the haematopoietic system is well known. Low blood lead levels will cause inhibition of delta-aminolaevulinic acid dehydratase activity. It is the most sensitive of the parameters and becomes reduced already at blood lead levels of 100 µg/L. About two to three weeks later, this will result in an increase in delta-aminolaevulinic acid in the blood and its elevated excretion in the urine. Delta-aminolaevulinic acid has been assumed to be responsible for neurotoxicity and a number of other effects. In addition, inhibition of cellular functions requiring zinc and calcium has been discussed because lead is known to interfere with calcium. Also ferrochelatase, an enzyme responsible for iron incorporation into porphyrin, is inhibited, which will cause an increase in erythrocyte porphyrin. This will result in elevated excretion of coproporphyrin III in urine and anaemia with basophilic stippling.

In addition to the bone marrow and the nervous system, also the kidneys and smooth muscles are affected by lead poisoning. Manifestations of acute and subacute poisoning include abdominal pain, nausea and a transient renal proximal tubular dysfunction similar to Fanconi syndrome. Chronic exposure may lead to anorexia, lethargy, irritability, ataxia, weakness of muscles, colicky abdominal pain, reduced intelligence, renal damage, hypertension, visual disturbances and lead lines in the tubular bones found by radiology.

Diagnostic parameters should include determination of lead and delta-aminolaevulinic acid levels in the patient's blood and urine and of the erythrocyte protoporphyrin concentration.

Asymptomatic patients with blood lead levels below 250 µg/L do not require treatment. Pa-

tients exhibiting higher levels and clinical signs, respectively, (as in the above case) should receive antidote therapy with a chelating agent. In Germany, the medicinal product DMPS (dimercaptopropane sulfonate) has been approved for this indication. However, this product is not manufactured and supplied at present. In the USA, where long-term experience with lead poisoning exists due to a high exposure of the population, the chelating agent DMSA (2,3-dimercaptosuccinic acid) has been recommended, which is even more effective. The older chelating agents, EDTA (ethylenediaminetetraacetic acid) and BAL (British anti-lewisite, dimercaprol) have become obsolete based on recent evidence because they are toxic on their own and possibly increase lead absorption.

Therapy is performed in several phases: Initially, the lead contained in the blood compartment is removed by means of the chelating agent. During chronic lead exposure, lead is accumulated in the bones and from there only slowly re-distributed in the blood. This is why after the first treatment cycle, treatment should be discontinued for at least 14 days. During this period, lead can be mobilized from the bones and return to the blood where it binds to the chelating agent and is excreted.

Based on the massively elevated blood and urine lead levels found, it can be assumed that in the above case the patient suffered from severe chronic lead poisoning. Given the characteristic manifestations including marked anaemia, anorexia and ataxia, it has been assumed that poisoning had set in already before October 2007, i.e. before the patient noticed the symptoms. He had become intoxicated by smoking lead-contaminated cannabis.

Evaluation of the case described
Based on the toxic blood lead level, the elevated porphyrin and delta-aminolaevulinic acid levels in the urine as well as the characteristic manifestations including colicky abdominal pain, hypertension, ataxia, anorexia and anaemia, and in the absence of other causes, a causal relationship is to be rated as confirmed.

3.2.3.5 Rust remover spray

Lethal case – Association with the use of rust remover/corrosion-protective spray cannot be ruled out
A 69-year-old male had treated the underbody of his car with a lubricant/penetrating oil. He had used a commercial rust remover spray consisting of petrol hydrocarbons as a main component and carbon dioxide as a propellant. Molybdenum disulfide was contained in amounts not requiring labelling. The spray had been applied in a lying position under the car for about 15 minutes on a windless day in front of a carport. No special protective clothing, particularly no respiratory protection had been worn by the patient. Immediately after this operation, the patient developed acute dyspnoea, nausea and circulatory shock. In spite of early resuscitation measures, the patient died at the intensive care unit of a hospital ca. four hours after the onset of first symptoms without having regained consciousness.

Since an association of the severe shock with the inhalation of the lubricant could not be excluded, the criminal investigation department was informed. The latter had a post-mortem examination carried out. The cause of death has not been fully elucidated so far in spite of extensive expert examinations.

Manifestations/course
No serious diseases were reported in the deceased patient's medical history. After spraying of the lubricant, he had suddenly complained of nausea and severe dyspnoea. His wife reported that he had touched his throat several times and cried "I cannot breathe anymore." He had repeatedly expectorated thick

yellow mucus. Cough and retching had then increased. Since she had deemed the situation to be life-threatening, she had called the emergency medical service immediately. When the latter arrived after a few minutes, they found the patient already in an acrotic and cyanotic condition. Immediate resuscitation measures resulted in a stabilization of circulation in the still unconscious patient on the scene after about 40 minutes, and he was admitted to the intensive care unit of a hospital.

On admission, the deeply comatose patient, who was artificially respirated, showed the typical signs of a circulatory shock (blood pressure not measurable, irregular cardiac action, heart rate 70/min). On auscultation, both lungs were ventilated and a few fine rales were heard at the bases. The patient's body temperature had dropped to 31.8 °C. In spite of intensive medical therapy including maximum doses of catecholamines, fluid supply, buffering of metabolic acidosis and ventilation with high oxygen concentration, stabilization of circulation could not be achieved anymore. The patient died approximately four hours after resuscitation measures had been initiated.

Post-mortem findings included pronounced general arteriosclerosis, particularly of the coronary vessels, and signs of recurrent myocardial infarctions suffered in the past. However, no recent myocardial damage was found. Macroscopic examination of the lungs did not result in any pathological findings that could have explained the patient's death. According to the post-mortem report, the severe pathological changes of the cardiovascular system found in the patient could have led to his death at any point in time, however, not inevitably at the time when death actually occurred. An obvious cause of death was not stated in the most-mortem records.

Notes

Both the way the accident happened and the clinical course, as well as the evaluation of the post-mortem records suggest recurrent myocardial infarction to have been the most probable cause of death. However, post-mortem findings of the lungs do not exclude pulmonary illness caused by aspiration of the lubricant used. Further analyses to detect residues of the product used in the lung tissue might have produced more precise results. However, this possibility was omitted since in the experts' opinion, no change of the assumed cause of death could have been expected.

This tragic death has again drawn attention to health damage possibly attributable to the use of chemical products in the form of aerosol sprays. According to the safety data sheet, the product concerned is not classified as harmful to health. It is stated that general personal protection measures are sufficient during use. No respiratory protection was required as long as the room was well ventilated. It seems that this information was not alarming enough as a warning.

Aliphatic hydrocarbons are known to have a toxic effect on the lungs. Accidental ingestion of even minor quantities may lead to aspiration which, in turn, may result in most severe pulmonary manifestations with a possibly lethal outcome. In most cases, symptoms will only include cough and temporary breathing difficulty. There is, however, also the possibility that chemical pneumonia with a long duration of the disease may develop. In very rare cases, rapidly developing and life-threatening symptoms were observed including severe cough and early cyanosis. Causes that could be established included glottis or pulmonary oedema, pleuritis or pneumothorax, again in very rare cases only.

According to the present state of knowledge gained from comparable accident reports, more and more indications have suggested that the

possibly toxic effect on the lungs may be attributed to additives or solvents contained in aerosols. It may also be assumed that the very fine dispersion of the spray mist results in critical droplet sizes so that components of the chemical product may penetrate deeply into the smallest alveoli and cause toxic effects in these structures. In the opinion of the BfR, further research is urgently required in this field. Therefore, a number of research projects has been initiated by the institute which are dealing for example with surface sealant sprays.

Evaluation of the case described

Based on the information given on the temporal relationship between the use of the chemical product and the appearance of the symptoms described, a causal relationship between the inhalation of rust remover aerosol containing penetrating oil and the patient's death is possible.

4 Annex

4.1 Spectrum of cases reported during the period 1 January–31 December 2007

Table 12: 4 086 reports vs. degree of severity of health disturbances, classified by children and adults, with the adult cases differentiated by exposure in the private sphere and the working environment (except for cases with a causal relationship rated as "absent" or "excluded")

Incriminated products/uses	Reports, total numbers					Health impairment moderate/severe				
First level Second level Third level	*Total*	*Children*	*Adults*	*Home*	*Work*	*Total*	*Children*	*Adults*	*Home*	*Work*
I. Medicinal products	180	11	169	2	167	5	2	3	2	1
II. Veterinary medicinal products	3		3		3					
III. Chemical products	2.440	30	2.410	24	2.386	166	7	159	12	147
Wastes, solid	27		27		27	1		1		1
Waste gases	179		179	2	177	10		10	2	8
Sewage	16		16		16					
Paints and related materials	146		146	4	142	9		9	2	7
Paint removers/strippers	9		9		9					
Alkyd resin paints										
Emulsion paints	7		7		7					
Artist's painting materials										
Glossy paints	23		32		32	1		1		1
Parquetry sealers	1		1		1	1		1		1
Pigments	1		1		1					
Primers	15		15	3	12	3		3	2	1
Paint thinners	51	3	51		51	3		3		3
Fire lighting products	3	3				2	2			
Building materials, auxiliary products	22		22	2	20	3		3	1	2
Building materials	123		123		123	19		19		19
Fuels, solid; auxiliary products	3		3		3					
Fuels, liquid; auxiliary products	29	5	24		24	1	1			
Petrol	12		12		12					
Ethanol for technical use	4	1	3		3					
Lamp oil	4	4				1	1			
Fuels, gaseous	2		2		2					
Office materials, chemical	19		19	1	18	1		1		1
Decoration materials	2		2		2					
Dental materials	5		5		5					

Incriminated products/uses	Reports, total numbers					Health impairment moderate/severe				
First level Second level Third level	*Total*	*Chil-dren*	*A-dults*	*Home*	*Work*	*Total*	*Chil-dren*	*A-dults*	*Home*	*Work*
Disinfectants/sterilizers	369		369	2	367	14		14	1	13
Deodorants for technical use	6	1	5		5					
Diagnostic agents/reagents	2		2		2					
Printing, auxiliary products	3		3		3					
De-icing products	1		1		1					
Fire extinguishing media	15		15		15	1		1		1
Flame retardants										
Galvanic cells	87		87		87	4		4		4
Dry cells										
Button batteries										
Accumulators	87		87		87	4		4		4
Galvanizing agents	1		1		1					
Galvanizing agents, auxiliary products	2		2		2					
Gases for technical use	2		2		2					
Antifreezes	2		2		2					
Glass-working, auxiliary products										
Rubber, production materials	3		3		3					
Semiconductors, production materials										
Household auxiliary products, chemical-technical										
Hydraulic fluids	26		26		26					
Refrigerants	3		3		3					
Ceramics, auxiliary products	1		1		1					
Ceramic materials	2		2		2					
Glues	87		87	2	85	5		5	1	4
Coolants	13		13		13					
Plastics, starting materials	14		14		14	1		1		1
Plastics, formulating materials	3		3		3					
Leather processing products										
Luminophors	6		6	1	5					
Solvents for technical use	60		60	1	59,3		3		3	
Soldering and welding products (except welding fumes)	3		3		3					

Incriminated products/uses	Reports, total numbers					Health impairment moderate/severe				
First level Second level Third level	*Total*	*Chil-dren*	*A-dults*	*Home*	*Work*	*Total*	*Chil-dren*	*A-dults*	*Home*	*Work*
Measuring equipment, chemical-technical										
Heating meters										
Mercury thermometers										
Thermometer fluids										
Metallurgy, auxiliary products	13		13		13	3		3		3
Dairy, auxiliary products										
Paper-making, auxiliary products										
Photography, auxiliary products	9		9		9					
Radioisotopes, radionuclides										
Cleaning products	778	19	759	10	749	72	4	68	5	63
Drain cleaners	15		15		15	3		3		3
All-purpose cleaners	47	2	45		45	2		2		2
Oven and grill cleaners	27	3	24		24					
Cleansers for electronic products										
Descaling products	19		19	3	16	1		1	1	
Front wall and stone cleaners	4		4		4					
Stain removers	2		2		2	1		1		1
Floor polishes	4	1	3		3					
Washing-up detergents (manual use)	9		9		9					
Dishwasher detergents	10	1	9		9	1		1		1
Dishwasher cleaners	6		6		6	2		2		2
Glass cleaners	6		6	1	5	1		1	1	
Industrial cleaners	76		76	1	75	11		11		11
Rinsing additive for dishwashers	9	1	8		8					
Plastic cleaners										
Glossy paint cleaners										
Milking machine cleaners	70	2	68		68	8	1	7		7
Metal cleaners	23		23		23	1		1		1
Furniture polishes	1	1								
Soot remover	1		1		1	1		1		1
Lavatory cleansers	38	5	33	3	30	4		4	2	2

Incriminated products/uses	Reports, total numbers					Health impairment moderate/severe				
First level Second level Third level	*Total*	*Chil-dren*	*A-dults*	*Home*	*Work*	*Total*	*Chil-dren*	*A-dults*	*Home*	*Work*
Shoe and leather cleaners	4	1	3	3		3	1	2	2	
Carpet/upholstery cleaners										
Detergents										
Detergents, auxiliary products	10		10		10					
Joke articles										
Lubricants	24		24	1	23	2		2	1	1
Welding fumes	24		24		24					
Dust-laying oils										
Toys										
Textile, auxiliary products	5		5	2	3	3		3	2	1
Propellants/sprays	2		2		2					
Water treatment products	11	1	10		10	2		2		2
Pet shop products	2	1	1		1					
Unknown	108		108		108	5		5		5
IV. Cosmetics/personal hygiene products	71		71	7	64	6		6	3	3
Hair care products	25		25	1	24	1		1	1	
Permanent wave products	4		4		4					
Depilatory products										
Hair dyes/colorants	20		20	1	19	1		1	1	
Hair conditioners										
Hair tonics										
Shampoos										
Skin care products	30		30	3	27	3		3	1	2
Bath oils/salts	2		2		2					
Tanning products	1		1	1						
Creams/ointments/lotions	5		5	2	3	2		2	1	1
Deodorants										
Face tonics										
Make-up products										
Oils										
Perfumes/after shaves	3		3		3					
Powders	1		1		1					
Soaps	16		16		16	1		1		1
Sun blockers										
Oral care/dental products	10		10	1	9	1		1		1
Nail care products	2		2		2					

Incriminated products/uses	Reports, total numbers					Health impairment moderate/severe				
First level Second level Third level	*Total*	*Chil-dren*	*A-dults*	*Home*	*Work*	*Total*	*Chil-dren*	*A-dults*	*Home*	*Work*
V. Pesticides	107	5	102	8	34	11		11	3	8
Acaricides	1		1		1					
Fungicides	9		9		9	2		2		2
Herbicides	22		22		22	2		2		2
Wood preservatives	9	5	4	13						
Insecticides	25		25	6	19	3		3	3	
Carbamates										
Chlorinated hydrocarbons										
Phosphoric esters	9		9	2	7	2		2	2	
Pyrethroids	6		6	1	5					
Molluscicides	1		1		1					
Repellents										
Rodenticides	1		1		1					
Anticoagulants										
Phosphates										
Seed dressings	1		1		1					
VI. Agrochemicals other than pesticides	10		10		10	1		1		1
Fertilizers	4		4		4	1		1		1
Plant care products										
Growth regulators										
VII. Substances of abuse	2		2	2		1		1	1	
VIII. Plants	8	5	3		3					
IX. Fungi	13	6	7	6	1	5	1	4	4	
X. Animals	2	1	1		1					
XI. Foods and beverages	49	2	47	20	27	7	1	6	6	
Alcoholic beverages	7		7	2	5	2		2	2	
Food additives	1		1		1					
Tobacco and tobacco prod.	2	1	1	1						
Food supplements	11		11	11		2		2	2	
XII. Warfare/anti-riot agents	2		2		2					
Pyrotechnic products										
Tear gas										
XIII. Miscellaneous	112		112	1	111	8		8		8
Textiles	10		10		10					
Clothing	10		10		10					
Furnishing fabrics										
XIV. Primary substances	1.152	2	1.150	9	1.141	113		113	5	108
XV. Industrial accidents	6		6		6	1		1		1

4.2 Notification form for cases of poisoning

Bundesinstitut für Risikobewertung
Dokumentations- und Bewertungsstelle
für Vergiftungen
Postfach 33 00 13

14191 Berlin

Stempel, Telefon-Nummer und Unterschrift der/des Ärztin/Arztes

Mitteilung bei Vergiftungen
nach § 16e Abs. 2 des Chemikaliengesetzes
(Telefon: 01888-412-3460, Fax: 01888-412-3929. E-Mail: giftdok@bfr.bund.de

1. Angaben zur/zum Patientin/en:

Alter: Jahre ☐ Monate (bei Kindern unter 3 Jahren) ☐ ☐ männlich ☐ weiblich Schwangerschaft (**freiwillig** auszufüllen) ☐ ja ☐ nein

2. Vergiftung ☐ **Verdacht** ☐

Unbedingt Handelsname der Zubereitung/des Biozid-Produktes oder Stoffname, aufgenommene Menge und Hersteller (Vertreiber); ggf. vermutete Ursache

a.

b.

c.

3. Exposition ☐ akut ☐ chronisch ☐ oral ☐ inhalativ ☐ Haut ☐ Auge sonstiges, welche

Art der Vergiftung:	☐ akzidentell (Unfall)	☐ gewerblich	☐ Verwechslung	
	☐ suizidale Handlung	☐ Abusus	☐ Umwelt	☐ Sonstiges
Ort:	☐ Arbeitsplatz	☐ im Haus	☐ Schule	
	☐ Kindergarten	☐ im Freien	☐ Sonstiges	
Labor-Nachweis:	☐ ja	☐ nein		
Behandlung:	☐ keine	☐ ambulant	☐ stationär	
Verlauf:	☐ nicht bekannt	☐ vollständige Heilung	☐ Defektheilung	☐ Tod
	☐ Spätschäden (nicht auszuschließen)			

(**freiwillig** auszufüllen)

4. Symptome, Verlauf – stichwortartig – (ggf. anonymisierte Befunde, Epikrise beilegen)

4.3 Notification form for industrial accidents

BfR-Fragebogen zur Expositionsermittlung bei Stör- und Transportunfällen

Pers. Nummer

weiblich ☐ männliich ☐ Erwachsene(r) ☐ Kind ☐

Bereich I

Unmittelbar Betroffene(r)

(Bitte Eintrag in die Landkarte)

Direkt am Unfallort ☐
Nahe Unfallort ☐
☐ m

Arbeiter(in) ☐
Feuerwehr ☐
Polizei/Rettungsdienst ☐
Privatperson ☐
Sonstige(r) ☐

Erstexposition Uhrzeit ☐ Datum ☐
Dauer ständig ☐ nicht ständig Stunden/Tage ☐
Schutzmaßnahmen ja ☐ nein ☐
Symptome ja ☐ nein ☐
(Wenn ja, bitte Dokumentation auf dem Meldebogen)

Bereich II

Nicht unmittelbar Betroffene(r)

(Bitte Eintrag in die Landkarte)

Entfernung vom Unfallort
☐ m
☐ km

Anwohner ☐
Beschäftigte(r)/Arbeitnehmer(in) ☐
Sonstige(r) ☐ ☐

Erstexposition Uhrzeit ☐ Datum ☐
Dauer ständig ☐ nicht ständig Stunden/Tage ☐
Symptome ja ☐ nein ☐
(Wenn ja, bitte Dokumentation auf dem Meldebogen)

Biomonitoring **Stoff:** ☐

Blutentnahme ☐ Datum ☐ Zeitpunkt ☐ Konzentration ☐
Urinprobe ☐ Datum ☐ Zeitpunkt ☐ Konzentration ☐
Spontanurin ☐ 24h Sammelurin ☐ Kreatinin ☐

4.4 List of Poison Control Centres in Germany

Berlin	BBGes – Giftnotruf Berlin Institut für Toxikologie Klinische Toxikologie und Giftnotruf Berlin	Oranienburger Str. 285	D-13437 Berlin	Phone: +49 (0) 30-192 40 Fax: +49 (0) 30-30 68 67 21 E-Mail@giftnotruf.de www.giftnotruf.de
Bonn	Informationszentrale gegen Vergiftungen Zentrum für Kinderheilkunde Universitätsklinikum Bonn	Adenauerallee 119	D-53113 Bonn	Phone: +49 (0) 2 28-19 240 Fax: +49 (0) 2 28-2 87 33 14 GIZBN@ukb.uni-bonn.de www.meb.uni-bonn.de/ giftzentrale
Erfurt	Gemeinsames Giftinformations- zentrum der Länder Mecklenburg-Vorpommern, Sachsen, Sachsen-Anhalt und Thüringen	Nordhäuser Str. 74	D-99089 Erfurt	Phone: +49 (0) 3 61-73 07 30 Fax: +49 (0) 3 61-7 30 73 17 Info@ggiz-erfurt.de www.ggiz-erfurt.de
Freiburg	Zentrum für Kinderheilkunde und Jugendmedizin Vergiftungs-Informations-Zentrale	Mathildenstr. 1	D-79106 Freiburg	Phone: +49 (0) 7 61-19 240 Fax: +49 (0) 7 61-2 70 44 57 giftinfo@kikli.ukl.uni-freiburg.de www.giftberatung.de
Göttingen	Giftinformationszentrum-Nord der Länder Bremen, Hamburg, Nieder- sachsen und Schleswig-Holstein (GIZ-Nord) Universität Göttingen – Bereich Humanmedizin	Robert Koch-Str. 40	D-37075 Göttingen	Phone: +49 (0) 5 51-38 31 80 Fax: +49 (0) 5 51-3 83 18 81 giznord@giz-nord.de www.giz-nord.de
Homburg	Informations- und Behandlungs- zentrum für Vergiftungen des Saarlandes Klinik für Kinder- und Jugendmedizin	Kirrberger Str. Gebäude 9	D-66421 Homburg/ Saar	Phone: +49 (0) 68 41-19 240 +49 (0) 68 41-16 28 314 Fax: +49 (0) 68 41-16 28 438 kigift@uniklinikum-saarland.de www.uniklinikum-saarland.de/de/ einrichtungen/andere/giftzentrale
Mainz	Klinische Toxikologie und Beratungsstelle bei Vergiftungen der Länder Rheinland-Pfalz und Hessen Universitätsklinikum	Langenbeckstr. 1	D-55131 Mainz	Phone: +49 (0) 61 31-19 240 +49 (0) 61 31-23 24 66 Fax: +49 (0) 61 31-23 24 69 +49 (0) 61 31-23 24 68 giftinfo@giftinfo.uni-mainz.de www.giftinfo.uni-mainz.de

Munich	Giftnotruf München Toxikologische Abteilung der II. Medizinischen Klinik und Poliklinik, rechts der Isar der Technischen Universität München	Ismaninger Str. 22	D-81675 Munich	Phone: +49 (0) 89-1 92 40 Fax: +49 (0) 89-41 40 24 67 tox@lrz.tum.de www.toxinfo.org
Nurem-berg	Giftnotrufzentrale Nürnberg Medizinische Klinik 2, Klinikum Nürnberg Lehrstuhl Innere Medizin-Gerontologie, Universität Erlangen-Nürnberg	Prof.-Ernst-Nathan-Str. 1	D-90419 Nurem-berg	Phone: +49 (0) 9 11-3 98 26 65 Fax: +49 (0) 9 11-3 98 21 92 Giftnotruf: +49 (0) 9 11-3 98 24 51 or +49 (0) 9 11-3 98 26 65 muehlberg@ klinikum-nuernberg.de www.giftinformation.de

4.5 Press releases on toxicological problems issued by the BfR in 2007

Childproof oil lamps are possible!
New design burners can effectively protect children from poisoning
02/2007, 18 April 2007

Fewer experimental animals but same degree of safety for consumers!
BfR advocates shorter procedure for testing reprotoxic effects of chemicals
04/2007, 9 May 2007

Detergent and cleaning agent formulations must be notified to the Federal Institute for Risk Assessment
Electronic notification aids available to make processing easier
06/2007, 5 June 2007

Bitter apricot kernels can lead to poisoning
Federal Institute for Risk Assessment believes that the packaging should carry warnings
07/2007, 7 June 2007

Chromium (VI) in leather clothing and shoes problematic for allergy sufferers!
BfR recommends strictly limiting levels in leather goods
10/2007, 2 July 2007

BfR repeats its warning about henna tattoos
The ingredients may open the door to allergic reactions
14/2007, 18 July 2007

It seems that ultrafine dust from laser printers and photocopiers does not contain toner particles
Final report on the pilot study expected towards the end of the year
18/2007, 16 October 2007

4.6 List of abbreviations (German notation) used in the brochure

Abbreviation	Meaning
µg/h	Quantity per unit of time in micrograms per hour
µg/L	Quantity per volume in micrograms per litre
ADH	Antidiuretic hormone
BAL	British anti-lewisite, dimercaprol
BfR	Bundesinstitut für Risikobewertung – Federal Institute for Risk Assessment
BG	Berufsgenossenschaften – institutions for statutory accident insurance and prevention for trade and industry in Germany
BgVV	Bundesinstitut für gesundheitlichen Verbraucherschutz und Veterinärmedizin – Federal Institute for Health Protection of Consumers and Veterinary Medicine
BMI	Body mass index
BVL	Bundesamt für Verbraucherschutz und Lebensmittel – Federal Office for Consumer Protection and Food Safety
CEN	Comité Européen de Normalisation – European Committee for Standardization
CFC	Chlorofluorocarbons
ChemG	Chemikaliengesetz – German Chemicals Act
CK	Creatinine kinase
CNS	Central nervous system
CRP	Capsule-reactive protein
CVC	Central venous catheter
DIN	Deutsches Institut für Normung – German Institute for Standardization
EAN	European Article Number
EDTA	Ethylenediaminetetraacetic acid
EMG	Elektromyography
ESR	Erythrocyte sedimentation rate
FAO	Food and Agriculture Organization
gamma-GT	Gamma glutamyl transferase
GHS	Globally Harmonized System of Classification and Labelling of Chemicals
GOT	Glutamate oxaloacetate transaminase
GPT	Glutamate pyruvate transaminase
ha	Hectare
Hb	Haemoglobin
i.v.	Intravenous
IMO	International Maritime Organisation
IPPC	International Plant Protection Convention
ISPM	International Standards for Phytosanitary Measures
mmHg	Millimeters of mercury
mmol/L	Millimoles per litre
PCC	Poison Control Centre
PEG	Percutaneous endoscopic gastrostomy
PET	Polyethylene terephthalate
PI element	Product identification element
PRINS	Product information system

TRGS	Technische Regeln für Gefahrstoffe – German Technical Rules for Hazardous Substances
TSH	Thyroid-stimulating hormone
U/L	Units per litre
UBA	Umweltbundesamt – German Federal Environment Agency
UN	United Nations
WRMG	Wasch- und Reinigungsmittelgesetz – German Detergents and Cleaning Agents Act
XML file	Extensible markup language file
ZIP file	Data compression and archival format file

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