INFORMATION

Cases of Poisoning Reported by Physicians

2004

BfR

Risiken erkennen – Gesundheit schützen

Cases of Poisoning Reported by Physicians in 2004
Published by: BfR Press and Public Relations Office
Editors: Poison and Product Documentation Centre at the BfR
No of copies printed: 1000
Typesetting and printing: Werbedruck Schreckhase, www.schreckhase.de
Printed on chlorine-free paper

ISBN 3-938163-08-9
ISSN 1435-4047

Cases of Poisoning Reported by Physicians 2004

Poison and Product Documentation Centre at the Federal Institute for Risk Assessment
11th Report (2004)

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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 laid the foundation "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 ascribed 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 Poison and Product Documentation Centre at the Federal Institute for Risk Assessment (BfR).

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

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

Within the meaning of the Chemicals Act, the term of poisoning designates all cases in which health impairment has occurred, as well as suspected cases of poisoning. Under the Act, also the Poison Information and Treatment Centres (Poison Control Centres, PCC) 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", "none" or "cannot be assessed". The rules applied in the assessment of individual cases have been described in detail in the previous annual reports.

Differentiated analyses and evaluation of the data on cases form the basis for the estimation of toxic risks in humans. For these purposes, the data on cases in humans are continuously documented as case data sets and case reports. Information on identified risks is passed on to ministries, manufacturers and industrial associations in the form of rapid communications or annual summarizing reports by means of the product information system PRINS (see Chapter 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 BfR publishes annual reports on the knowledge gained from the cases of poisoning reported by physicians. These publications are available on request in writing at the Pressestelle of the Federal Institute for Risk Assessment, Thielallee 88-92, D-14195 Berlin, Germany. In part, they have also been published as

electronic documents on the internet (ww.bfr.bund.de).

A graphical representation of these tasks and procedures is shown in Fig. 1.

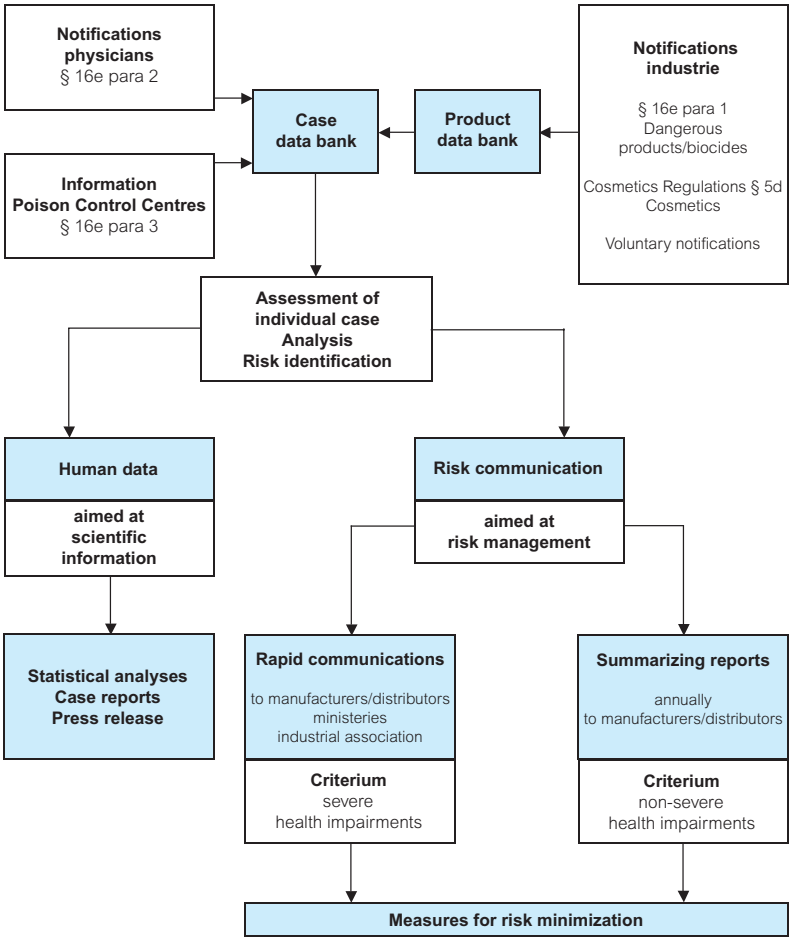


Fig. 1: Terms of reference of the Poison and Product Documentation Centre

1.3 Product data bank (poison information data bank)

1.3.1 Figures

At he end of 2004, 185 487 documents on individual products had been recorded in the poison information data bank maintained by the BfR, which can be accessed by the Poison Control Centres in Germany thus supporting their activities in providing consultation and treatment in cases of poisoning. The structure of the data bank and the different types of product data sets have been described in detail in previous reports. The number of reports on products received by the Centre for Recording of Poisonings at the BfR increased by 23 458 documents in 2004 (Fig. 2).

1.3.2 Collaboration between the BfR, industry and reporting Poison Control Centres

More than 90 % of product data on cosmetics received by the BfR are submitted by manufacturers and distributors in electronic form, while the major part of reports made on a voluntary basis, reports on dangerous preparations and biocidal products is still submitted on paper forms.

Until the end of the year, 1 699 product formulations were received by the BfR through the electronic information procedure (EMIL) elaborated in cooperation with the Poison Control Centres and the German Cosmetics, Toiletries, Perfumes, and Detergents Association (Industrieverband Körperpflege und Waschmittel e.V. –

Notifications

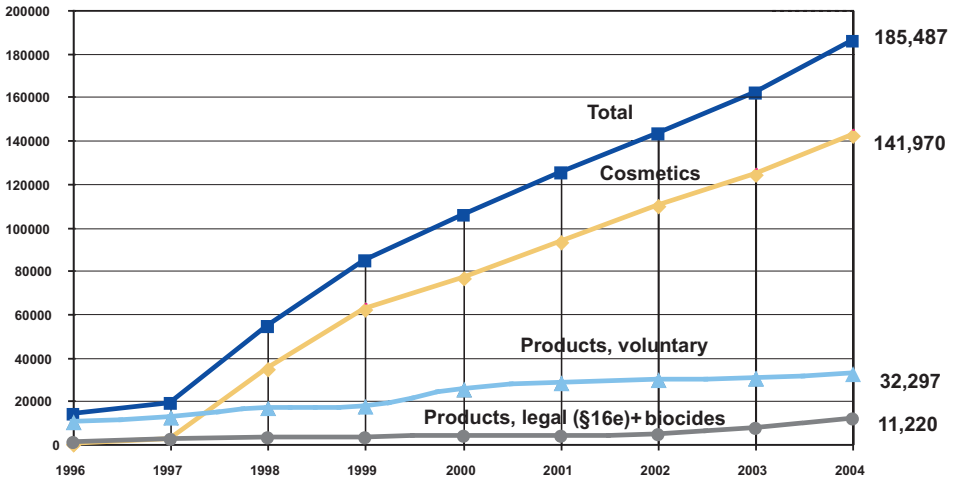


Fig. 2: Notifications on products received since 1997 and transmission of information to the German Poison Control Centres

IKW), which is guided by the notification procedure for cosmetics. The data were transmitted by diskette and e-mail. The envisaged end point of electronic data transmission is online data recording and data transmission in the framework of a central poison information data bank.

Of the dangerous preparations and biocidal products notifiable under §16e para 1 of the Chemicals Act, 11 220 data sets have been distributed by transmission to the Poison Control Centres so far (Fig. 3).

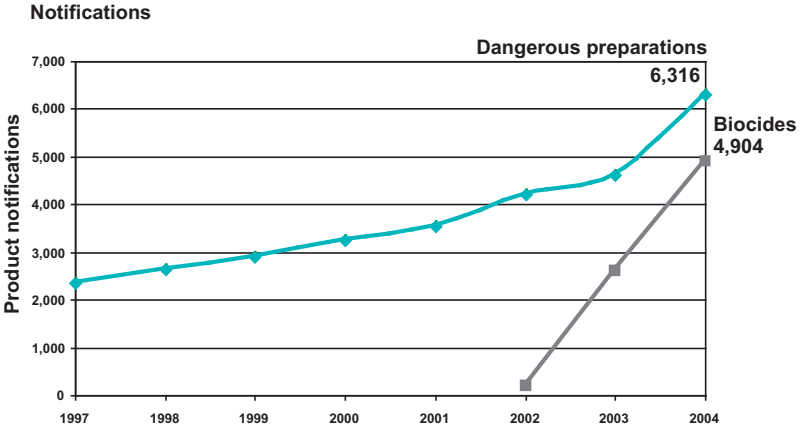


Fig. 3: Notifications under §16e para 1 of the Chemicals Act: legal products and biocidal products

2 Case reports by physicians

2.1 Evaluation of reports

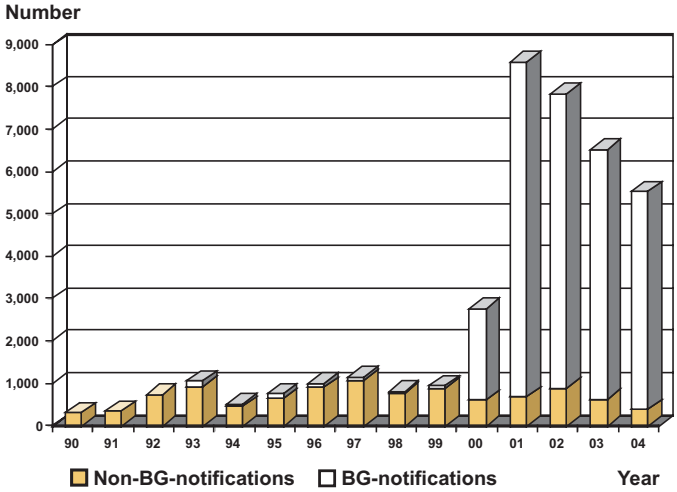


Fig. 4: Cases reported (BG notifications 100 % = 5 155; non-BG notifications 100 % = 386)

In the period between 1 August 1990, i.e. the beginning of the compulsory notification, and 31 December 2004, altogether 39 071 reports on cases of poisoning or suspected cases of poisoning were received by the BfR. In 2004, the reporting year considered, 5 541 notifications were received (Fig. 4).

The increased number of notifications received in 2000 was due to an agreement with the Berufsgenossenschaften (BG, professional insurance bodies in Germany responsible for occupational safety, health protection and accident insurance). According to this agreement, all notifications on cases of acute health impairment after contact with chemicals or chemical products are directly reported to the BfR by the Berufsgenossenschaften.

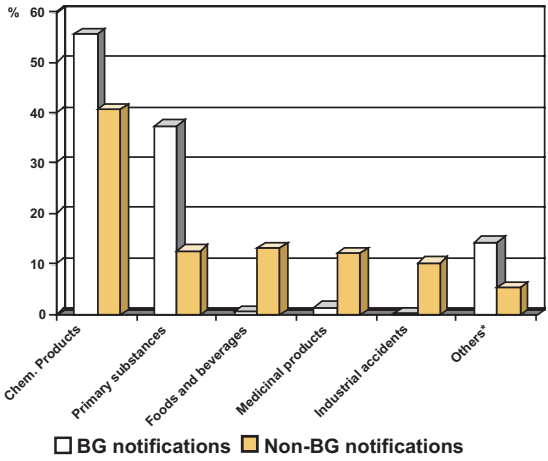
2.2 Reports on cases of poisoning in 2004

2.2.1 Origin

In 2004, 5 155 cases, i.e. 93 % of all cases notified, were reported by the Berufsgenossenschaften. The remaining 386 notifications (7 %) were essentially submitted by hospitals and medical practitioners. Single notifications were also received from pharmacies, poison control centres, the Arzneimittelkommission der Deutschen Ärzteschaft (Drug Commission of the German Medical Profession) or the Arzneimittelkommission der Deutschen Apotheker (Drug Commission of the German Pharmacists), among others.

2.2.2 Spectrum of cases reported

Fig. 5 provides a synoptic view of the spectrum of product groups involved in the cases reported. In 2004, as before, poisonings by chemical



* Others: Cosmetics/personal hygiene products, pesticides, agrochemicals, plants, fungi, animals, veterinary medicines, weapons, others

Fig. 5: Spectrum of cases reported (BG notifications 100 % = 5 155; non-BG notifications 100 % = 386)

products and primary substances have remained in top position among the total of cases reported by the Berufsgenossenschaften. All other product groups play a minor role with shares of less than 2 % each.

As expected, the spectrum of substances and products involved in poisonings is somewhat different in the reports received from hospitals and those received from medical practitioners. Also among these, notifications related to chemical products ranked first in the reporting year. They are followed, at a clear distance, by the primary substances that are likewise subject to compulsory notification. Next in the ranking are health complaints caused by foods, beverages 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 2004 have been classified by product application groups (assignment of toxicants according to their intended use).

2.2.3 Causes of poisoning

The Berufsgenossenschaften almost exclusively reported cases of exposure to poisons in the context of occupational accidents (ca. 96 % of

	BG notifications (100 % = 5 155 notifications)		Non-BG notifications (100 % = 386 notifications)	
Chemical products	55.7 %	(2 872 cases)	40.7 %	(157 cases)
Primary substances	37.6 %	(1 936 cases)	12.7 %	(49 cases)
Foods and beverages	0.7 %	(36 cases)	13.2 %	(51 cases)
Medicinal products	1.6 %	(22 cases)	12.2 %	(47 cases)
Industrial accidents	0.4 %	(20 cases)	10.4 %	(40 cases)
Others	5.4 %	(285 cases)	14.5 %	(56 cases)

Table 1: Spectrum of notifications (repeat listing of cases possible)

cases). The remaining 4 % of cases referred to accidents that occurred during the common use of a product or the cause of the accident was unknown.

Also among the reports submitted by hospitals and medical practitioners, accidents were the predominant cause of poisoning (58 %) followed by exposure during common use (25 %). Suicidal action was reported in no more than 1.8 % of cases. In the remaining cases, the cause has been unknown.

On principle, acute poisoning takes a dominating position among the reports (Table 2). This is due to the fact that the agreement on the transmission of reports on cases of poisoning by the Berufsgenossenschaften expressly provides for the submission of reports on acute cases of poisoning only.

2.2.4 Age structure and sex distribution

In 2004, the share of poisonings in adults among the total of cases reported was 96.8 %.

The cases submitted by the Berufsgenossenschaften were exclusively those involving adults. The share of cases in adults predominated also among the reports received from hospitals and medical practitioners while the share of children involved was 43 % (Table 3).

2.2.5 Degree of severity of health impairment

Also in 2004, 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 impairment is more often reported by medical practitioners or physicians working in hospitals because they also receive reports on suicide attempts (Table 5).

	BG notifications (100 % = 5 155 notifications)		Non-BG notifications (100 % = 386 notifications)	
Acute	99.9 %	(5 149 cases)	83.2 %	(321 cases)
Chronic	0.1 %	(4 cases)	15.8 %	(61 cases)
Unknown	0 %	(2 cases)	1 %	(4 cases)

Table 2: Duration of exposure

	BG notifications (100 % = 5 155 notifications)		Non-BG notifications (100 % = 386 notifications)	
Children	0 %	(0 cases)	43.1 %	(166 cases)
Adults	100 %	(5 154 cases)	55.4 %	(214 cases)
Unknown	0 %	(1 case)	1.5 %	(6 cases)

Table 3: Age groups

	BG notifications (100 % = 5 155 notifications)		Non-BG notifications (100 % = 386 notifications)	
Male	62.3 %	(3 211 cases)	44 %	(170 cases)
Female	22.0 %	(1 134 cases)	44.3 %	(171 cases)
Unknown	15.7 %	(810 cases)	11.7 %	(45 cases)

Table 4: Sex distribution

The product groups involved most frequently with regard to the degree of severity of health effects 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 (45 cases). Of course, the toxicants reported from occupational environments were different from those reported from the private sphere because, for example, the availability of certain product groups is a different one.

One of the reasons for the high number of cases involving lamp oil may be seen in the specific ascertainment of such cases in collaboration with ESPED (Erhebungseinheit für seltene pädiatrische Erkrankungen in Deutschland – clinical registration unit for rare paediatric diseases in Germany) cooperating with almost all paediatric hospitals in Germany.

2.2.6 Outcome of illnesses

For the notifications submitted by the Berufsgenossenschaften, the outcome is unknown in ca. 85 % of cases. The reason is that in the majority of cases, the report submitted is that by the so-called "Durchgangsarzt" ("transition doctor" appointed by the Berufsgenossenschaft). The report form is completed after the patient's first presentation. Therefore, such report does

	BG notifications (100 % = 5 155 notifications)		Non-BG notifications (100 % = 386 notifications)	
None	1.4 %	(70 cases)	13.5 %	(52 cases)
Minor	90.5 %	(4 669 cases)	60.4 %	(233 cases)
Moderate	6.5 %	(334 cases)	17.6 %	(68 cases)
Severe	0.1 %	(6 cases)	3.6 %	(14 cases)
Cannot be assessed	1.5 %	(76 cases)	4.9 %	(19 cases)

Table 5: Degree of severity of health disturbances

	Health impairment		
Product groups	Minor	Moderate	Severe
Primary substances	1 727	160	1
Cleansing products	814	58	
Industrial cleansers	58	6	
All-purpose cleansers	55		
Oven and grill cleansers	34	2	
Disinfectants/sterilizers	377	8	
Paints and related materials	236	11	1
Paint thinners	107	5	
Building materials	132	25	
Glues	110	3	
Sewage		2	3
Galvanic cells	101	5	1

Table 6: Product groups involved most frequently, by degree of severity of health impairment (BG notifications 100 % = 5 155 notifications)

	Health impairment		
Product groups	Minor	Moderate	Severe
Industrial accidents	40		
Foods and beverages	34	8	4
Food supplements	25	4	3
Lamp oil	24	24	3
Primary substances	31	15	2
Cleansing products	14	2	
Cosmetic creams/ lotion	10	1	
Fire lighting products	1	5	2

Table 7: Product groups involved most frequently, by degree of severity of health impairment (Non-BG notifications 100 % = 386 notifications)

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 the disease. 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 254 cases (67 %). In 118 cases (31 %), the outcome was unknown; in nine cases (2 %), late damage could not be excluded or partial recovery was reported.

Altogether seven deaths were reported in 2004, two of these by the Berufsgenossenschaften and five, by hospitals and medical practitioners.

The fatal two cases reported from workplaces were poisonings by gases such as hydrogen sulfide from an industrial sewage collection tank (cf. Chapter 3.3.6).

In the preceding year, regrettably also two deaths were reported that referred to children who had accidentally ingested paraffin-containing colourless lamp oil (cf. Chapter 3.3.1).

In addition, two deaths were reported that had been due to consumption of leaves of colchicum being mistaken for those of bear's garlic (cf. Chapter 3.3.11) and one suicide involving the pesticide, parathion.

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, hobby articles, cosmetics, plant protection and pest control products and corresponding products for commercial use have been informed about reports received by the BfR on cases of health impairment associated with their products.

2.3.1 Rapid communications

If reports on **severe** health risks (except those related to suicide attempts) are received by the BfR, it 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 responsible ministries, the Federal Ministry of Consumer Protection, Food and Agriculture, the Federal Ministry for the Environment, Nature Conservation and Nuclear Safety, and the Federal Ministry of Health and Social Security as well as the Federal Office for Consumer Protection and Food Safety.

Between 1 January 1998 and 31 December 2004, altogether 21 rapid communications were prepared and communicated. A synoptic view of these is given in Table 8. For explanations with regard to individual cases until 2003, reference is made to the 2002 and 2003 Annual Reports. In the reporting year of 2004, two rapid communications were distributed. The cases concerned were two fatal ones in children associated with the ingestion of colourless paraffins from a garden torch and an oil lamp. The case reports are described in detail in Chapters 3.3.1.2. and 3.3.1.3.

Year	Product	Toxicologically relevant substance	Person exposed	Outcome	Proposal by BfR (P) and results (R)
1998	Impregnating agent	Fluorinated hydrocarbons	Adult	Death	P: Warnings for asthmatics R: Accepted
1998	Disinfectant	Quaternary ammonium compounds (surfactants)	Elderly adult	Death	P: Information, labelling „corrosive“ R: Accepted
1999	Toilet drain cleanser	Sodium hydroxide	Adult	Caustic burns	None
1999	Solvent	Petrol	Adult	Pulmonary oedema	None
1999	Depilatory cream	Thioglycolic acid	Adult	Scars	None
1999	Disinfectant	Quaternary ammonium compounds (surfactants)	Elderly adult	Death	P: Information, labelling
1999	Industrial cleanser	Sodium hydroxide	Young child	Caustic burns	P: Information
1999	Medicinal product	Dimenhydrinate	Infant	Death	P: Warnings
2000	Cream bath product	Surfactants	Elderly adult	Death	P: Information
2000	Lamp oil	Paraffins	Young child	Severe pneumonia	P: Partial ban R: Accepted, paraffin substitute
2001	Disinfectant	Alkylamine (surfactant)	Elderly adult	Death	P: Information

Year	Product	Toxicologically relevant substance	Person exposed	Outcome	Proposal by BfR (P) and results (R)
2001	Tea (biodrug)	Atropa belladonna	Adolescent	Respiratory insufficiency	P: Information
2002	Lavatory cleaner	Surfactant	Elderly adult	Caustic burns	P: Information
2002	Mild detergent	Surfactant	Elderly adult	Death	P: Information
2003	Cleansing product	Surfactant	Elderly adult	Respiratory insufficiency	P: Information
2003	Food supplement	Proteins	Adult	Severe allergy	P: Information
2003	Fumigant	Sulfuryl difluoride	Adult	Death	P: Information
2003	Drain cleanser	Potassium hydroxide solution	Child	Severe caustic burns	P: Information
2003	Disinfectant	Peracetic acid	Adult	Respiratory insufficiency	P: Information
2004	Garden torch	Paraffins, colourless	Infant	Respiratory insufficiency, death	P: Information, additional EU ban on colourless / unscented paraffins R: Accepted
2004	Oil lamp	Paraffins, colourless	Infant	Respiratory insufficiency, death	P: Information, additional EU ban on colourless/unscented paraffins R: Accepted

Table 8: Rapid communications 1 January 1998 – 31 December 2004

2.3.2 Summary reports

Notifications referring to **non-severe** health impairment caused by chemical products in occupational or private environments are transmitted to the manufacturers/distributors in the first quarter of each new year in a summarized form. As requested by manufacturers, also suicides/suicide attempts have been included in the summary notifications since 2003 irrespective of the degree of severity of poisoning. Thus, manufacturers and distributors gain knowledge on possible risks involved in the handling of their products, which enables them to exercise responsible care with regard to their products. If they find the information provided to be insufficient, additional information can be obtained from the BfR. Much use has been made of this opportunity. The information provided for the manufacturer is a contribution to increase product safety and thus, to improve consumer protection. There has been great interest in such information. For example, accident analyses have revealed that eye injuries caused by chemical products have frequently occurred in spite of wearing safety goggles. The safety data sheet should therefore point out "closely fitting safety goggles".

Summary reports for the year 2004 referred to 303 products and were formally transmitted to 148 manufacturers. The table below (Table 9) provides a synoptic view of product application groups (minimum three listings) of the 2004 summary reports. Strikingly high numbers have been recorded for cleansing products (90) and disinfectants (61).

First level		Second level		Third level	
Agrochemicals	7				
Chemical products	254	Building materials, auxiliary products	4		
		Building materials	6		
		Fuels, liquid	14	Lamp oil	14
		Office materials, chemical	13		
		Disinfectants/sterilizers	61		
		Glass-working, auxiliary products	3		
		Glues	3		
		Metallurgy, auxiliary products	3		
		Cleansing products	90	Descaling products	3
				Dishwasher detergents	4
				Dishwasher cleansers	3
				Industrial cleansers	9
				Milking machine cleansers	11
				Lavatory cleansers	13
				Detergents, auxiliary products	4
		Water treatment products	3		
Cosmetics/ personal hygiene products	18	Skin care products	15	Creams	10
Pesticides	24	Fungicides	4		
		Herbicides	7		
		Insecticides	9		

Table 9: Product groups in 2004 summary reports

Table 10 shows the number of moderate health disturbances associated with the product groups in 2004. The remaining product groups were involved in minor health impairment.
The BfR also performs cumulative data analyses of case reports. If trends become apparent, the manufacturers of the products confirmed are informed. In turn, manufacturers are requested by the BfR to communicate comparable data and trends that may serve to improve product safety.

First level		Second level		Third level	
Agrochemicals	1				
Chemical products	36	Paints and related materials	1		
		Building materials	1		
		Fuels, liquid	7	Lamp oil	7
		Office materials, chemical	4		
		Disinfectants/sterilizers	3		
		Galvanizing agents, auxiliary products	2		
		Glass-working, auxiliary products	1		
		Coolants	1		
		Metallurgy, auxiliary products	2		
		Cleaning products	10	Floor polishes	1
				Industrial cleaners	1
				Milking machine cleaners	2
				Furniture polishers	1
Cosmetics/ personal hygiene products	2	Hair care products	1	Dyes/colorants	1
		Skin care products	1	Creams	1
Pesticides	2	Insecticides	2	Phosphoric esters	1

Table 10: Product groups associated with moderate health disturbances of summary reports in 2004

3 Selected toxicological problems

3.1 Risk of aspiration carried by petroleum distillates and paraffins

As repeatedly reported earlier, liquid fuels containing paraffins and petroleum distillates that are used in ornamental oil lamps, garden torches, for grill lighting and fire-breathing, carry a high potential risk. Very low quantities, often only a little sip, may result in severe chemical pneumonia. In Germany, already five deaths in infants and young children have been recorded since 1990. In the reporting year of 2004, two infants died of the consequences of aspiration of colourless paraffin-containing lamp oils (see also case reports).

In addition to the regular documentation of cases under §16e of the Chemicals Act , the BfR has recorded cases of poisoning involving lamp oils in collaboration with the clinical registration unit for rare paediatric diseases in Germany (ESPED) and almost all German paediatric hospitals since 1 March 2000. A detailed report on the first part of the study (ESPED I: 1 March 2000–28 February 2003) was published in the annual report "Cases of Poisoning Reported by Physicians in 2003". Since lamp oil substitutes (rape seed methyl ester, high-viscosity mineral oils and paraffins) are being placed on the market, the study will be continued until 31 December 2006.

The ESPED study "Lamp oil poisoning in Germany" has proved to be a reliable instrument of postmarketing control. It has reliably described the introduction of substitute substances and the residual risks posed by lamp oils for infants and young children. The figures documented so far demonstrate that the frequency of lamp oil accidents requiring inpatient treatment has continued to be on a decrease in Germany. The ban on coloured and scented lamp oils containing paraffins or kerosene that was introduced in Germany on 1 January 1999, the placing on the market of substitutes and the warning to consumers issued by the most different institutions and the media appears to have taken effect. A comparable trend has also been recorded by the German Poison Control Centres. In 2004, as already in the reporting period of 2003, no single case of health impairment due to the new substitutes was documented, neither at the BfR nor at the German Poison Control Centres.

3.1.1 Reports in the ESPED study, state as of 31 December 2004

Between 1 March 2000 and 31 December 2004, the BfR received 616 case reports from ESPED with a total number of 458 questionnaires being returned (67 %). 411 of these cases could be validated as lamp oil ingestion with a 40 % rate of pneumonia (in 165 infants and young children). In the majority of cases (61 %), pneumonia was caused by lamp oils containing paraffins or petroleum distillates that were either old products (i.e. coloured or scented products sold before the ban) or uncoloured and unscented products **not subject to the ban so far.** Observations made by different parties have indicated that the uncoloured and unscented products containing paraffins/petroleum distillates that are not subject to the ban are more aggressively advertised and sold with increasing market shares by wholesalers and retailers. A possible reason is that these products are a good fuel for garden torches and for lighting of charcoal (products for grill lighting).

3.1.2 Measures to be taken

Alarmed by the two tragic deaths in 2004 that were caused by products containing paraffins and petroleum distillates (lamp oil in one case and liquid fuel for garden torches in the other), the Federal Institute for Risk Assessment and the Ministry for the Environment, Nature Conservation and Nuclear Safety have again (as already in 1993/1996) demanded a ban on all

products of such type on the EU level. At present, a risk survey is performed by the EU in all its member states in order to achieve an appropriate decision. Until such a decision is achieved, it is of utmost importance to keenly protect children and to draw attention to substitute fuels (e.g. on a rape oil basis). In October 2002, an EU standard for the design of childproof oil lamps took effect (EN 14059: Decorative oil lamps – Safety requirements and test methods), which, however, has not yet been taken up by the German industry in spite of persisting accidents. Also the results of the ESPED study have suggested that the passive protection of children can be improved essentially, given the fact that children have very frequently ingested the toxicant from non-childproof oil lamps. When grilling is performed in the presence of children, paraffin-/kerosene-containing liquid products for grill lighting should not be used. The BfR has pointed out this special risk in press releases.

3.1.3 Overall evaluations of liquids involving aspiration risks

Evaluations of all notifications received by the BfR of cases associated with liquids involving aspiration risks such as lamp oils, liquid products for grill lighting and fire eating/breathing as well as case reports of the ESPED study have shown a decreasing tendency. In these evaluations, the essential share in the figures is represented by the ESPED study data (ca. 85 %). The total number of cases recorded at the BfR has distinctly decreased, while the share of cases of aspiration pneumonia has shown a slight decrease. This tendency becomes evident even if these figures refer to those cases only where knowledge of the formulation of the product involved has suggested the ingestion of paraffin-containing liquids (Fig. 6). Thus, the results of the ESPED study and notifications under §16e have demonstrated the fact of a decreasing total number of ingestion of liquids involving aspiration risks in Germany.

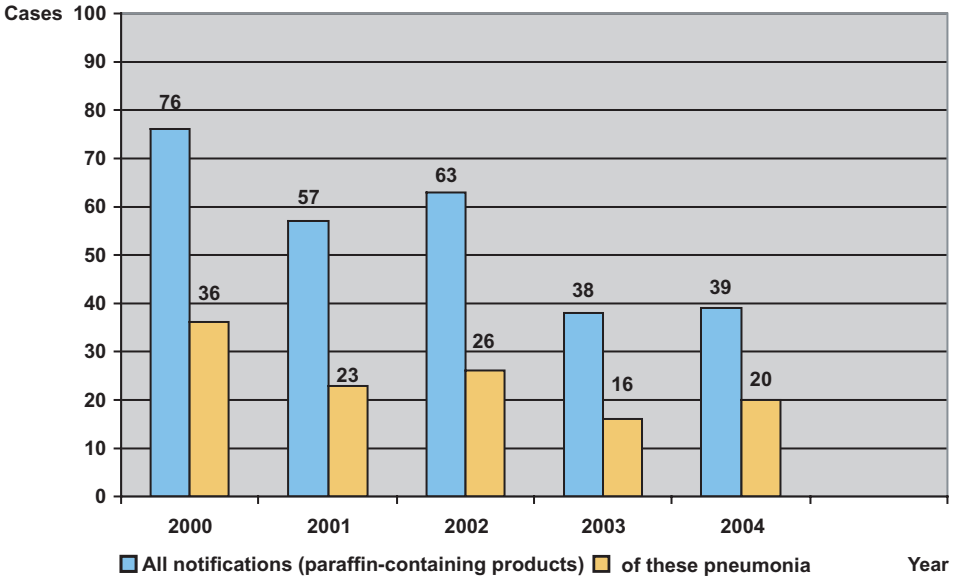


Fig. 6: Frequency of notifications under §16e Chemicals Act of cases involving paraffin-containing products from 1 January 2000 – 31 December 2004 (linear trend, the figure for 2000 with regard to ESPED cases was obtained by linear extrapolation since the study started on 1 March 2000)

The severe health impairments caused by colourless lamp oils and liquid products for grill lighting and fire eating/breathing have shown that the protection of the population, particularly of infants and young children, has to be further improved. Appropriate measures on an EU level are expected to be initiated in 2005.

3.2 Health impairments caused by toner

Single reports on health impairments caused by toners were received from the field of occupational medicine. They primarily referred to health complaints involving the mucosal membranes such as rhinitis, eye and throat irritation and asthma-like cough. One of these cases was described in the annual report "Cases of Poisoning Reported by Physicians in 2002" by the Federal Institute for Risk Assessment and information provided for physicians on the manifestations and relationships observed.

Until the end of 2004, physicians and Berufsgenossenschaften reported to the BfR 48 cases involving toners (reporting year 2000: 1 case; 2001: 5 cases; 2002: 11 cases; 2003: 5 cases; 2004: 26 cases). 15 cases were reported by physicians working in hospitals, nine by medical practitioners and two, by Poison Control Centres (three by others). 19 reports were received from Berufsgenossenschaften. The persons involved were exclusively adults (24 females, 21 males, three cases unknown). Most of the exposures (46) occurred at the workplace, only two of them in the private sphere. In most cases, the exposure was chronic (26), but also acute cases occurred (20, in two cases unknown). The route of exposure occurring most frequently was inhalation (42), but also exposure through the skin (10) and the eyes (2) and one case of ingestion were reported (repeated listing possible). The health impairments experienced by the persons affected were predominantly classified as "minor" (28). "Moderate" health impairments were observed in 15 cases, no impairment in three cases. In two cases, the health impairment could not be assessed on the basis of the data available. The health impairments observed referred mainly to the respiratory tract including cough (20), rhinitis (16), bronchitis (13), but also dyspnoea (12) and bronchial asthma (9). Also eye irritation, headache and allergies (9) were reported.

The Interessengemeinschaft der Tonergeschädigten (ITG, a self-help group of persons affected by health damage due to toners) has stated the number of persons affected to be at least 700. This was reported on a hearing of the ITG performed at the BfR on 1 September 2004. Printing and copying processes are complex physical and chemical processes associated with the liberation and emission into the indoor air of volatile organic compounds of different chemical groups, microparticles from toners and papers and gases. As a result, users of laser printers and copying machines are exposed to a higher or lower degree to a number of substances, among these also substances involving health hazards. For the evaluation of possible health damage caused by toners, the BfR has been collaborating with other federal institutions, such as the Federal Institute for Occupational Safety and Health (BAuA/FIOSH), the Federal Institute for Materials Research and Testing (BAM) and the Federal Environmental Agency (UBA) all of which have already dealt with the problem in the context of scientific tasks and studies. A BfR pilot study on health risks posed by toners is envisaged.

The case report below demonstrates how difficult an evaluation of symptoms associated with exposure to toner dusts may be.

Case report
Health impairment after contact with toner in a patient suffering from atopic diathesis

A 42-year-old female patient had been suffering from cough and sudden dyspnoea since 1985. Having moved into a newly furnished office in 1989, she began to suffer increas-

ingly from breathing difficulty at her workplace. The patient attributed her complaints to the impact of dust emitted by copying machines and printers. She was examined and her medical condition assessed, with a tentative diagnosis of obstructive disease of the respiratory tract. There was no sufficient evidence to incriminate the patient's occupation as the cause of her breathing difficulties.

Manifestations/course
The case history revealed certain indications of frequent respiratory tract complaints at the workplace.

When packaging deep-frozen products in the spring of 1985, the patient experienced for the first time cough and an oppressive feeling when breathing. These manifestations abated in her private home. This was followed by manifestations such as a runny nose, sneezing and irritation of the conjunctivae of the eyes. Later, she also developed manifestations on her hands, particularly after exposure to dust emitted during reconstruction work in her office. Reportedly, she developed 'influenza-like' complaints particularly when working at copying machines or laser printers. During weekends and holidays, her condition improved clearly. Asthma-like complaints requiring increased administration of medicines and allergic rhinoconjunctivitis were stated. However, examinations performed to determine exposure at the workplace did not reveal any clear evidence of an occupational cause of the patient's bronchial asthma. Various occupational provocation tests were carried out on the basis of the patient's assumptions about substances that might have triggered the complaints. After working at a copying machine, inhalation of dust brought along from her workplace as well as after staying in an archive of medical files, the patient developed breathing difficulties comparable to those experienced at her workplace. However, measuring techniques were unable to unequivocally detect any reaction of the respiratory tract in these provocation tests. It was assumed that the patient's complaints might have to be attributed to a sick building syndrome. It was stated that no risk of a trend-setting deterioration of the disease was seen as that could be associated with a continuation of her previous occupation. The last expert opinion of 1996 concluded that the patient was suffering from a rhinopathy due to house dust mites which had been partly caused by exposure to such mites. In this context, the exposure to house dust mites in the patient's home was considered as less intensive than that at the workplace because the patient had taken measures to control the infestation by house dust mites in her private home. However, no sufficient evidence was found that would have permitted to attribute the bronchial disease of the patient to antigenic influences at the workplace or to the incriminated action of dusts emitted by copying machines and printers. Great importance was attributed to the patient's high cigarette consumption as a cause of the persistence of her chronic bronchial asthma. Furthermore, a sensitisation to cat epithelium was found to play an additional role in the unspecific increase of responsiveness of the bronchial system.

Notes
In the case described, a subjective health impairment was experienced at the workplace by the patient who had been suffering from an underlying allergic disease. Nevertheless, no evidence of a workplace-associated cause leading to occupational disease was found by examinations performed with regard to dust exposure at the workplace.

3.3 Case reports

3.3.1 Cases of poisoning by paraffins

3.3.1.1 Liquid products for grill lighting

Respiratory insufficiency in a young child after ingestion of a liquid product for grill lighting

A two-year old boy drank and aspirated an unknown quantity of a liquid product for grill lighting. As a consequence, artificial respiration had to be performed. In the further course, the patient developed subglottic granulomas, in addition to pneumonia. He was referred to inpatient treatment, which lasted for almost three weeks and resulted in complete recovery.

Manifestations/course

After ingestion, the child showed signs of respiratory insufficiency. Since primary oxygen supply was insufficient as a therapy, the boy had to be intubated and respirated.

On admission to hospital, the little patient was analgosedated and kept under mechanical ventilation applied equally on both sides of the chest. Auscultation revealed crepitation over the lung fields. Other organ findings were normal. Pneumonia, which could also be verified radiologically, receded slowly so that respiration could be withdrawn from day 4 and extubation performed on day 6. In the further course, a marked inspiratory stridor was found to be present. Bronchoscopy was therefore performed on day 10, which revealed subglottic granulomas. The patient remained under intubation and artificial respiration. Three days later, bronchoscopy was repeated under laser conditions at an ENT hospital. Except for a moderate mucosal swelling, other manifestations were not found to persist. After cortisone administration and suprarenin inhalation, extubation could be performed three hours later. Stridor was no longer found to be present. A secondary infection with *Haemophilus influenzae* detected in the tracheal secretion was treated with antibiotics. After 18 days, the patient had completely recovered and was discharged.

Notes

The detailed composition of the liquid involved was not available. In most cases, the only relevant components contained in liquid products for grill lighting are hydrocarbons such as petrol, paraffin oil, isoparaffins, kerosene and, less often, also isopropanol. Investigations into eleven product formulations performed at the Federal Institute for Risk Assessment (BfR) revealed as ingredients: lamp oils in six, kerosene in three and petrol in two products. The two products containing petrol, however, had been available on the market only until 2001.

Ingestion of petrol or kerosene is mostly followed by the typical foetor ex ore since these substances are largely excreted through the respiratory tract. In the case described above, such typical smell was not described, however, the authors of the report may just have failed to do so. The hydrocarbons concerned have chain lengths between C_9 and C_{15} and involve a high risk of aspiration because of their physicochemical properties such as low viscosity, low surface tension and low vapour pressure. They readily pass the epiglottis by creeping and thus may cause severe chemical pneumonitis. Aspiration of amounts as low as < 1 mL may induce pneumonia in humans. The cardinal sign is an initial and often persistent cough. In addition, vomiting may occur. This may be followed by dyspnoea and/or tachypnoea, cyanosis and less frequently, by somnolence. In cases of pulmonary manifestations, pneumonitis may develop in ca. 25-50 % of cases. However, also in the event of an initial absence of manifestations, pneumonitis may develop in 10-20 % of cases. Death due to progressive pulmonary oedema is

also possible. Less often, pneumatoceles have been observed. In cases of ingestion of >1mL/kg b.w. or suspected aspiration it is always recommended to seek medical advice in a hospital. In all patients suffering from initial manifestations, clinical and/or radiological examinations are required to exclude pneumonia. X-ray examination should be performed two hours after ingestion but not earlier. Clinically asymptomatic patients with pathological X-ray findings should undergo clinical observation for 6-12 hours. The aspiration problem associated with lamp oils for use in ornamental lamps, liquid fuels used by fire breathers and also liquids for grill lighting has already been comprehensively dealt with by the Federal Health Office (BGA), the Federal Institute for Health Protection of Consumers and Veterinary Medicine (BgVV) and their successor institution, the Federal Institute for Risk Assessment (BfR).

Evaluation of the case described:
In the case described above, a causal relationship between the ingestion and the manifestations observed has been rated as probable on the basis of the information given on the temporal relationship and in the absence of other causes, for the severe health impairment suffered by the patient.

3.3.1.2 Garden torch

3.3.1.3 Oil lamp

Severe health impairment with lethal outcome in two infants after ingestion of colourless and unscented lamp oils containing paraffin

In the context of notifications of cases of poisoning under § 16e para 2 of the German Chemicals Act, two severe cases of health impairment with a lethal outcome were reported to the Federal Institute for Risk Assessment (BfR). The notifications referred to a girl aged 13 months (date of accident 16 May 2004) and a boy aged one year and eight months. In both cases, the substances involved were colourless and odourless lamp oils on a paraffin basis. Both children died from the sequelae of lamp oil aspiration, in spite of intensive medical treatment.

Case No 1: Garden torch
When playing in the garden, a girl aged 13 months drank an unidentified quantity of clear and odourless lamp oil contained in a garden torch. The manufacturer of the product has remained unknown so far. According to analy-

Fig. 7: Garden torch

ses performed, the product involved consisted of paraffins (long-chain alkanes, fractions C_9 - C_{14}) and was labelled with R 65 under the German Regulations on Dangerous Substances and Materials (Gefahrstoffverordnung – GefStoffV).

Manifestations/course
The child was reported to have coughed, retched and vomited several times immediately after ingestion. After an emergency physician had referred her to a hospital which

took place without delay, the little patient's condition deteriorated dramatically, as seen by signs of respiratory insufficiency, increase of heart rate and cyanosis. She was artificially respirated and transferred to the paediatric intensive care unit of a large hospital. On arrival, a decompensated respiratory acidosis with a pH of 7.2 was already found to be present. Chest X-ray revealed extended accumulation of fluid in both lungs, with pleural effusion right in the sense of an extended chemical pneumonia. In the further course, the clinical picture showed a pronounced acute respiratory distress syndrome (ARDS) which developed shortly afterwards. In spite of massive measures of intensive medical care, no oxygen saturation could be achieved even at the highest ventilation pressure available. After a sudden decrease of the heart rate followed by cardiac arrest, cardiac massage, intratracheal administration of three doses of adrenaline and defibrillation remained unsuccessful. The child died after ca. twelve hours from the sequelae of lamp oil aspiration, having developed a severe pneumonia and destruction of lung tissue, which were confirmed histologically.

Evaluation of the case described:
Based on the information received on the temporal relationship between ingestion and manifestations, a causal relationship is probable.

Case No 2: Oil lamp
A boy aged 20 months drank an unknown amount of a colourless and unscented paraffin-containing oil from a lamp (a heavy glass bottle equipped with a metal ring that reportedly had held a wick). However, it has also been considered as possible that the boy had only sucked from the wick because the latter was found beside the bottle. The lamp had been placed on the terrace. The manufacturer of the product was known. Also in this case, the substance involved consisted of paraffins both according to the product label submitted and the analyses performed.

Fig. 8: Oil lamp

Manifestations/course
The child was reported to have coughed immediately and vomited later on. After admission to the nearest hospital, the boy was intubated and respirated while developing an increasing clouding of consciousness. Due to cardiac arrest, cardiopulmonary resuscitation (by mechanical measures and medication) over a short period became necessary and as a result, temporary haemodynamic stabilization was achieved. When respiratory insufficiency continued to deteriorate, the boy was transferred by helicopter to a university hospital. In spite of aggressive respiration and repeated catecholamine administration, a respiratory and haemodynamic stabilization could not be achieved again when the patient developed right ventricular failure. A thoracic ECCPAD implantation was performed (extracorporeal membrane oxygenation). In the further course, the patient became anuretic. Under conditions of a considerable generalized metabolic disturbance, the patient developed

progressive hyperkalaemia and haemolysis. A reduction of potassium levels could be achieved by haemodialysis that had to be performed because of renal failure unresponsive to therapy. Episodes of rising temperature remained largely refractory to therapy. In spite of massive measures of intensive medical treatment including aggressive respiration and extracorporeal membrane oxygenation, the patient died after three days from the sequelae of lamp oil aspiration which included development of multiple organ failure and brain damage.

Notes
Due to the particular hazard involved in lamp oils, the former Federal Institute for Health Protection of Consumers and Veterinary Medicine (BgVV) had demanded a ban on the marketing of lamp oils. In Germany, a ban on the marketing of coloured and scented lamp oils containing paraffin and kerosene was achieved in 1999. Since mid-2000, this ban has been effective on the European level. Obviously, this measure has not been adequate to protect infants and young children. The ban on marketing should be extended as soon as possible to include also colourless and unscented products. In a press release, the BfR has issued a warning not to use such lamp oils in the household.

When including the two notifications described above, altogether five deaths of children attributable to lamp oils containing paraffin and kerosene have been reported. Additionally, a number of children have suffered severe health damage. As a conclusion, such products are to be rated among those household chemicals which are most dangerous for children between one and three years of age. The potential hazard involved is to be attributed to the special physicochemical properties of these lamp oils. Ingestion of very low quantities of less than one gram may result in the oils 'creeping' into the lungs and causing severe inflammation commonly referred to as chemical pneumonia.

Since 1970, German poison control centres had received ever-increasing numbers of inquiries about lamp oil poisoning. In 1994, between 250 and 300 cases of chemical pneumonia in infants and young children were calculated to have occurred per 1000 of such inquiries. A decrease in the number of reported cases involving severe health damage was recorded for the first time after a number of preventive measures had been implemented by the predecessor institute of the Federal Institute for Risk Assessment. Such measures included child-resistant closures, warnings, labelling (risk phrase R 65, 'harmful'), and a ban on the marketing of scented and coloured lamp oils containing paraffin and kerosene for use by the private consumer (see Chapter 3.1).

3.3.2 Food supplements

3.3.2.1 Maca powder

Severe course in a case of eosinophilic vasculitis
A 22-year-old patient was suffering from an eosinophilic vasculitis associated with adult respiratory distress syndrome (ARDS) with a severe course. The cause of the disease could not be conclusively elucidated. The patient had taken a muscle building product over 20 days that was taken into consideration as a triggering agent. However, no allergy tests had been performed before the present report was recorded. The product contained Maca powder, vitamin E and zinc. The patient had to be respirated for seven days. Inpatient treatment lasted for 18 days.

Manifestations/course
The patient was admitted to hospital due to a swelling of lymph nodes in his right inguinal

region lasting for ten days. In addition, he complained of exhaustion, night sweat and cough. In order to exclude a malignant underlying disease, a lymph node puncture was performed under spinal anaesthesia. During this procedure, the patient already developed considerable dyspnoea associated with reduced gas exchange and a peripheral oxygen saturation of 84 % when breathing indoor air. At first, therapeutic attempts included non-invasive artificial respiration. Due to a further deterioration of the patient's condition, he was transferred to the intensive care unit on the following day. There, the striking signs of tachypnoea with respiratory rates of up to 30/min and a peripheral oxygen saturation of 88 % were recorded under conditions of oxygen supply by nasal tube. Because of a further deterioration (peripheral saturation 75 %), the patient was intubated and respirated. Still, the gas exchange was found to be extremely reduced. Bronchoscopy was performed without delay and revealed only low amounts of a yellow-brownish secretion without any obstruction of the airways. The mucosa was found to be normal except for reddening and petechial haemorrhages. The clinical picture found was that of a severe ARDS associated with pronounced confluent shadowing over both lungs revealed by X-ray and shadows from pleural effusions revealed by computer tomography. Based on a tentative diagnosis of an infectious-septic process, a broad-spectrum antibiotic therapy was initiated. Nevertheless, laboratory analysis revealed only a moderate increase of inflammatory parameters and a significant increase of eosinophils in the differential blood count (23.5 %, reference value: 2.7 %). After a septic process had been excluded, a tentative diagnosis of an allergic-immunological cause was assumed and therefore, it was decided to perform a probatory high-dose steroid administration. Already administration of the first dose of 500 mg of prednisolone resulted in a significant improvement of the patient's condition. Gas exchange parameters improved continuously, pulmonary infiltrates receded, and eosinophil levels returned to normal. Due to the clinical picture and the findings made by lymph node biopsy associated with a necrotizing vasculitis and considerable eosinophilia, the tentative diagnosis stated was that of an eosinophilic vasculitis of unclear origin. After seven days, extubation of the patient could be performed without any problems as he exhibited sufficient spontaneous respiration and a good vigilance. In parallel to the ARDS, the patient had developed a considerable coagulation disorder associated with thrombopenia, hypofibrinogenaemia and increased D-dimer levels as an expression of hyperfibrinolysis. However, there was no increased haemophilia.

Neither external nor internal medical history revealed any event or responsible agent that could be considered as a trigger for the allergic-immunological process observed in the patient. The muscle building product taken before the onset of the disease was taken into consideration as a possible cause. No similar cases have become known so far.

Notes

The muscle building product contained a root powder from the plant, *Lepidium meyenii*, also referred to as Maca, which is imported from Peru. In addition, the preparation contains vitamin E and zinc oxide. It is sold as a vitality-enhancing food supplement for health-conscious people. According to the responsible food control authority, it is marketable as a food.

Although closely related to the popular garden cress (*Lepidium sativum*), the perennial Maca plant has been almost unknown in Europe so far. Maca was cultivated as a crop plant in Peru

in pre-Columbian times already. The edible and nutrient-containing part of the plant is the tuber having a size of ca. 8 cm in diameter. The soft outer layers are rich in sugars. The more solid inner tissues of the tuber accumulate mainly starch, but also valuable proteins. The content of nutrients is even higher than that of cereals and potatoes. The Maca tuber contains ca. 60 % of carbohydrates (mainly starch, but also various types of sugar), 10-13 % proteins, 8-9 % dietary fibre and 2-3 % lipids, mainly fatty acids such as linoleic and oleic acid. In addition, it contains important minerals such as iron and iodine, but also calcium and magnesium. Other substances contained include alkaloids, tannins and saponins whose biological activity in humans still requires further research. Owing to its optimal ingredients, Maca became a medicinal plant surrounded by mysticism in the Andean region. It was used as a holy medicinal plant already by the Incas. World-wide, Maca powder has gained increasing popularity because it is said to enhance physical energy, endurance and stamina in athletes, etc.

Evaluation of the case described:
In the absence of results of allergy tests, a possible relationship cannot be assessed at present.

3.3.2.2 Atractylosides

Intrauterine hepatic damage of unclear origin after exposure to atractylosides
A female infant aged one month and 20 days was admitted to hospital due to an increasingly poor general condition. The findings made included an inadequate circulation due to vitamin-K deficiency associated with cholestasis under conditions of hepatopathy. An intrauterine hepatic damage due to the administration of plant products allegedly containing atractylosides was suspected. One of the products involved had been taken by the mother during the last three months of gestation and the second one, during the lactation period. Both products had been marketed as food supplements and were bought in a pharmacy. The report did not contain any information on why the expectant and later breast-feeding mother hat taken the preparations concerned. One of the preparations was labelled on the package with the warning: 'Do not use during pregnancy'. In the further course, a diagnosis of *progressive familial intrahepatic cholestasis* was established.

Manifestations/course
The child had been suffering from congenital icterus. One or two weeks before admittance to hospital, she developed a haematoma on her back. Two days before admittance to hospital, she suffered from nose bleeding. Her general state deteriorated, and on admittance, the child was in a deeply comatous condition. Due to an extended epidural haemorrhage right, the haematoma was immediately subjected to a neurosurgical relieving operation.

Laboratory analyses revealed increased GOT 253 U/L (reference range in children < 1 year: < 38 U/L), GPT 335 U/L (reference range in children < 1 year: < 36 U/L), bilirubin 3.5 mg/dL (reference range total bilirubin newborns < 13, adults < 1.1 mg/dL), AP 2340 U/L (reference range in children < 15 years. 110-700 U/L) and a Quick's value of 80 % (reference range 70-100 %). Galactosaemia, tyrosinaemia, alpha-1-antitrypsin deficiency, neonatal haemochromatosis, Niemann-Pick disease, Alagille syndrome and infectious hepatitis could be excluded. Hepatopathy persisted in the infant. Liver biopsy was performed to exclude a progressive familial intrahepatic cholestasis. The biopsy results revealed a picture of chronic hepatitis associated with giant cell transformation, intrahepatic bilirubinostasis as well as marked septal fibrosis and moderately floride inflammatory

activity. The histological picture was compatible with that of a protracted neonatal hepatitis. Similar pictures had been seen in cases of familial neonatal hepatitis, virus infections and also of toxic damage resulting from medicinal products. The eosinophilic inflammatory component could be an indication of a previous exposure to medicinal products, e.g. the preparations taken by the mother. Metabolic diseases such as viral infections that may also cause neonatal giant cell hepatitis were excluded by clinical examinations. By means of differential diagnosis, the investigators found that a toxic damage had to be considered as the most probable cause to explain the clinical picture presented. Nevertheless, a diagnosis of *progressive familial intrahepatic cholestasis* was made in the further course.

Notes

The two products involved were preparations used in traditional Chinese medicine (TCM). In China and Japan, there are corresponding traditional plant preparations that have been used to improve the immune system, among other purposes. The two food supplements were examined for hepatotoxic ingredients such as pyrrolizidine alkaloids and atractylosides. According to the labels, both preparations contain the rhizome of an Atractylodes species, among other ingredients. Both preparations contain *Atractylodes macrocephala* (Bai Zhu) as an ingredient in quantities of 12.4 % and 7.6 %, respectively. However, it could be detected only in the capsules taken by the mother during her pregnancy. The concentration detected in a capsule was below 10 µg.

Phytopharmaceuticals are widely used and are largely considered as harmless by the general population. However, on the whole, there has been an increasing number of reports on hepatotoxic effects of herbal medicines ranging from minor changes in hepatic parameters to severe liver damage. Particularly in South Africa, there have been severe cases of poisoning by the plant, *Callilepis laureola*, containing atractylosides. Atractylosides are diterpene glycosides that may cause fatal hepatic and renal necrosis in the mammalian organism and also in humans. They inhibit the oxidative phosphorylation in the liver mitochondria. Cases of acute poisoning by plants containing atractylosides in humans have been described and may result in acute hepatic failure. Also cases of renal damage have been described. Knowledge is scarce concerning their chronic toxicity. In literature, there has been no indication so far of intrauterine hepatic damage in an unborn child by atractylosides. In TCM, this plant has been described as having a "calming effect on restless foetuses". Both preparations seem to have been composed according to ancient traditional formulations of TCM that are not intended for dietary purposes but primarily for the treatment of a number of physical complaints, general weakness and also for an improvement of the immune system in cases of HIV infection or cancer, among other conditions.

Preparations that are predominantly intended to cure or relieve diseases must be considered as medicinal products and not as foods. Also according to assessments made by the food control authorities and the BfR, the products concerned have been suspected of belonging to the category of medicinal products.

Evaluation of the case described:

On the basis of the information given on the temporal relationship between the mother's exposure and the onset of the infant's disease, and given the diagnosis of a progressive familial intrahepatic cholestasis, a causal relationship cannot be established. However, the elevated transaminase levels found initially are not typical of a progressive familial intrahepatic cholestasis.

3.3.2.3 Ephedra alkaloids

Adverse reaction resulting from an ephedra-containing product

The BfR received a report on a suspected case of an adverse reaction to a food supplement that had been submitted by a pharmacy. A customer of the pharmacy had reported to suffer from health complaints after taking the preparation. Therefore, she was in doubt about the safety of the product and contacted the pharmacist asking him to check the package. According to the letter received from the pharmacy, the product concerned is a food supplement originating from the Netherlands and containing 20 mg ephedra alkaloids. It is used for weight reduction purposes. The product had been unknown to the BfR. Already in 2002, a joint press release had been issued by the Federal Institute for Health Protection of Consumers and Veterinary Medicine (BgVV) and the Federal Institute for Drugs and Medical Devices (BfArM) giving a warning against an uncontrolled use of ephedra-containing products.

Manifestations/course

The customer of the pharmacy had reported to suffer from hot flashes, nervousness and sleep disorders after taking the preparation. She reported to simultaneously have experienced a euphoric effect that had been so pronounced that she found it difficult to refrain from taking the product. The product had also taken effect with regard to the intended weight reduction. However, these side effects and the effect of addiction raised doubt in her as to whether the product was safe in terms of health.

Notes

Due to the ephedra alkaloids contained in the product according to the information given by the pharmacy, the product involved may have to be considered as a medicinal product. The herb, ephedra (*Ephedra sinica*) is a Chinese therapeutic agent. It is available on the market as a food supplement under the Chinese name of Ma Huang. Being a natural source of ephedrine, it has pharmacological properties. Its effects include vasoconstriction, circulatory stimulation, rising blood pressure, CNS stimulation, strong dehydration, suppression of appetite and broncho-spasmolysis. Possible adverse reactions include dilatation of the pupils, nervousness, tremor, sweating, cardiac arrhythmia, hypertension and at high doses, also convulsive seizures and mental changes. Form and character of the ephedra alkaloids naturally contained in the plant are similar to those of amphetamine. Therefore, products containing ephedra have been classified as medicinal products to be sold by pharmacies only In this way, quality, efficacy and safety of the products must be ensured.

Regrettably, products containing ephedra have been offered on the internet as food supplements or foods which is a practice avoiding authorization limitations and quality control. They are sold as appetite suppressant or remedy for hay fever. A study performed in the Netherlands on the quality and safety of ephedra-containing products revealed that in the majority of the products tested, the ephedra alkaloid quantities detected were higher than those stated in the labelling. Often, caffeine is added to the ingredients, increasing the effects of ephedra and thus the risk of harmful effects for the consumer.

In literature, there has been a great number of reports on health impairment associated with the use of ephedra-containing food supplements. After taking four tablets of a Ma Huang preparation for alleged weight reduction, a bodybuilder complained of severe pain in his right thorax and suffered myocardial infarction. In another case, a 54-year-old female suffered from hallucination associated with long-term use of food supplements containing ephedra (Clinical Toxicology 38 (2000) 5). Recently, it was re-

ported that a 22-year-old female was admitted to hospital presenting with tachycardia, nausea, tremor, abdominal pain and vomiting after having consumed a food supplement containing ephedrine and caffeine. Electrocardiography revealed manifestations of ischaemia (Clinical Toxicology 41 (2003) 6). The Food and Drug Administration (FDA) being responsible for the approval of medicinal products and food control in the USA has announced that it will ban the sale of all products containing ephedrine alkaloids. Also in the Netherlands, the use of ephedrine in products other than those classified as medicinal products has meanwhile been discontinued.

Already in 2002, the former BgVV has pointed out that such products should only be administered under control by a physician. Products for which a therapeutic effect is claimed in advertising have to be considered as medicinal products. Therefore, such products require authorization by the Federal Institute for Drugs and Medical Devices (BfArM). Products lacking such authorization are not marketable. In contrast, food supplements are foods of general consumption and must not be advertised by claiming medicinal effects. Responsibility for safety in terms of health rests with the manufacturer. Due to the direct sale of ephedrine-containing products on the internet, a complete control by the national control authorities is impossible.

Evaluation of the case described:
On the basis of the information given on the temporal relationship between the ingestion and the occurrence of the manifestations observed, and in the absence of other causes, a causal relationship has to be assumed in the case described.

3.3.3 Foods

3.3.3.1 Butterfish/Escolar

Caution when consuming smoked butterfish/escolar
A female patient and her partner experienced health complaints after the consumption of such fish that had been bought in a fresh state, stored in the refrigerator at 4 °C and undergone heat treatment. Manifestations persisted for four days. The patient became aware of the problem when reading comments on health reports from Australia published by the BfR.

Fig. 9: Butterfish/Escolar

Manifestations/course
Both partners experienced gastrointestinal complaints in the form of diarrhoea that persisted for three to four days, with stools of oily consistency and dark yellow colour. After 48 hours, a physician was consulted who sampled blood for examination and recommended to drink large amounts of fluid. Since there was no feedback from the physician consulted, it has been assumed that the results of chemical examinations were not alarming. No report was received from the attending physician.

Notes
In mid-2003, Australian health authorities reported health complaints associated with the consumption of escolar, also referred to as rudderfish. 98 cases had been recorded since 1999. In a press release, the BfR informed the public that in particularly sensitive persons, the consumption of large amounts of fish of the species *Lepidocybium flavobrunneum* (escolar) and *Ruvettus pretiosus* (oilfish) both belonging to the *Gempylidae* family (German terms: "Butterfisch" or "Buttermakrele") may cause health impairments such as diarrhoea, abdominal cramping, vomiting and headache and warned that caution be observed when eating such products. Experts have assumed as a presumptive cause the presence of poorly digestible or even indigestible wax esters that represent 90 % of the oil or fat in these two fish species. So far, it has remained unclear whether these wax esters are the only causes responsible for such illnesses or whether there are other factors playing a role as well. Such factors could possibly include certain allergenic fish proteins or biogenic amines (histamine, among others) that may form in fresh fish during extended storage periods. Another unknown factor consists in the quantity of fish that must be consumed to produce such health disturbances. The German terms of "Butterfisch" and "Buttermakrele" are collective terms used in the marketing of several high-fat fish species caught as by-catch in deep-sea fishing. In Germany, such fish has been available on the market for several years in the form of hot smoked fish cuts referred to as "geräucherte Buttermakrele", formerly "geräucherter Butterfisch". According to a study by the Federal Research Centre for Fisheries in Hamburg, waxy esters form more than 90 % of the oil or fat of the smoked "Butterfisch" and "Buttermakrele" marketed in Germany. The two cases described above are the first ones reported in Germany.

With regard to the toxicity of fishery products assigned to the family of *Gempylidae*, an expert opinion of 30 August 2004 by the Scientific Panel on Contaminants in the Food Chain (CONTAM) stated that according to the EFSA (European Food Safety Authority), it was not possible to establish, on the basis of case reports received, an intake level for such fish which would not lead to these adverse effects. By using appropriate practices of preparation, such as discarding the oil released, the occurrence of such symptoms may perhaps be avoided.

Evaluation of the case described:
On the basis of the information given in the two above cases on the temporal relationship between the ingestion and the occurrence of the manifestations observed, and in the absence of other causes, the existence of a causal relationship has to be assumed.

Other cases involving butterfish/escolar
Reports by lay persons after publication of the article on the internet.

Case No. 4592/04
After the consumption of 350 g of fish each, both partners suffered from severe diarrhoea persisting for five to six days. Their stools contained large quantities of fat excreted in the form of globules. However, this type of diarrhoea was not associated with pain as usual.

Case No. 4593/04
One day after the consumption of 300 g of fish, diarrhoea with stools of a yellow colour and waxy-oily consistency occurred that persisted until the next day. There were no other health complaints.

3.3.3.2 Shiitake mushroom

Shiitake dermatitis (flagellate dermatitis)
A dermatological outpatient department reported on a patient presenting with dermal manifestations after the ingestion of at least two raw shiitake mushrooms on two consecu-

tive days. The patient's wife had also eaten such mushrooms, however, without developing any health complaints.

Fig. 10: Shiitake mushroom

Manifestations/course
The changes of the skin observed were described by the physician on duty as linear erythema (similar to factitious urticaria) spreading over the entire body including the head. In addition, disseminated seropapules were seen. Furthermore, the patient stated to feel weak and abnormally tired. One month later, he still complained of skin irritation on mechanical stimulation. Treatment included systemic administration of cortisone which, however, was not taken by the patient. An allergy test was to be performed. The result remains to be seen.

Notes
The shiitake mushroom (*Lentinus edodes*) belongs to the family of *Tricholomataceae* and is a saprophytic fungus which colonises dead wood. Its cap has a diameter of up to 20 cm and is of brownish-grey colour with flat triangular scales, its gills are white-brownish and its spores colourless. It is highly valued as a food due to its excellent spicy taste. It has been ascribed extensive favourable effects on health. Particularly in Chinese and Japanese cooking, it has been a quite popular food. However, it is being cultivated and consumed in large amounts also in Germany. It is the second most popular mushroom in the world next to the button (table, white) mushroom. The beneficial properties and effects ascribed to this "overall healthy mushroom" include being a source of protein, potassium, zinc, vitamins B1, B2 and D, and more, an activator of the immune system, a reducer of the cholesterol level, and having favourable effects on the immune system in the treatment of cancer and AIDS. The main flavouring substances identified are sulfur compounds. They include lenthionine, tetrathiane and trithiolane as well as the amino acid, eritadenine.

In a few individuals, consumption of these mushrooms may have unpleasant consequences. Some hours after the meal, they will develop a so-called shiitake or flagellate dermatitis. The medieval penitents castigating themselves, also referred to as flagellants, lent their name to the clinical picture of the disease being characterised by skin lesions which resemble whiplashes on the trunk, the arms and legs and on the neck. In the past, such skin manifestations had been seen mainly after the ingestion of inadequately cooked mushrooms. It was, therefore recommended to eat shiitake mushrooms only if they had been thoroughly cooked or fried. However, recent reports have suggested that the type of preparation was of no influence on the health complaints developed by sensitive individuals.

The suspected cause of the intolerance reaction is the polysaccharide, lentinan, being a natural component of the mushroom. The substance appears to be heat-stable which is why it may cause the dermatitis to develop also after the ingestion of well-cooked and fried mush-

rooms. In spite of the large quantities of shiitake mushrooms cultivated world-wide, cases of shiitake dermatitis have been very rare in Germany. Obviously, a sensitive reaction is developed by a few individuals only while the causes have not yet been elucidated. It has been assumed that responsible factors may also include unknown co-factors in addition to the amount ingested and the type of preparation. Based on the number of cases described, the risk for the consumer seems to be low, according to the present state of knowledge.

Mainly Japanese authors have reported about workers on mushroom farms who had developed an allergic alveolitis after inhalation of shiitake spores. In this context, also cases of allergic contact dermatitis were mentioned that could be diagnostically confirmed by means of the patch test. As a sign of the allergic reaction, the skin rash was found to be associated with eosinophilia. Flagellate dermatitis was described for the first time in 1977 by Nakamura. In 1985, he reported on 30 cases observed in Japan within a period of nine years. They referred to patients presenting with severe erythema and pruritus after ingestion of the mushrooms in traditional Asian dishes. All his patients suffered from intensely pruritic, very small papules appearing closely together in lines. They reported these stripes to have developed within one or two days after the meal containing the mushrooms. The stripes expressing a Koebner phenomenon had obviously resulted from scratching of the skin. The manifestations disappeared after 20–30 days. Until 1991, Nakamura recorded a number of additional cases. Other authors reported on 58 patients presenting with shiitake dermatitis during the 1997–2001 period. In 33 of these cases, the disease had developed after the ingestion of sufficiently cooked/boiled mushrooms. In Germany, only single cases of this disease have occurred after consumption of this mushroom.

Evaluation of the case described:
On the basis of the information given on the temporal relationship between the ingestion and the occurrence of the manifestations observed, and in the absence of other causes, a causal relationship has been considered as probable.

3.3.4 Welding fumes

Moderate health impairment after welding of plastic material
A 39-year-old worker reported to have welded plastic material on two days for a period of altogether 17 hours. At his workplace, the exhaust hood under which the work was performed was defective. In addition, he had worn a defective gas mask for three hours. On the following evening, he experienced health complaints that caused him to seek medical advice in an outpatient department.

Manifestations/course
The patient reported influenza-like symptoms in the form of arthralgia over the last 36 hours. In addition, he suffered from severe cough and fever. Inhalation was associated with marked pain, and he experienced dyspnoea and decreasing vitality. His cigarette consumption was stated to be ten cigarettes per day. The findings of an outpatient examination performed two days later revealed that the patient was in a good general condition. Cardiovascular and pulmonary findings, as well as the status of the other organs examined were normal. No treatment was required, and the patient was recommended to avoid major physical strain and temporarily refrain from smoking.

Notes
The case described above was presumably due to exposure to fumes from plastic materials resulting from non-compliance with occupational safety regulations. The manifestations described were largely compatible with those of polymer

fume fever being similar to those of metal fume fever. During the processing of plastic materials, fluorocarbons in monomer or polymer form are released that may cause polymer fume fever. It is characterised by chest pain, choking fits, dry cough, fever, shivers and arthralgia. In most cases, such manifestations will disappear within one or two days after exposure. However, also protracted pneumonia associated with agonizing cough, retrosternal pain and general health impairment may occur. Chronic health damage has not been recorded. Exposure to fluorine gas and possibly hydrocyanic acid could not be excluded. Due to the short half-life of both substances, a toxicological analysis was no longer possible after two days had passed.

Health impairment after steel welding operations

During the welding of antimagnetic steel, a worker had inhaled chromium and nickel fumes, in spite of wearing a respirator. This resulted in moderate health impairment requiring inpatient treatment.

Fig. 11: Welding

Manifestations/course

Typical signs of inhalational poisoning were described including dyspnoea at rest, vertigo, cough and two episodes of vomiting. A blood gas analysis performed on the day of admission to the hospital revealed a partial insufficiency. An elevated carbon monoxide Hb level (CO-Hb) was found. Pulmonary oedema could be excluded by radiological examination. The patient's condition improved rapidly under oxygen supply and inhalatory administration of corticoids. He could be discharged in a symptom-free state on the following day.

Notes

The above case of moderate health impairment was possibly associated with the formation of chromium and nickel fumes during welding operations. A temporary partial respiratory insufficiency receded rapidly under appropriate treatment. Chromium and nickel fumes may cause irritation of the respiratory tract after inhalational exposure. Single cases of respiratory disease after occupational exposure to chromium dust and chromium compounds have been reported which were associated with functional pulmonary disorders. Inflammatory and asthma-like lung diseases were reported to have occurred after acute inhalational exposure. A sensitising effect on the respiratory tract has to be assumed.

3.3.5 Internal combustion engines

Industrial accident associated with an internal combustion engine

At his workplace, a 33-year-old patient had cut a concrete slab in an insufficiently ventilated room. The disk grinder used was powered by an internal combustion engine. In spite of occasional breaks, the patient had experienced health complaints after two hours of working. He was monitored at an intensive care unit for one day.

Manifestations/course

After having worked for approximately two hours, the patient experienced vertigo and

weakness. He could just leave the room before his legs gave way. There was no loss of consciousness nor breathing difficulty. He was immediately subjected to intensive medical treatment. The carbon monoxide Hb level (CO-Hb) established on the patient's arrival was 29.1 %. Under high-dose oxygen supply (15 L/min), the CO-Hb decreased to 2.1 %. Since it remained unclear whether other toxic gases had also been present in the room, the patient was monitored for another 24 hours and administered dexamethasone. On the following day, the patient could be discharged in a good general condition.

Notes
The circumstances described by the patient raised doubts as to whether the required measures of occupational safety had been complied with. Working in a poorly ventilated room with machinery powered by an internal combustion engine involves a considerable health risk for the operator. Possible organ damage due to oxygen deficiency may result in permanent brain damage or even acute death from suffocation.

Combustion gases from internal combustion engines contain 4–11 % carbon monoxide. Carbon monoxide is haemotoxic. It binds to haemoglobin to form carbon monoxide Hb (CO-Hb) by displacing the oxygen. The affinity of carbon monoxide to haemoglobin is 300 times higher than that of oxygen. This is the reason for the hazard posed by CO. Individuals differ considerably in their sensitivity to carbon monoxide in acute poisoning events. Because of their higher respiration rate and more intense metabolism, adolescents and small and slim persons are more at risk, as a rule, than adult and sturdy persons. Already at CO-Hb levels as low as 4 %, changes can be detected in psychomotor tests. As in the case described above, headache, weakness and vertigo will as a rule occur, if ca. 30 % of the haemoglobin has become bound by carbon monoxide. Levels above 40–50 % will result in collapse and unconsciousness. If the respiration is deprived of 75 % of the haemoglobin, the inevitable result will be death from suffocation. As compared to younger individuals, CO-Hb concentrations that may lead to death become lower with increasing age. Carbon monoxide poisoning is particularly often followed by late damage and secondary diseases that may occur mainly as sequelae of hypoxia experienced over a more or less extended period. Frequent sequelae include brain damage characterized by different manifestations because the central nervous system is highly sensitive in its response to hypoxia. Other sequelae recorded include myocardial necrosis and pneumonia. Also changes in the peripheral nerves or even paralysis have been reported. Similar to the central manifestations, they are in part caused by primary vascular damage.

The German MAK (maximale Arbeitsplatzkonzentration – maximum admissible concentration at the workplace) has been set at 30 mL/m^3 (33 mg/m^3), and the BAT (Biologischer Arbeitsstofftoleranzwert – biological threshold limit value), at 5 % CO-Hb in whole blood at the end of the exposure period.

Evaluation of the case described:
On the basis of the information given on the temporal relationship between carbon monoxide inhalation and occurrence of the manifestations observed, and in the presence of clearly elevated blood levels, a causal relationship has been confirmed.

3.3.6 Sewage collector tank

Serious industrial accidents in an industrial sewage collector tank
The bottom of a sewage collector tank (depth ca. 3 m, capacity 60 m^3, manhole 1.50 m^2) of a plant producing leather fibre was to be cleaned by means of a fire hose. For this pur-

pose, a worker wearing a gas mask entered the tank over a ladder and flushed the tank. The estimated outside air temperature was 28 °C. Another worker stood at the entrance of the tank at a visible distance. Having finished the cleaning work after ca. 30 min, the worker wearing the gas mask climbed up the ladder. When his head was already above the level of the tank manhole, he took off the mask and handed it over to his colleague responsible for supervision. At that moment, he fell backwards into the sump of the tank. The worker standing on ground level immediately sought the help of two colleagues, who unfortunately entered the tank without wearing protective masks and taking any protective precautions. One of them and the first worker affected could only be recovered dead by the fire brigade. The third worker was rescued alive. He suffered a severe brain damage. Obviously, hydrogen sulfide had formed and the safety precautions for working in sewage tanks had probably not been complied with. No measurements were performed on the scene neither before nor after the accident had happened.

Manifestations/course

1. Case No. 3951/04

The deceased had cleaned the sewage tank wearing a filter mask. When he had climbed up the ladder and taken off the mask standing on the last rungs, he fell backwards into the tank for unknown reasons. He could only be recovered in a dead state. Post-mortem findings indicated an acute poisoning by gases from the sewage tank. On post-mortem, the body surface and lung sections exhibited a markedly putrid smell. Lung findings revealed oedema and tissue haemorrhage. Furthermore, clear signs of mucosal irritation were found. Such findings may be explained by an inhalation of hydrogen sulfide. There were no signs of drowning found neither by post-mortem examination nor by toxicological-chemical analysis.

2. Case No. 3805/04

A 51-year-old male who had tried to rescue the first worker affected by the accident without taking protective measures and suffering from respiratory insufficiency and acute pulmonary oedema was transported, by an emergency ambulance, to the intensive care unit of a university hospital. On admission to hospital, the patient was in an analgosedated, intubated and respirated state and his circulation was stable. The peripheral oxygen saturation level was 86 %, with an FiO2 of 1.0. The causative agent could not be identified. The cause assumed was inhalation of hydrogen sulfide having become released in the tank. Also a formation of hydrogen cyanide could not be excluded. Still on the day of admission, the patient was subjected to bronchoscopy that revealed a massive aspiration of gastric contents. The bronchial mucosa was highly sensitive and oedematous. These manifestations disappeared under antibiotic therapy and systemic and inhalatory administration of steroids as well as adrenaline inhalation. Respiration therapy which also required tracheotomy could be discontinued after seven days. However, the patient remained comatose. As a response to pain stimulus, he spontaneously opened his eyes without visual fixation and did not respond when accosted. He temporarily exhibited swallowing and chewing movements and an anisocoria right with persisting reaction to light. He was completely paralysed (tetraplegic) and incontinent. The cranial computer tomography performed did not reveal any pathological findings. In the further course, the patient suffered from convulsive seizures that could be controlled effectively by medication. A severe cerebral psychosyndrome was diagnosed. To optimize nursing care, percutaneous endo-

scopic gastrostomy was performed. For further rehabilitation, the patient was transferred to a neurological rehabilitation centre. The severe cerebral damage will probably result in irreversible sequelae. The subsequent course remains to be seen.

3. Case No. 3950/04
The second worker who came to rescue the first one could only be recovered when already dead.

Post-mortem findings revealed signs of acute oxygen deficiency associated with indications of a possible poisoning by hydrogen sulfide. Findings included a faeces-like smell of lung sections and mucosal haemorrhage probably caused by toxaemia. The toxicological-chemical expert opinion stated that highly volatile organic compounds were detected in the lung tissue by gas chromatography which, judged by experience, suggested a non-massive inhalation of sludge digestion gases. Blood taken from the left ventricle revealed an excess water content of 29 %.

On this basis, it had to be assumed that the deceased had lost consciousness due to the inhalation of sewage gases and died from drowning. Based on toxicological-chemical experience, death from drowning is suggested by water levels above 5 %.

Notes
Hydrogen sulfide is an extremely toxic irritant gas. Due to its higher density as compared to air, it accumulates on the bottom of manure tanks, well shafts and in sewer systems where it is formed in the process of anaerobic digestion of organic material. It is a colourless gas with a putrid smell (resembling that of rotten eggs) that may form explosive mixtures with oxygen. Its smell cannot be perceived at higher concentrations because it paralyses the olfactory nerve. It exerts a direct depressive action on the central nervous system and inhibits cytochrome oxidase to a higher degree than hydrogen cyanide does. Due to its quick absorption after inhalational exposure, poisoning by this gas is characterized by an apoplectiform course associated with a rapid onset of unconsciousness. Being a weak acid, hydrogen sulfide will also act as a local irritant.

In the following, H_2S concentrations are listed together with typical cardinal signs:

H_2S concentration (ppm)	Cardinal signs
0.025-0.13	Olfactory threshold
0.30	Clearly perceptible smell
10-100	Irritation of eyes, throat and nose
100-150	Paralysis of the olfactory nerve
>150	On inhalation for > 30 min: headache, vertigo, diarrhoea
300-500	Pulmonary oedema
500-700	Inhalation for half an hour can be lethal
>1400	Apoplectiform lethal poisoning, death after taking a few breaths

In the cases involved in the severe industrial accident described above, occupational safety rules had obviously not been complied with. Investigations revealed that no hazard analysis had been performed. There had been neither an inspection of the tank where the accident happened nor any internal instructions for entering it.

For the inspection of such tanks, the wearing of personal protective equipment and rescue equipment is required by law. For example, entering such a tank is only permitted for persons roped up with block-and-tackle equipment.

Therefore, rescue of persons is only permitted in cooperation with the fire brigade using appropriate respiratory protection. A simple roping-up with the lifeline of the rescuer is insufficient. There are also rules with regard to the wearing of respirators. Prior to entering such tanks, the ambient atmosphere in the tank has to be measured by means of a measuring instrument developed especially for this purpose. The measuring result will decide on the protective measures to be taken. The use of filter-type respirators will depend on the prevailing ambient atmosphere while self-contained apparatus can be used irrespective of the ambient atmosphere. This implicates that filter respirators must not be used in cases of unknown ambient conditions or of possible detrimental changes in the composition of the ambient conditions. In addition, the multi-gas filter mask used by the first victim of the accident was to be used only until March 2004. It has to be concluded that the severe accident resulting in two deaths among three persons involved could have been prevented if the applicable rules had been complied with.

Evaluation of the cases described:
On the basis of the information given on the temporal relationship between the inhalational exposure to hydrogen sulfide and the occurrence of health impairments in the three tragic cases described, and in the absence of other causes, a causal relationship has been considered as probable.

3.3.7 Battery acid

Severe eye burns after exposure to battery acid
A 34-year-old patient was involved in an industrial accident when splashes of battery acid hit both of his eyes. The scene of the accident was a storage area where probably a battery exploded. The patient suffered a severe eye injury, particularly in his left eye. He required inpatient treatment for two weeks. The possibility of a further development of a lens opacity requiring a cataract operation remains to be seen.

Manifestations/course
On admission to hospital, the patient's visual acuity was severely reduced. Treatment included thorough irrigation with lactated Ringer's solution and BSS (balanced salt solution). X-ray findings of the orbital cavity were normal. Corneal erosions were found in both eyes, and hyphaema in the left eye. The latter was gradually absorbed except for a residual coagulum. However, the patient developed a glaucoma with an intraocular pressure of up to 42 mm Hg (17±3 mm Hg, on average, in healthy persons, this value is exceeded in persons suffering from glaucoma). To relieve the patient's condition, he was treated by administration of acetazolamide. After two weeks, the patient was discharged. Vision of the right eye was completely restored, and the anterior segment found to be normal. The residual visual acuity of the left eye was only 0.25. The conjunctiva was hyperaemic. In addition, a loss of iris pigment and its deposition in the anterior chamber and a sphincter lesion were found. The pupil was misshapen. Findings also included a minor corneal scar. The patient developed a slight lens opacity. Findings regarding the accessible ocular fundus were normal. The pupil response to light was only minimal. The patient was referred to further outpatient treatment. To reduce the intraocular pressure, he was administered brinzolamide and locally, brimonidine and timolol eyedrops. In the event of an increasing lens opacity, the patient may require a cataract operation involving the implantation of a posterior chamber lens.

Notes
Motor vehicle batteries contain sulfuric acid in a 32 % concentration to act as an electrolyte between the positive plate consisting of lead oxide and the negative plate consisting of pure lead. In accidents, above all those involving explosion, the corrosive effect is decisive. Absorption is not to be expected. With the exception of the hydrofluoric and sulfuric ones having an oxidative effect, acids will penetrate tissues less rapidly than bases. The coagulation of proteins caused by the hydrogen ions liberated will result in a relative protection against a deep penetration of acids. Minor eye injuries are associated with hyperaemia or chemosis of the conjunctiva and loss of the epithelium of the cornea, while the underlying corneal stroma remains clear. Such cases will heal within a few days without sequelae. Severe burns are characterized by extended and mainly deeper damage. Damage will include large parts of the conjunctiva and the underlying tissue. Visible blood vessels will be thrombosed and appear in a brownish-black colour. The cornea becomes cloudy, and the iris will exhibit a dirty-grey discoloration. Lens opacity (cataract) as well as protracted inflammation and glaucoma may occur. Eye burns are always to be considered as emergencies. As a first aid measure, decisive importance is attributed to immediate ocular irrigation with at least 1.5 L water that should be administered by a helper because in severe cases, the person affected by the accident will be unable to perform an effective irrigation, if any. Afterwards, the patient should see a specialist. Water as an irrigation fluid will mostly be available in sufficient quantities. Intensive irrigation will result in the dilution effect intended. However, water will also increase the oedema and permeability of the cornea. Therefore, saline isotonic with tears or hypertonic saline should be preferably used. Lactated Ringer's solution – as was used in the above case – is buffered and thus more effective than physiological saline. BSS (balanced salt solution) having the same osmolarity as the aqueous humour and a neutral pH is even more suitable. It was developed especially for ophthalmologic operations. It can prevent the development of corneal oedema and protect the endothelium. The subsequent procedure will depend on the degree of severity of the damage suffered.

Evaluation of the case described:
On the basis of the information given on the temporal relationship between the exposure of the eyes and the occurrence of the manifestations observed, and in the absence of other causes, a causal relationship has been confirmed.

Fig. 12: Motor vehicle battery

Health impairments due to starter batteries or automobile accumulators/storage batteries have accounted for a major part of reports submitted to the BfR (n=597), particularly of those submitted by the professional insurance bodies (Berufsgenossenschaften: 590). Fortunately, the number of such cases has been decreasing since 2001 (2001: 176 cases, 2002: 161 cases, 2003: 129 cases, 2004: 96 cases). Most often, the eyes were affected (n=452), but there were also reports referring to skin exposure (n=129), inhalational exposure (n=53) and ingestion (n=4). The majority of cases involved only minor health

impairment (n=533); in 35 reports, the health impairment suffered was evaluated as moderate. 21 cases reported could not be evaluated with regard to the degree of severity, and in seven cases, no manifestations had been recorded. The only case where a patient was affected by a severe health impairment was the one described above. The majority of incidents involved unexpected gas deflagration or explosion of accumulators resulting in acid splashing up from accumulators causing burns, mostly in the eyes.

With regard to the mechanism of accidents, three major types can be distinguished.

1. During installation and removal of batteries, short circuits between the accumulator battery posts may be caused by conductive tools such as spanners. This may result in explosion.
2. Accidents may occur when batteries are recharged.
3. During transport, for example when carrying a battery, splashes may be released due to stumbling or if the battery is put down roughly.

Although most accidents of this type happened at the workplace, the private consumer may be at risk as well. Particularly in the autumn and winter months, many starter batteries are exchanged in a DIY procedure. Often, people doing so are not aware of the risk involved. Utmost care should be exercised when exchanging or recharging batteries. It is recommended to follow all instructions given e.g. on new batteries in the form of stickers or pictograms. It is recommended to always wear safety goggles and protective clothing when performing such operations. Regular maintenance is important. Batteries should be recharged only by means of appropriate loading devices and in well-ventilated rooms. Sparking (e.g. from cigarettes) and open fire must be avoided at any rate. After the recharging process, the battery should be allowed to outgas for eight hours prior to being installed (risk of formation of oxyhydrogen gas).

When connecting the battery, care must be taken that all current consumers in the vehicle such as light, radio etc. are switched off.

Already in its 2001 Annual Report, the former Federal Institute for Health Protection of Consumers and Veterinary Medicine (BgVV) has drawn attention to the problem of health impairment due to starter batteries and accumulators.

3.3.8 Glow sticks

Eye injury caused by glow stick
At a company event, glow sticks were handed out to the participants. An 18-year old male manipulated one of these sticks so that it broke apart and splashes of the liquid contained hit his face and left eye. According to the respective safety data sheet, the product contained 8–12 % tert-butyl alcohol and 4–5

Fig. 13: Glow stick

% hydrogen peroxide (70 %). Since ocular irrigation could be performed already three minutes later at the company's medical service rooms, permanent damage to the patient's health was not to be expected.

Manifestations/course
The patient complained of extremely painful smarting in his eye and face. His left eye and facial area were intensely reddened, and the green fluorescent colorant was well visible. A thorough irrigation of the eye with Ringer's solution was initiated immediately. In addition, an attempt was made to remove the liquid from the patient's face and hair. The ophthalmologist consulted diagnosed a chemical burn of the conjunctiva. Permanent damage was not to be expected since eye irrigation had been performed early enough.

Notes
Based on the report submitted by the company doctor, attention is drawn to a number of facts in this case.

- The liquid was very difficult to remove. It could not be removed at all from the patient's hair. The process of removal from the face and eye, although performed by means of thorough irrigation, took a very long time, and a quantity of 1 L of Ringer's solution had to be used, with pain always flaring up when the irrigation was interrupted.
- No warning whatsoever was found on the product indicating that the substance contained was harmful to the eyes. The safety data sheet stated merely, "moderate eye irritation". Given the experience made, the attending physician considered such information as a kind of "understatement".

Glow sticks consist of two liquids contained in a plastic tube. By bending the sticks, the two liquids become mixed, thus producing a glow. The safety data sheet states the following information with regard to health risks: "Direct contact with this material may cause moderate eye irritation". Enquiries made with the distributor of the product revealed that no similar case had become known so far. The distributor, who has been given a detailed description of the case, will consider to provide additional warnings on the product packaging. The result remains to be seen.

Evaluation of the case described:
On the basis of the information given on the temporal relationship between the exposure of the skin and eye and the occurrence of the manifestations observed, and in the absence of other causes, a causal relationship has been confirmed.

3.3.9 Multiple chemicals

Multiple chemical sensitivity
A 36-year-old female biological laboratory assistant presented with multiple health complaints at an environmental health clinic. She had been occupationally exposed to a variety of chemicals, particularly to solvents. After a change of her workplace, she developed a hypersensitivity to chemicals, mainly to solvents. At her former workplace, she had worked mainly with acetonitrile, methanol and toluene. The occupational safety conditions were described as other than optimal. According to information given by the patient, there had not been enough safety cabinets, and the rooms had been very small. Regularly, she had to work overtime. Since late 2002, she began to suffer from health problems that improved during her annual leave. Since she quitted her job in early 2004, she has found her health to improve slowly but continuously.

Manifestations/course
The patient complained of night sweat and sleeplessness, nausea and diarrhoea. In addition, she stated to suffer from dizziness, ver-

tigo, poor concentration and bad memory. She complained of panic attacks, anxiety states, tachycardia, cardiac arrhythmia, circulatory problems, speech disorders and headache. She reported to have frequently developed migraine after contact with chemicals. In indoor situations, she suffered from respiratory problems. In addition, she suffered from tinnitus and skin rash. Altogether, she reported her state of health to vary considerably.

Below, a report by the patient herself is cited: "Finally, I had no longer the mental capacity to operate a technical device. My forgetfulness caused loss of time and an additional workload. Another reason for quitting my job was that due to my dizziness, I made mistakes when driving. I did not want to end up sticking to a tree with my car. In the end, there was simply nothing working normally with me. When I thought that all that was only due to stress, I took a time-out for myself. I started going to work by bicycle as often as possible (ca. 18 km through the countryside). This resulted in a temporary subsiding of my symptomatology." Concerning her medical history, the patient reported to have undergone subtotal thyroidectomy due to adenoma of the thyroid gland in 2002.

Findings of physical examinations were normal as were the clinical-chemical parameters of routine laboratory analysis. A psychiatric examination indicated the presence of an unspecific somatoform disorder and additionally, of dysthymia and panic disorder. Gratifyingly, it was found that the patient obviously had managed to considerably improve her state of health by means of a number of health-promoting measures taken on her own initiative. However, the examiners considered an extended regeneration period of several months as necessary for her to completely regain her health and stress tolerance. They stated that after that period, there was a realistic chance for her to return to work as a trained laboratory assistant. However, optimal working conditions should be ensured if possible.

Notes

The clinical picture seen is that of a so-called multiple chemical sensitivity (MCS). The aetiology and pathogenesis of her complaints have not yet been conclusively elucidated. MCS can be described in a most appropriate way as a process with multifactorial causes. It is a sensitivity that is associated by the patients with exposure to chemicals and characterized by recurrent manifestations in several organ systems. The symptomatology is mostly unspecific and includes, for example, headache, vertigo, tiredness, weakness of concentration, cardiac and circulatory complaints, gastrointestinal complaints, dermal and mucosal symptoms, myalgia and arthralgia. The symptoms are attributed to exposure to a great number of chemically unrelated substances which likewise cannot be assumed to have any specific effect, e.g. on the receptor level. There is no dose-effect relationship. The concentrations of the substances incriminated have been far below those leading to health problems in the general population. Neither clinical nor laboratory tests have shown any correlation with the complaints reported by the patients, which are often experienced as very serious and as a considerable impairment of their quality of life. In addition to toxicological triggering factors, a variety of other factors such as stress, electromagnetic fields and microorganisms may play a role in the development of MCS. Substances stated most often by patients affected include solvents, dust, smoke, pesticides, foods and medicinal products. Threshold values at which symptoms are triggered are extremely low. A variety of possible causes of MCS can be imagined: Factors that have been

discussed include an overreaction of the immune system, disorders of the olfactory system or of the olfactory-limbic system. Mental mechanisms based on anxiety disorders play a role. On account of insufficient data available on the genetic predisposition to develop MCS, genetic testing is not recommended.

Evaluation of the case described:
On the basis of the information given on the temporal relationship between chronic exposure to solvents and the occurrence of manifestations associated with a minor health impairment, and in the absence of other causes, a causal relationship has to be rated as possible in the case described. In addition to a possible triggering of sensitization to solvents due to long-term occupational exposure, the development of symptoms had been most probably also caused by psychosomatic factors. Other possible co-factors in the development of the symptomatology described are the inappropriate industrial safety conditions and the non-optimal organization of the work resulting in regular overtime hours. In all probability, according to the assessment by the environmental health clinic, a combination of influencing factors had caused the hypersensitivity and persistent complaints.

3.3.10 Henna tattoos

Allergic local reaction associated with henna tattoo
An 18-year-old female sought medical advice from a general practitioner after having a tattoo made ten days earlier in Malta. No data could be obtained on the product name or the manufacturer. The patient was subjected to an extended topical treatment resulting in a complete regression of her health complaints.

Manifestations/course
The patient presented with local erythema and swelling of the skin in the area of the tattoo. A beginning keloid formation receded completely on administration of a cortisone ointment.

Notes
More and more cases of contact dermatitis associated with henna tattoos have been described in literature. Henna, an extract of the plant, Lawsonia, has been known for centuries in many cultures as a means to dye hair and nails and for decorative body painting. Also in Germany, wearing tattoos is very popular, particularly among adolescents. Henna tattoos (also referred to as temporary tattoos) are not tattoos in the proper sense because the colorant is applied **onto the surface** of the skin. Such techniques are subject to the legal provisions on cosmetics under the European Cosmetics Directive and the German Cosmetics Regulations.

The most frequently observed undesirable consequences of such tattooing include severe allergic reactions and inflammations. In most cases, the active substance, paraphenylene diamine (PPD) is the cause of the allergic reaction. It is used in henna to darken its colour shade, and when making black henna tattoos, it is applied onto the skin and may penetrate into it. It is also known as a hair dye. Persons who have experienced sensitisation to PPD may exhibit allergic reactions to this substance for their entire lifetime. Other sources of risk include contaminants in the colour mixtures as well as certain azo dyes that may split and form carcinogenic aromatic amines.

While cosmetics are subject to legal regulations stipulated by the German Foods and Other Commodities Act, the German Cosmetics Regulations and the European Cosmetics Directive, tattoo dyes are still not subject to any comparable legal regulation. Up to the present, there have been no legal provisions on tattoo dyes referring to the degree of purity, quality and testing for safety in terms of health. A national regu-

lation is being prepared at present. Tattoos and permanent make-up should only be performed using colorants that comply with the requirements of the European Cosmetics Directive and the German Cosmetics Regulations, i.e. that have been tested and approved for the use in cosmetics. Problematic colorants containing substances that are hazardous due to their carcinogenic, mutagenic or sensitising properties or reproductive toxicity or may form aromatic amines by splitting should be banned for such uses. Efforts should be made to ensure an appropriate training and health control of persons who carry out tattooing and apply permanent make-up. The BfR has already commented on the health risks involved in tattoos and permanent make-up.

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

3.3.11 Plants – Colchicum autumnale

Colchicum poisoning in a married couple
A 83-year-old woman and her 90-year-old husband were found dead in their flat. In the couple's refrigerator, leaves of bear's garlic (*Allium ursinum*) and colchicum (120 and 170 g, respectively) were found. When collecting them in the vicinity of their home, the couple had obviously accidentally mistaken the green leaves of colchicum for those of bear's garlic and had eaten both. Chemical-toxicological examinations revealed blood levels of colchicine in the lethal range.

Manifestations/course
From the report by the public prosecution office, it was concluded that massive diarrhoea had set in after the meal. No information was available on other manifestations since deaths had probably occurred several days ago. Possibly, both partners died almost at the same time. Inspection of the sites where their bodies were found and external findings did not permit any conclusions as to the cause of death. From an objective point of view, there were neither indications of violence or trauma of any kind nor of a suicidal intent. Post-mortem findings included signs of advanced putrefaction of the bodies. Initially, the cause of death could not be clarified unequivocally. Blood and urine as well as gastric contents and parts of inner organs were stored and kept for further investigation.

Findings resulting from chemical-toxicological analyses included: In the female corpse, the colchicine levels detected in urine, in heart blood and in blood from the femoral vein were 783, 98.3 and 78.4 ng/mL, respectively. In the male corpse, the colchicine levels detected in heart blood and blood from the femoral vein were somewhat lower (36.6 and 22.7 ng/mL, respectively). This confirmed lethal poisoning by colchicine in both cases.

Notes
The popularity of bear's garlic tempts many people to pick the plant in the forest nearby. Again and again, collecting of the plant in the spring season, particularly in the month of May, has led to colchicum being mistaken for bear's garlic, resulting in tragic consequences. The leaves of bear's garlic and colchicum sprout at the same time of the year. Mistakes involving the lily of the valley (*Convallaria majalis*) are less dangerous. The leaves of the three plants are quite similar in appearance. However, there are distinguishing features that should be given attention. The relatively slim leaves of bear's garlic have stalks, being similar to the long and slim leaves of the lily of the valley. In contrast, the leaves of colchicum lack stalks. The smell of

bear's garlic is similar to that of garlic, but weaker, while the two other plants do not smell of garlic. But again, caution should be exercised when testing the smell: If bear's garlic has already been collected before, the smell of its juice adhering to the fingers could suggest a garlic smell emanating from what is actually colchicum or lily of the valley.

All parts of the colchicum plant contain the cytotoxic substance, colchicine, which is a mitotic poison blocking cell division (capsule: 0.4–1.4 %, flower: 0.8–1.8 %, leaves: < 0.2 %, bulb: 0.08-0.2 %). The doses considered as potentially lethal are 1–1.5 g seeds for children and 5 g seeds (1 g corresponds to ca. 200 seeds) or 50–60 g leaves for adults. Administration of colchicine for medical purposes is indicated e.g. for treatment of acute attacks of gout. Accumulation in the leukocytes inhibits leukocyte migration and thus, phagocytosis. This prevents the crystallization of uric acid. Therapeutic doses do not result in an inhibition of mitosis. At toxic doses, mitosis inhibition will result in cell death and thus, multiple organ damage. Among the most sensitive tissues are those with the highest cell division rate such as intestinal epithelium, bone marrow and hair follicle. Other effects include disturbances of intracellular transport and membrane function resulting in an inhibition of the secretion of neurotransmitters, hormones, immunoglobulins and collagen synthesis.

Toxicity is very high, with a potentially lethal dose in adults of ca. 7–8 mg (in individuals with renal insufficiency, 3 mg only). However, also cases of survival at higher doses have been described. In general, colchicine levels in the plasma of > 35 ng/mL and in urine of > 1,5 µg/mL are considered as lethal. As demonstrated by the two cases of poisoning described above, also lower doses may obviously result in death.

Colchicine is readily absorbed. It is characterized by a pronounced enterohepatic circulation and a high volume of distribution with accumu-

Fig. 14: Bear's garlic

Fig. 15: Lily of the valley

Fig. 16: Colchicum autumnale

lation on repeated intake. The typical clinical picture of poisoning is characterized by three stages:

- After an initial symptom-free interval of 2-6-14 hours, the gastrointestinal stage will be most prominent with a sore and burning sensation in mouth and throat, vomiting, tenesmus, watery and bloody diarrhoea, exsiccosis and leukocytosis.
- Multiple organ damage will follow after 24–72 hours. Manifestations will involve the nervous system resulting in disorientation, convulsions, weakness of muscles, somnolence, sopor and coma. The cardiovascular system will develop hypotension, shock and arrhythmia. The respiratory tract will be affected, with tachypnoea, central respiratory depression, respiratory arrest, pulmonary infiltration and lung oedema. The gastrointestinal tract will be involved with melanorrhoea and liver dysfunction. Acute renal failure may occur. The haematopoietic system will react with granulocytopenia, thrombocytopenia and pancytopenia. The clinical picture may become even more serious by metabolic disorders and changes of laboratory parameters associated with metabolic acidosis, electrolyte disturbance and consumptive coagulopathy. This stage will persist for ca. one week. In the majority of cases, death occurs within 1–3 days due to toxic cardiovascular failure, acute pulmonary oedema, septicaemia or cerebral oedema.
- Patients who survive this stage will recover from the seventh to tenths day onwards. The convalescent stage will be associated with loss of hair, mostly presenting as a complete alopecia. In the course of illness, the patient's condition may become affected by numerous other complications.

For treatment, decisive importance is attributed to primary detoxification, i.e. removal of the poison because there are almost no effective means of secondary detoxification. So far, no colchicine-specific Fab fragments are commercially available. There have been no suggestions of effective measures for secondary detoxification so far. This means that only symptomatic treatment can be performed.

Evaluation of the case described:
In the two above cases with a tragic outcome, the relationship between ingestion of colchicum leaves and lethal outcome was confirmed by chemical-toxicological analysis.

3.3.12 Animals – Vipera berus

Poisonous snake bite
During a holiday spent in Poland, an 8-year-old girl was bitten by a snake. When playing in the grass, the girl felt a brief and strong pain on her right hand and saw a brown-grey snake gliding away. The patient developed a life-threatening condition. She was admitted to the nearest hospital where she was administered an antiserum. From there, she was transferred to a major paediatric hospital in Poland and later, to a specialized hospital in Germany. It took one week for the child to recover.

Manifestations/course
When the mother and father had a close look at their daughter's hand, they noticed not only the two punctures but also a ring forming around the injury. They immediately went off to the hospital in the nearby town. Soon, the girl began to suffer from strong pain, progressive swelling, nausea and headache. "The swelling on her arm increased from minute to minute", reported her father. In spite of administration of an antiserum (unspecified anti-snake-bite serum), immobilization and cooling of the extremities, antibiotic shielding by means of amoxicillin, clavulanic acid and metronidazole combined with antihistamines and glucocorticoids as well as administration of anti-tetanus prophylaxis, the patient's condition deteriorated. In the course of the day,

she developed persisting nausea and experienced repeated vomiting. The livid discoloration and increasing swelling of her right arm extended up to her shoulder. Findings included a slight arterial hypotension with a systolic blood pressure of 90 mmHg. During the night, the patient was very restless and suffered from states of panic. On the next morning, the local findings had deteriorated with a blue-black discoloration of the patient's hand. The patient's general condition had deteriorated to such a degree that she was almost no longer able to sit up without support. As a consequence, she was transferred to a major paediatric hospital in Poland. There, a central venous catheter was attached to the left femoral vein and the initial therapy continued. On the following day, her general condition stabilized and the swelling decreased slightly. In the evening of that day, the girl was transferred to the intensive care unit of a specialized hospital in Germany by emergency flight. There, clinical findings described the child as being in a proper general condition, awake, responsive and cooperative. Findings included a massive painful swelling and a marbled-livid discoloration of the entire right arm and the right shoulder which had partly extended to the right thoracic wall. The radial pulse was vigorously palpable. The status of her other organs was also found to be normal.

Laboratory examinations performed after two days in the period of increasing swelling revealed thrombocytopenia of 33 000/nL (reference ranges 150–350 (x103/µL), an Hb decrease to 7.4 g/dL (reference range 12–16 g/dL) without clear signs of haemolysis. In addition, findings included a CK increase to 3 231 U/L (reference range for creatine kinase < 70 U/L) on the third day and an increase of GPT to 162 U/L (reference range < 17 U/L). Resting electrocardiography revealed a borderline PQ interval (0.17) and a QT interval near the normal upper limit (0.36).

The therapy which consisted of immobilization and cooling of the arm, administration of antibiotics (for seven days) and of glucocorticoids, as well as anaesthetic treatment by administration of metamizole and piritramide were continued. Because of increasing swelling and extension into the shoulder and thorax regions and due to thrombocytopenia and Hb decrease one day after admission of the patient to hospital, it was decided to administer another dose of antiserum against adder's poison which was well tolerated. Subsequently, the swelling subsided slowly, and the livid discoloration faded. Also the laboratory parameters returned to normal levels. After four days, the little patient was in a stable condition and could be transferred to a paediatric hospital situated not far from her parent's place of residence. After physiotherapeutic treatment, the mobility of the little patient's arm and her health were completely restored.

Notes

The only wildlife snakes living in Europe are those of the family Viperidae. The respective species are:

Vipera ammodytes (nosehorn viper, Western sand viper)
Vipera aspis (European asp, asp viper)
Vipera berus (adder, common viper, common adder, cross adder)
Vipera lebetina (blunt-nosed viper, Levantine viper, Levant viper)
Vipera latasti (Lataste's viper)
Vipera ursinii (Orsini's viper, meadow viper)
Vipera xanthina (Ottoman viper, coastal viper)

Based on the geographical assignment and the assignment with the help of pictures, the

species that had most probably been involved in this case was the adder (Vipera berus). Accidents involving snake bites occur particularly often between April and October. With regard to the course of disease after snake bites, it is difficult to make reliable statements because manifestations will essentially depend on the quantity of snake poison entering the body. Since the case described above occurred in May, the snake had possibly accumulated a major quantity of poison after the hibernation period. A poi-

Fig. 17: Vipera berus

soning due to snake bite has to be considered as a complex poisoning by neurotoxins and haemotoxins, among others. In the majority of cases, only local effects will be most prominent. Dangerous or lethal cases of poisoning have been observed rarely. In addition to local reactions such as bite marks associated with erythema, oedema, pain, blue-red discoloration of the skin, haematoma, blistering, necrosis and swelling of lymph nodes, systemic reactions may occur. These include anxiety, dizziness, vertigo, headache, tachycardia, weakness, sweating, vomiting and diarrhoea. Haemorrhages and coagulopathy associated with bleeding and thrombosis will be the most prominent manifestations if vipers are involved; in the context of a consumptive coagulopathy, the parameters of bleeding and coagulation will exhibit pathological changes. Primarily, hypotension and shock will result from increased capillary permeability, however, they may also result from blood loss associated with consumptive coagulopathy. These conditions may, in turn, result in acute renal failure. Also damage to the heart and respiratory disturbances have been reported. As a therapy, the limb affected should be immobilized. Application of any kind of tourniquet may result in severe subsequent damage (necrosis) and therefore must not be performed. All other measures will be symptomatic. Antisera should be administered in the event of a massive local reaction associated with considerable systemic effects. The administration of antiserum in cases of adder bites has been questioned on the basis of experience made in Sweden and Switzerland. Physicians working in hospitals consider pre-testing to be unnecessary if the action of the snake poison is rated as more dangerous than the risk of a possible anaphylactic adverse effect. Depending on the geographic distribution of poisonous snakes, different types of antiserum are administered. The information required has to be obtained from the responsible regional poison control centres.

Evaluation of the case described:
On the basis of the information given on the temporal relationship between the exposure of the skin by bite and the occurrence of the manifestations observed, and in the absence of other causes, a causal relationship has been confirmed. The degree of severity of the health impairment has been classified as moderate.

4 Annex

4.1 Overview of reported cases of poisoning in the period of 1 January–31 December 2004

Table 11: 5 530 reports vs. degree of severity of health disturbances, classified by children and adults, with the adult cases differentiated by exposures in the private sphere and in working environments (except for those with a degree of probability of "no relationship").

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	129	33	96	10	85	2		2	1	1
II. Veterinary medicinal products	9		7		7					
III. Chemical products	3022	100	2922	17	2904	214	34	180	2	178
Wastes, solid	36		36		36	2		2		2
Waste gases	224	1	223	1	222	8		8		8
Sewage	18		18		18	5		5		5
Paints and related materials	255	1	254	1	253	14		14		14
Paint removers/strippers	9		9	1	8					
Alkyd resin paints										
Emulsion paints	2		2		2	1		1		1
Artists pai nting materials	1		1		1					
Lacquers/varnishes	53		53		53	1		1		1
Parquetry sealers	1		1		1					
Pigments	1		1		1					
Primers	10		10		10	5				
Paint thinners	114	1	113		113	5		5		5
Fire lighting products	9	9				7				
Building materials, auxiliary products	26		26		26	2		2		2
Building materials	160		160		160	25		25		25
Fuels, liquid	96	56	40		40	30	26	4		4
Petrol	26		26		26	3		3		3
Ethanol for technical use	6		6		6					
Lamp oil	56	56				26	26			
Fuels, gaseous	2		2		2					
Office materials, chemical	32		32		32	8		8		8
Decoration materials										
Dental materials	37		37	1	36	1		1		1
Disinfectants/sterilizers	393		393		393	8		8		8
Deodorants for technical use	5	2	3		3					
Diagnostics/reagents	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
Printing, auxiliary products	4		4		4					
Insulating materials for electric equipment										
De-icing products										
Fire extinguishing media	21		21		21					
Fire retardants										
Galvanic cells	116	4	112		112	6		6		6
Dry cells	15	2	13		13	1		1		1
Button batteries	2	2								
Accumulators	100		100		100			6		6
Galvanizing agents	3		3		3					
Galvanizing agents, auxiliary products	3		3		3	2		2		2
Gases for technical use	2		2		2					
Antifreezes	1		1		1					
Glass-working, auxiliary products	3		3		3	1		1		1
Rubber, production materials	2		2		2					
Semiconductors, production materials										
Household auxiliary products, chemical-technical										
Hydraulic fluids	37		37		37					
Refrigerants	12		12		12	1		1		1
Ceramics, auxiliary products	2		2		2					
Ceramic materials	1		1		1					
Glues	121	1	120	5	115	3		3		3
Coolants	23		23		23	1		1		1
Plastics, starting materials	24		24		24	4		4		4
Plastics, formulating materials	4		4		4	2		2		2
Leather processing products	2		2		2					
Luminophors	3		3		3					
Solvents for technical use	65		65	1	63	2		2		2
Soldering and welding products (except welding fumes)	6		6		6					
Measuring equipment, chemical-technical	8	1	7		7					
Heating meters	1	1								

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
Mercury thermometers	1		1		1					
Thermometer fluids	4		4		4					
Metallurgy, auxiliary products	30		30	1	29	4		4	1	3
Dairy, auxiliary products										
Papermaking, auxiliary products										
Photography, auxiliary products	5		5		5					
Cleaning products	920	22	898	7	891	60	1	59	1	58
Drain cleanser	18	1	17	1	16	3		3		3
All-purpose cleaners	55		55		55					
Oven and grill cleaners	36		36		36	2		2		2
Electronics cleaners										
Descaling products	35	4	31	1	30					
Front wall and stone cleaners	4		4		4			1		1
Stain removers	4	1	3		3	1				
Floor polishes	4	1	3		3	1		1		1
Dishwashing products, manual	8	1	7		7					
Dishwashing products, machine	20	3	17		17					
Dishwasher cleaners	12		12		12	1		1		1
Glass cleaners	2		2		2					
Industrial cleaners	65		65		65	6		6		6
Rinsing additives for dishwashers	6		6		6					
Plastic cleaners	4		4		4					
Lacquer cleaners										
Milking machine cleaners	29		29		29	5		5		5
Metal cleaners	22				22	5		5		5
Furniture polishers	2	2				1	1			
Soot removers										
Lavatory cleaners	30	2	28		28					
Shoe and leather cleaners	1		1	1						
Carpet/upholstery cleaners										
Detergents	17	2	15		15	1		1		1

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
Detergents, auxiliary products	6	1	5	2	3	1		1		1
Joke articles	1	1								
Lubricants	27		27		27	2		2		2
Welding fumes	57		57		57	2		2		2
Dust-laying oils	1		1		1					
Toys										
Textile, auxiliary products	2		2		2					
Propellants/sprays	3		3		3					
Water treatment products	5		5		5					
Pet shop products	1		1		1					
IV. Cosmetics/personal hygiene products	75	7	68	15	52	4		4	3	1
Hair care products	21	1	20	2	18	1		1	1	
Permanent wave products	7		7		7					
Depilatory agents	1		1	1						
Dyes/colorants	8		8	1	7	1		1	1	
Conditioners	3		3		3					
Hair tonics										
Shampoos	1	1								
Skin care products	44	4	40	10	29	2		2	1	1
Bath oils/ salts	5	1	4		4					
Tanning products										
Creams/ointments	14	2	12	9	3	1		1	1	
Deodorants	4		4		4					
Cleansers	1	1								
Make-up	1		1		1					
Oils										
Perfumes/after shaves	2		2		2					
Powders										
Soaps	15		15	1	14	1		1		1
Sun blockers										
Dental products	4		4	1	3					
Nail care products	4	1	3	1	2	1		1	1	
V. Pesticides	97	2	95	5	90	5		5	2	3
Acaricides										
Fungicides	11		11	1	10	1		1		1
Herbicides	20		20		20	1		1		1
Wood preservatives;	4		4	1	3				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
Insecticides	28	1	27	3	24	4		4		2
Carbamates	1		1		1					
Chlorinated hydrocarbons	1		1	1						
Phosphoric esters	6		6	2	4	3		3	2	1
Pyrethroids	2	1	1		1					
Molluscicides										
Repellents	1		1		1					
Rodenticides	3	1	2		2					
Anti-coagulants										
Phosphates										
Seed dressings										
VI. Agrochemicals (other than pesticides)	10		22		22	2		2		
Fertilizers			10		10	1		1		1
Growth regulators										
VII. Substances of abuse										
VIII. Plants	19	11	8	3	5	2		2	2	
IX. Fungi	3		3	1	2					
X. Animals	4	1	3		3	2	1	1		1
XI. Foods and beverages	86	5	78	41	36	15	1	11	8	3
Alcoholic beverages	16		16	1	15	2		2	1	1
Food additives	2		2		2					
Tobacco and tobacco products	3	1	2	1						
Food supplements	33	2	29	29		7	1	4	4	
XII. Warfare/anti-riot agents	4		4		4					
Pyrotechnic products										
Tear gas	1		1		1					
XIII. Miscellaneous	106	1	104	1	103	4	1	3		3
Textiles	38		38		38					
Clothing	36		36		36					
Furnishing fabrics	60									
XIV. Basic elements	1981	3	1977	19	1955	177	2		10	164
XV. Industrial accidents	60		60		60					

4.2 Notification form

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 List of Poison Control Centres

Berlin	BBGes – Giftnotruf Berlin Institut für Toxikologie Klinische Toxikologie und Giftnotruf Berlin	Oranienburger Str. 285	D-13437 Berlin	Phone: +49-30-19240 Fax: +49-0-30 68 67 21 E-Mail@giftnotruf.de www.giftnotruf.de
Berlin	Charité – Universitätsmedizin Berlin Campus Virchow Klinikum Klinik für Nephrologie und internistische Intensivmedizin, Giftinformation	Augustenburger Platz 1	D-13353 Berlin	Phone: +49-30-4 50 65 35 55 Fax: +49-30-4 50 55 39 15 giftinfo@charite.de www.charite.de/rv/nephro
Bonn	Informationszentrale gegen Vergiftungen Zentrum für Kinderheilkunde Universitätsklinikum Bonn	Adenauerallee 119	D-53113 Bonn	Phone: +49-2 28-19240 Fax: +49-2 28-2 87 33 14 GIZBN@ukb.uni-bonn.de www.meb.uni-bonn.de/ giftzentrale
Erfurt	Gemeinsames Giftinformationszentrum der Länder Mecklenburg-Vorpommern, Sachsen, Sachsen-Anhalt und Thüringen	Nordhäuser Str. 74	D-99089 Erfurt	Phone: +49-3 61-73 07 30 Fax: +49-3 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: +49-7 61-19240 Fax: +49-7 61-2 70 44 57 giftinfo@kikli.ukl.uni-freiburg.de www.giftberatung.de
Göttingen	Giftinformationszentrum-Nord der Länder Bremen, Hamburg, Niedersachsen und Schleswig-Holstein (GIZ-Nord) Universität Göttingen – Bereich Humanmedizin	Robert Koch-Str. 40	D-37075 Göttingen	Phone: +49-5 51-19240 Fax: +49-5 51-3 83 18 81 giznord@giz-nord.de www.Giz-Nord.de
Homburg	Informations- und Beratungszentrum für Vergiftungsfälle Klinik für Kinder- und Jugendmedizin		D-66421 Homburg/ Saar	Phone: +49-68 41-1 92 40 +49-6841-1628314 Fax: +49-6841-1628438 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: +49-6131-19240 +49-6131-232466 Fax: +49-6131-232469 +49-6131-176605 giftinfo@giftinfo.uni-mainz.de www.giftinfo.uni-mainz.de
München	Giftnotruf München Toxikologische Abteilung der II. Medizinischen Klinik und Poliklinik, rechts der Isar der Technischen Universität München	Ismaninger Str. 22	D-81675 München	Phone: +49-89-19240 tox@lrz.tu-muenchen.de www.toxinfo.org
Nürnberg	Giftnotrufzentrale Nürnberg Medizinische Klinik 2, Klinikum Nürnberg Lehrstuhl Innere Medizin-Gerontologie, Universität Erlangen-Nürnberg	Prof.-Ernst-Nathan-Str. 1	D-90419 Nürnberg	Phone: +49-911-398 2665 Phone: +49-911-398 2192 muehlberg@klinikum-nuernberg.de www.giftinformation.de Giftnotruf: +49-911-3982451 oder +49-911-3982665

4.4 Press releases on toxicological problems issued by the BfR in 2004

Tattoos and permanent make-up are not without risk
The colours used for this purpose have not been tested
03/2004, 10 April 2004

Two new child fatalities caused by lamp oils! BfR in favour of extending its ban on sale to clear and non-perfumed products
07/2004, 14 July 2004

Enjoyment with unpleasant consequences
Skin reactions may occur after eating shiitake mushrooms
10/2004, 19 August 2004

Exercise caution when handling Scoubidou bands
Volatile organic solvents, critical plasticisers and other problematic substances detected
12/2004, 28 September 2004

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