INFORMATION

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Cases of Poisoning Reported by Physicians in 2010

Poison and Product Documentation Centre at the Federal Institute for Risk Assessment – 17th Report (2010)

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Preface

Professor Dr. Dr. Andreas Hensel

Dr. Axel Hahn

Dear Reader,

On 1 August 1990, the requirement of compulsory reporting of cases of poisoning by attending physicians within the framework of the Chemicals Act came into force. This was to complete, in a meaningful way, the reporting system for adverse effects of medicinal products. The documentation of accidents involving chemical products will enable attending physicians to obtain valuable data for their on-site activities and thus, to develop effective measures of prevention and therapy at a very early date. It has been the purpose of this Act to ensure that the assessment of chemical substances was not to rely on toxicological data from animal studies alone. Rather, the specific health assessment required should be based on data from poisoning accidents in humans that unfortunately continue to occur.

The authors take great pleasure to publish and offer to you the latest, i.e. 17th Report by the Poison and Product Documentation Centre. To illustrate a specific risk, the principle of and the chances for protecting the population that are based on the reports by physicians in cases of poisoning as required under § 16 e of the Chemicals Act, a recent case that has been well examined and documented shall serve as an example:

A girl aged two years and eleven months had ingested a rust-removing and descaling agent containing nitric acid which had been sold mainly in Turkish retail shops all over Germany. She suffered most severe chemical burns and had to be admitted to the intensive care unit of a hospital.

It took 12 days of intensive medical and surgical treatment until the little patient's condition could be stabilized to a degree permitting a careful reintroduction of food intake a few days later. After six weeks of inpatient treatment the child could be discharged under conditions of a gastrostoma and referred to outpatient paediatric care for three more months. Fortunately, follow-up examinations

performed about ten months after the incident showed a favourable course of the healing process. It is expected that the paediatric surgery procedures required will not result in any permanent impairment of the gastrointestinal tract and the functioning of digestion.

In cooperation with the German poison information centres, the Federal Institute for Risk Assessment (BfR) initiated immediate investigations into the case and assessment of the product involved. It is named Por Çöz and contains 25 % nitric acid. It was found that in the 1999 to 2010 period, altogether 134 cases had occurred that were associated with the use of this rust remover and descaler, with severe health damage suffered in some of the cases. It is interesting to note that this product had become popular particularly via the internet as the result of recommendations and reviews by a great number of different users emphasizing its enormous cleaning power, however, without drawing attention to its dangerous chemical effects.

As a result of comprehensive investigations by BfR, a rapid communication to the Turkish manufacturer, the German distributor and the responsible ministries, and based on a subsequently performed scientific risk assessment by BfR, the Federal Environment Agency (Umweltbundesamt – UBA) informed the EU Commission and the other EU Member States about the temporary ban on the placing on the German market of the cleaning agent named Por Çöz. It was possible to submit to the EU unequivocal evidence of a risk posed by nitric acid for human safety and health under Art. 15 of the Detergents Regulation.

As a result, the EU Commission has extended the ban on the placing this product on the market for another year and considers a permanent restriction in the future of the use of nitric acid in consumer goods sold in the EU. Based on the case series involving Por Çöz, BfR also submitted a CLH report entitled Proposal for Harmonised Classification and Labelling to the European Chemicals Agency (ECHA) to achieve an unequivocal labelling and classification of nitric acid on the European level. All of these measures will most probably result in a discontinuation of the use of the dangerous substance, nitric acid in consumer goods in the European Union.

Already in the past, the risk potential of dangerous lamp oils and grill lighter fluids had been identified by the BFR documentation and assessment of reported cases of poisoning and on this basis, the legal provisions for containers and hazard statements had been harmonized for all European consumers. Likewise, the case of the nitric acid-containing product, Por Çöz has again demonstrated that committed monitoring activity and scientific evaluation of undesirable effects of products may reduce risks in a highly effective and sustainable manner.

Therefore, attending physicians, poison information centres and also the general public are asked for their active support also in the future.

Professor Dr. Dr. Andreas Hensel
President of the Federal Institute for
Risk Assessment

Dr. Axel Hahn
Head of Unit
Poison and Product Documentation Centre

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1 Introduction

1.1 Underlying legislation: §16e Chemicals Act

On 1 August 1990, the requirement of compulsory reporting of poisonings by attending physicians within the framework of the Chemicals Act (Chemikaliengesetz – ChemG) came into force. This compulsory reporting is a meaningful counterpart to the reporting of adverse reactions to medicinal products. In addition to compulsory reporting of cases of poisoning, compulsory notification of dangerous preparations (formulations) was introduced at the same time. Poison information centres had to undertake to report their relevant knowledge of the situation with regard to poisoning incidents in Germany. All these activities merge at BfR at the Poison and Product Documentation Centre, where also the secretariat of the Committee for the Assessment of Poisonings is hosted.

It has been the purpose and objective of this legal provision in the German Chemicals Act to receive from physicians well documented findings on health complaints in humans caused by chemical products. It serves to provide valuable data on the incidence of poisoning accidents, doses and effects of chemicals and products in humans. On the basis of such data, effective measures of prevention can be recommended at a very early date. It has been the specific purpose of legislation that the toxicological assessment of chemical substances and products should not rely on toxicological data from animal studies alone. The data obtained from cases of poisoning in humans should be used as far as possible to minimize toxicological studies in animals and thus, make an active contribution to animal welfare.

The reporting and systematic evaluation of cases of poisoning represents a legal provision that is useful for both humans and animals and unique on the global level. The cases of poisoning reported by physicians have been compiled, assessed and evaluated at BfR in direct cooperation with attending physicians and the German poison information centres for more than 20 years now. The annual reports being published in a German as well as an English version have met with a most affirmative response among the scientific community owing to their dealing with toxicological issues of current interest, proposals for preventive measures and the presentation of individual case reports.

In addition, ministries, companies and industrial associations are informed about adverse effects of chemical products (toxicovigilance) through a well-working product information system (PRINS) either immediately by rapid communications (in severe cases of poisoning) or at annual intervals by summary reports (in all other cases).

Compulsory reporting

According to the Chemicals Act, reporting refers to illnesses or suspected poisonings as well as cases of unintentional exposure associated with the following substances or toxicants:

- Chemical substances and products used in the household, e.g. detergents and cleaning agents, hobby and DIY articles;
- Cosmetics;
- Detergents and cleaning agents;
- Pest control products;
- Plant protection products;
- Wood preservatives;
- Chemicals used at the workplace;
- Dangerous chemical substances present in the environment, including those released during industrial accidents;
- Poisonous plants including mushrooms; and
- Poisonous animals.

1.2 What does the term “poisoning” mean?

The term, poisoning, refers to illnesses caused by exposure of the human body to chemical substances or products as determined by their chemical and physical properties. In the majority of cases, the substances involved are not single ones but chemical products composed of a number of single substances in the sense of a formulation. For many poisons of animal or plant origin, full knowledge of their specific toxic effects is still missing. Therefore, toxicological research into these effects must continue.

The practice of human toxicology, i.e. the science dealing with the effects of toxic substances in humans, requires special knowledge and a long-standing experience. This applies in particular to the assessment of cases of poisoning. For the assessment of cases of poisoning in humans, toxicological findings and knowledge obtained from animal studies may be helpful to a limited extent only.

Within the meaning of the Chemicals Act, the term of poisoning designates all cases in which health impairment has occurred. Reporting is also required for suspected cases of poisoning. Poisoning may occur through a variety of routes of exposure to a product, e.g. after oral or inhalational exposure or after contact with the eyes or the skin.

Health impairments in the sense of adverse effects or allergic reactions occurring during or after the customary use of a product are to be reported to BfR, irrespective of the proper or improper use. BfR may also be informed of accidents involving a product which did not result in any health impairment (asymptomatic cases). Information on asymptomatic cases with documented exposure may provide useful information with regard to a risk potential and help define the safety range of the use of a product.

In addition, poison information centres are legally obliged to inform BfR about occurrences of general importance that have come to their knowledge so that trends may be identified at an early date and considerations made with regard to preventive action.

1.3 Principles of clinical toxicology

The assessment of cases of poisoning is based on the established principles of clinical toxicology in the sense of an expert judgement. The following queries have to be answered.

- Does the patient suffer from a disease or condition showing manifestations that can be clearly described?
- Is there any evidence existing or to be established that exposure to specific substances or products has taken place? Is it possible to confirm such exposure by laboratory evidence?
- Is there any evidence of an association, i.e. a causal relationship between the disease or condition/manifestations, and the exposure?

1.4 Standards for the assessment of poisonings

A systematic, uniform and harmonized documentation of reports of cases of poisoning by physicians and their assessment are the essential prerequisites for adequately confirmed and timely hazard identification. All single reports by physicians are recorded in a standardized and harmonized way.

As in all other fields of medicine (e.g. assessment of cases in occupational medicine), cases of poisoning must be assessed on the three different assessment levels described above, guided by objective criteria. For the medical assessment of a case, it has been particularly helpful to consider the individual manifestations as entities in their own right where the degree of severity of the health disorder is weighted correspondingly. This will provide a clear basis for the assessment by differential diagnostic considerations.

For the assessment of cases of poisoning by BfR, standardized instruments are available, which were either adopted and modified or developed at the institute. These instruments have been described in detail in the 2009 annual report. For details, see Annex 5.1 to this brochure. The degree of severity of manifestations (symptoms and signs) and conditions is assessed on the basis of the international poisoning severity score (PSS)[1] (see Table 1).

The most important element for the assessment of both acute and chronic poisonings is seen in the BfR three-level model presented in Chapter 5.1.1, Fig. 25. It was developed in analogy to the assessment of the causal relationship in the recording of adverse effects of medicinal products to enable a differentiated assessment of individual cases of health impairment from poisoning.

PSS grade		German (BfR)	
0	None	keiner	No symptoms or signs
1	Minor	leicht	Mild, transient and spontaneously resolving symptoms or signs
2	Moderate	mittel	Pronounced or prolonged symptoms or signs
3	Severe	schwer	Severe or life-threatening symptoms or signs
4	Fatal		Death

Table 1: Poisoning severity score (PSS): International standardized severity grading of health disorders in cases of poisoning

The advantage of the BfR three-level model assessment consists in a reduction of assessment efforts to three single levels which are logically interconnected.

- Is there a justifiable temporal and spatial association between the exposure and the occurrence of health impairment?
- Are there manifestations known from other case reports, or can they be explained by the mechanisms of action?
- Is there an association between symptomatology and exposure, i.e. are the signs and symptoms temporally associated with dechallenge (symptomatology subsiding after termination of exposure) or rechallenge (symptomatology aggravating on re-exposure)?

The assessment of exposure and health disorders/manifestations is supported by two BfR matrix models: a model to determine the degree of probability of exposure (Chapter 5.1.2, Table 15) and another one to assess the causal relationship between health disorder/manifestations and exposure (Chapter 5.1.3, Table 16).

[1] *Persson HE, Sjöberg GK, Haines JA, Pronczuk de Garbino J. Poisoning Severity Score. Grading of Acute Poisoning. Clin. Toxicol. 1998; 36(3):205–213.*

1.5 Procedure of assessment and risk communication

The reports received on health impairments associated with chemicals are subjected to an assessment procedure. The causal relationship between the toxicant absorbed and the symptomatology observed can be classified as "none", "possible", "probable", "confirmed", or "cannot be assessed".

The estimation of toxic risks for humans is based on differentiated analyses and assessments. For these purposes, the data on cases in humans are continuously documented in the form of case data sets and case reports. Information on identified risks is passed on to the responsible ministries, manufacturers and industrial associations in the form of rapid communications or to the manufacturers in the form of annual summarizing reports disseminated by way of the product information system PRINS (see Chapter 4.3). The responsible manufacturers and/or distributors are requested to transmit to BfR information on measures envisaged by them to improve product safety.

The knowledge gained during this process is published by BfR in its annual reports under the title, Cases of Poisoning Reported by Physicians. These reports and other publications are available on request by writing to Pressestelle, Bundesinstitut für Risikobewertung, Max-Dohrn-Str. 8–10, 10589 Berlin, GERMANY. These publications may also be accessed on the internet (www.bfr.bund.de).

For a summary of the terms of reference of the BfR Poison and Product Documentation Centre and the respective procedures, please refer to Fig. 26 in Annex 5.2.

1.6 Toxicological history (case history)

The case history is one of the most important elements of information to be obtained by a physician on a patient's condition, forming the essential basis for a plausible assessment of a case of disease. For this purpose, a general case history will comprise at least seven parts:

1. Elucidation of current complaints with special reference to the temporal development of the patient's condition;
2. Previous diseases and medical examinations;
3. Differential diagnostic considerations;
4. Medical history provided by persons other than the patient (sometimes referred to as heteroanamnesis);
5. Family history;
6. Social history; and
7. Travelling history.

In general, toxicological health impairments should be dealt with according to the same principles as for medical conditions of general character. However, items 5 to 7 are of minor importance as compared to a general medical history.

For a toxicological case history, a number of other facts are of particular importance. These include:

1. The routes of exposure (oral, dermal, inhalational etc.);
2. The dose and duration of exposure (acute/chronic);
3. The toxicant(s) that have caused the health impairment; and
4. The spatial and temporal relationship between the toxicant(s) involved and the manifestations observed.

An accurate and plausible toxicological assessment of the health impairment observed should be preceded by elucidation of the special toxicological data.

Routes of exposure (oral, dermal, inhalational etc.)
For any type of health impairment due to toxicants it is important to take special account of the route or path of exposure. In many cases, substances are ingested by mistake (oral route of exposure). Inhalation is the route of exposure second in frequency in cases of poisoning. Exposure through the skin, i.e. the dermal route, ranks third in frequency. Often, the routes of exposure are combined, e.g. oral and inhalational or oral and dermal route. Quite frequently, above all in occupational accidents, but also in those affecting children, it is dermal exposure that leads to health impairment, particularly if clothing contaminated after spillage of substances or products is not removed early enough. Depending on the duration of exposure, considerable quantities may be absorbed, particularly after previous damage to the skin barrier due to contact with irritating or corrosive substances.

Dose and duration of exposure (acute/chronic)
Almost without exception, it is very difficult to make a precise estimate of the dose absorbed unless sufficient evidence is provided by direct observations (e.g. two sips of a liquid or differences in quantities of substances kept in transparent vessels). This is quite difficult in cases of exposure by inhalation, particularly if taking place outdoors. The doses released and absorbed by inhalation will depend on a variety of parameters (room size, room furnishings, ventilation, temperature etc.) and on the direction of spreading. Outdoors, the latter will be determined to a considerable degree by the meteorological conditions (e.g. wind speed and direction). There are no reliable calculation methods available at present. Thus, also specialists have to rely on estimates, which most often will be based on a worst case scenario.

Toxicant
For the assessment of health impairment due to chemical products such as household products, paints, lacquers/varnishes, glues, insecticides etc., it is important to undoubtedly identify and document the responsible substance or product on the one hand and the resulting symptomatology, on the other. For a differentiated assessment of health effects it is also important to identify the dynamics and severity of the manifestations observed, in addition to the dose and route of exposure.

In this context, unequivocal identification of the responsible product is the most important information to be obtained by the attending physician. Based on the experience gained so far this means that for an assessment of health risks involved it is imperative for the attending physician to know not only the correct product or trade name of a product but also its current formulation.

1.7 Poison information database

The BfR poison information database serves to support the poison information centres in providing consultation and treatment in cases of poisoning by making available product formulations notified by manufacturers/distributors for purposes of emergency health response.

To this aim, industry is obliged to supply BfR with product information on biocides, detergents and cleaning agents and certain dangerous preparations intended for consumer use. The legal basis for such notifications is provided by § 16 e para 1 of the Chemicals Act (Chemikaliengesetz – ChemG), and § 10 of the Detergents and Cleaning Agents Act (Wasch- und Reinigungsmittelgesetz – WRMG). Until 2007, BfR also received notifications of formulations of cosmetics. In addition, companies may provide BfR with product information on a voluntary basis to enable fast and competent advice by a poison information centre in cases of accidents.

By the end of December 2010, a total of 86 984 documents containing product information were kept at the BfR product database. Of these, 8 323 were new notifications of products that had been added in 2010 alone.

So far, 49 355 legally required product notifications have been transmitted to the poison information centres. Of these, 9 910 referred to dangerous preparations, 13 844 to biocides and 25 601 to detergents and cleaning agents (Fig. 1). In addition, data on 37 629 products notified on a voluntary basis were submitted to the poison information centres.

In 2007, the Detergents and Cleaning Agents Act stipulated for the first time that these data should be submitted to BfR in electronic form. To this purpose, BfR had developed an XML data exchange format (XWRMG), which has shown an excellent performance. In its wake, another electronic data exchange format (XProductNotification) was made available to the companies free of charge permitting computerized notification of all products (both notifications on a legal as well as on a voluntary basis). Already at present, the majority of product notifications are received by BfR in electronic form. The corresponding formats and add-ons are available for downloading from the BfR homepage at www.bfr.bund.de/en/notifications_of_formulations-10144.html.

All product data notified are edited by BfR in a well-established manner and then transmitted to the poison information centres. This procedure has been carried out in electronic form for many years.

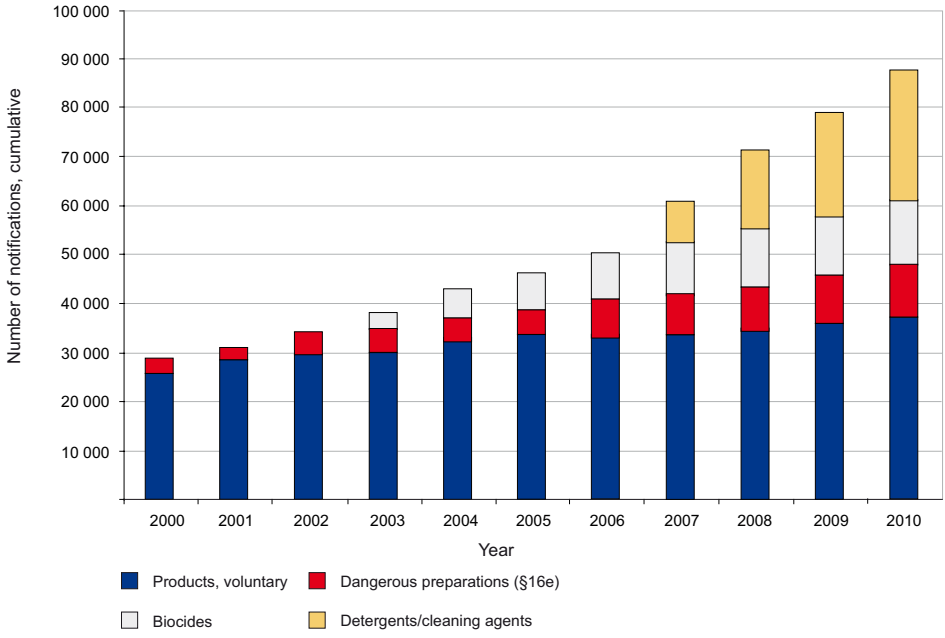

Fig. 1: Notifications of products received since 2000 and transmission of information to the German poison information centres

1.8 First BfR User Conference on Product Notifications

On 29 October 2010, the first BfR conference of users of the product notification system took place with more than 70 participants from all parts of Germany. Being the first of its kind, this event was guided by the consideration that the legal obligation to notify products may give rise to a number of practical problems that need to be addressed as soon as possible in the interest of a good customer support and smooth work flow.

Particularly companies complying for the first time with the obligation to notify their products have shown a considerable need for information, which can be met in an efficient way by regularly organizing such events. Hence, the first User Conference was above all to address representatives of industry, but also of poison information centres receiving reports on formulations, and government authorities involved in chemicals legislation and monitoring.

Fig. 2: First BfR User Conference on Product Notifications, October 2010

The event was structured around a number of practical topics. The participants were welcomed by the President of BfR, Prof. Dr. Dr. Andreas Hensel, who outlined the framework of the legal terms of reference of this institution and pointed out the importance of the issue for consumer health protection. Other presentations provided detailed information on the procedures and the necessities of product information, data security and information exchange between the companies involved, BfR and poison information centres. An important criterion consists in the completeness, correctness and unambiguousness of product notifications providing poison information centres with a comprehensive and reliable basis for emergency health response. A high level of data protection is warranted both at BfR and the poison information centres. Data are transmitted using a certified encryption system. At BfR, all documents are stored in a theft-proof manner and with access protection. All BfR staff are bound to observe secrecy.

A new uniform and electronic notification procedure for product notifications was presented, which is to enable easier handling and speeding up of the notification process. It is applicable to all product groups. In addition, users are supplied with an MS Excel input assistant. An intensive exchange of information developed in the context of preparatory working projects and envisaged regulatory provisions regarding a harmonized exchange format in the context of Article 45 of the CLP Regulation[2] (see Chapter 1.9). For the transition period to a final European implementation, product notification is regulated in a modified Chemicals Act. During the event and the breaks, lively discussions took place between the participants of the conference and BfR staff members. The conference will be held once a year at regular intervals. It is intended to develop into a constructive and informative dialogue between BfR and its clients.

1.9 Classification and labelling of products: The CLP Regulation

The CLP Regulation has been in effect already since 20 January 2009. It refers above all to new elements and provisions of the classification and labelling of substances and products.

[2] *Regulation (EC) No. 1272/2008 of the European Parliament and of the Council of 16 December 2008 on classification, labelling and packaging of substances and mixtures*

For the first time, compulsory notification of products for purposes of emergency health response was introduced by this Regulation. Under Article 45, compulsory notification shall apply to all products classified as hazardous on the basis of their health or physical effects. As a result, there will be a considerable increase in the number of products that have to be notified in the future.

With the new data exchange format, XProduct-Notification, BfR has made provisions to cope with the high number of product notifications to be expected, also taking into account the new classification and labelling elements for substances and products.

In autumn 2011, the German Chemicals Act has been harmonized with the current European legislation.

1.10 Current topics

1.10.1 Eye injuries caused by chemical products

Eye injuries account for the foremost share of reports by physicians under § 16 e Chemicals Act (ChemG). Only in relatively rare cases, the products having caused the accidents on record are mentioned in these reports. However, the name of the product involved is highly important for specific preventive measures and an early recognition of risks. This is why a specific analysis of products involved was carried out for all cases of eye injuries reported in 2010. This analysis has exceeded the number provided for in the framework of summary reports in the BfR product information system (PRINS, see Chapter 4.3) because all products reported were included. In contrast to the summary reports, the analysis also included medicinal products as well as products manufactured abroad, products whose manufacturer had remained unknown and those produced by more than one manufacturer. All of these are not taken into account in the summary reports.

For 282 (12.4 %) of the 2 266 cases of eye injury reported to BfR in 2010, the product involved was specifically named. For each case, only one product was reported. Of the 282 products reported, 264 (93.6 %) had caused minor eye injuries. Six (2.1 %) cases were classified as moderate and for another six (2.1 %), a degree of severity was not specified or could not be assessed. In the category of severe eye injuries, no specific product names were reported.

The moderate eye injuries had been caused by an agricultural surface disinfectant (quicklime), an herbicide, a commercial surface/metal cleaner, a hardener and a two-component adhesive, respectively.

Among the causative agents of the cases of minor severity, disinfectants (102 cases, corresponding to 38.6 %) and cleaning agents (97 cases, corresponding to 36.7 %) were predominant. Of the disinfectants involved, ca. 40 % represented surface and hand disinfectants and 20 %, instrument disinfectants. In 21 out of 264 (7.9 %) cases, eye injury had been caused by medicinal products. Herbicides and pesticides were reported to have been involved in 17 (6.4 %) of the cases of minor severity.

The cases of eye injuries lacking data on the degree of severity had been caused by a medical sclerosing agent, a cosmetic and food additive, a commercial dishwashing detergent, an instrument disinfectant and an agricultural surface disinfectant. Other cases that were not assigned a degree of severity included three reports involving an alcoholic hand disinfectant, two involving two surface disinfectants and one involving a crack filling material used as an auxiliary product in the construction sector.

In a summarizing view, 191 (67.7 %) of the products reported most frequently in the context of eye injuries were represented by the groups of cleaning agents (32.3 %), disinfectants (24.8 %), pesticides (6.7 %), adhesives (2.1 %) and detergents (1.8 %).

From another perspective, the exact product name was reported in 70 (30.7 %) of 228 cases of eye injury caused by disinfectants. Also for the cases of eye injury caused by cleaning agents, a specific product was named only in 91 (15.5 %) of 588 reports. In the cases of eye injury caused by pesticides, the product involved was reported in 19 (48.7 %) of 39 cases. For the seven cases of eye injury due to detergents, five products were named.

Altogether, among the reports on cases of eye injury under § 16 e ChemG, the number of reported products allowing an unequivocal identification of the product name and formulation is very low. However, risk assessment, early recognition of specific hazards and injury prevention are only possible for products whose specific trade name and formulations are known. In this respect, deficits have become evident which have to be attributed to insufficient information submitted by physicians in the context of compulsory reporting under § 16 e ChemG. Therefore, BfR kindly asks attending physicians to submit concrete details with regard to the product incriminated, the medical history and the manifestations observed. This is the only way to jointly develop approaches to a prevention of eye injuries and other risks.

1.10.2 Cases of poisoning reported to BfR under § 16 e ChemG and the corresponding consultation by telephone provided by the Berlin poison information centre (Giftnotruf Berlin) in 2007

(MA thesis by Ms. Emine Kurtal, Berlin School of Public Health, Charité Berlin)

Legislation introduced in 1990 assigned the obligation to report cases of poisoning (§ 16 e para 2 ChemG) to the attending physicians and not to the German poison information centres. The latter option had been a subject of extensive and in part controversial discussion prior to passing such legislation. This legal provision has given rise to debate again and again, for the reason alone that unlike the reporting of communicable diseases, occupational accidents etc., reporting of cases of poisoning cannot be charged by attending physicians as a medical service.

As the result of an initial lack of acceptance among physicians, reporting developed very slowly. In contrast, there was a continuous increase in telephone enquiries on poisonings received by the German poison information centres providing information in a round-the-clock consulting service on a national level.

The two data sources available, i.e. the Cases of Poisoning Reported by Physicians, and records of telephone enquiries to the German poison information centres are different, on principle. There are differences as to the data processing technology used and the quality of records. Owing to a good cooperation particularly within the National Committee for the Assessment of Poisonings, and as a result of two research projects conducted by the Federal Ministry for the Environment, Nature Conservation and Nuclear Safety (BMU) (EVA – Recording of cases of poisoning and evaluation at the poisoning information and treatment centres, 1994; TDI – Toxicological Documentation and Information Network of the BMU, 2006), the definitions and categorization systems used for

	Cases of Poisoning Reported by Physicians § 16e ChemG	Telephone enquiries to poison information centres
Data acquisition	After termination of treatment	- During the consultation - Often very early during exposure
Evaluation and assessment	By attending physicians	By calling party (parents, lay persons, physicians etc.)
Knowledge base	Medical expertise	Evaluation of the situation based on alleged manifestations, changes in behaviour (often not based on medical expertise)
Range of toxicants	Chemical products/substances	Entire range of possible toxicants
Background	Treated cases of poisoning following exposure	- Suspected poisoning after alleged exposure; - Request for toxicological consultation, also for preventive reasons; - Exposure to very low quantities; Cases of poisoning after relevant exposure
Medical findings	Data based on medical findings	Findings available at a later date in most cases
Documentation	Authorized documentation: - official report by physician; - medical report with signature	Records of telephone calls, authorized medical documentation only in the course of a follow-up
Time of notice	After report is received (weeks or months after the time of poisoning)	In close temporal relationship with possible time of poisoning

Table 2: Comparison of reports to BfR and telephone enquiries to poison information centres

the documentation of cases of poisoning have been harmonized and adapted.

As shown in Table 2, important differences between the data obtained from reported cases of poisoning and those based on telephone enquiries to poison information centres include:

- Time of data acquisition;
- Evaluation and assessment of the reporting/calling party;
- Knowledge base;
- Range and background of the reports/telephone enquiries; and
- Medical findings and technical documentation required.

Because of these differences, legislation had decided to confer the task of compulsory reporting upon the attending physicians from 1990 onwards.

The discrepancy between the number of cases of poisoning reported by physicians and the telephone enquiries to German poison information centres had already been examined in the context of the EVA research project conducted at the Max von Pettenkofer Institute of the former German Federal Health Office:

In a study involving four poison information centres in Berlin, Munich, Freiburg and Mainz, which were the largest ones in Germany at that time, it was possible for the first time to estimate

the number of cases of poisoning by chemical products for the year 1993. It was calculated that among the 120 000 consultations provided by the 17 different poison information centres per year, 28 000–30 000 (ca. 25 %) referred to cases of poisoning by chemical products. No differentiation was made at that time as to the type and dose of exposure or degree of severity of the health disorders recorded. During the same period, German physicians reported about 1 100 cases of poisoning to the former Federal Health Office.

The new approach to assessment

As described above, a first estimate of the number of cases of poisoning by chemicals was presented in 1993. Owing to the results of the MA thesis by Ms. Emine Kurtal, it has now become possible to evaluate also the numbers, the quality and representativeness of the reports of cases of poisoning by physicians under § 16 e para 2 ChemG for Germany.

By means of BfR research funding, telephone enquiries on poisonings dealt with by the Berlin poison information centre in 2007 were recorded according to the same categories as those applied to cases of poisoning reported by physicians at BfR. In this way, it became possible for the first time to create an immediate comparability of cases that had been a subject of telephone consultation at the Berlin poison information centre and those reported to BfR (§ 16 e para 2 ChemG) after termination of treatment. Afterwards, the principle of post-categorization of cases was applied to the 2007 annual reports of the other nine German poison information centres. As a result, is has become possible to estimate the share of cases of poisoning reported by attending physicians to BfR. In addition, the processed data material served to compare these data with the number of poisonings listed by the statistics of causes of death from the German Federal Statistical Office.

Results

In 2007, the nine German poison information centres received a total of 53 599 telephone enquiries on health disorders associated with exposure to toxicants reportable under § 16 e ChemG. This corresponds to a share of about 26 % as referred to the total number of ca. 206 000 telephone enquiries on poisonings in Germany during the same year. A similar share, namely ca. 25 %, had been established in the first estimate in 1993. In 2007, BfR received 3 717 reports on cases of poisoning, corresponding to 6.9 % as referred to the total number of telephone enquiries to poison information centres involving reportable toxicants. In contrast to the telephone enquiries, such reports to BfR were recorded only after termination of a treatment, therapy and/or hospitalization, in the sense of a final medical assessment.

As compared to the poison information centres, BfR has recorded far fewer cases of poisoning in children but many more cases related to occupational health and safety. Analysis of the degree of severity of poisonings under § 16 e ChemG has shown that on the national level more than 911 cases recorded at German poison information centres were classified as “moderate” or “severe”. This is opposed by only 292 cases classified as “moderate” or “severe” that were recorded at BfR in the same year.

For an appropriate rating of the reports under § 16 e para 2 ChemG it is important that in comparison to the German poison information centres, only a low share of spontaneous reports on cases with a minor degree of severity is received by BfR, however, as much as about one third, referred to the category of cases with a moderate and severe course. Therefore, what concerns relevant health impairment and risks associated with chemical substances and products, the analyses based on compulsory reporting of cases by physicians can be regarded as providing good evidence.

With regard to fatal cases of poisoning under § 16 e para 2 ChemG, BfR received far fewer documented cases in 2007 (7) than did the poison information centres (48). Nevertheless, BfR is informed about these deaths by way of the regular reports from the poison information centres (§ 16 e para 3 ChemG). Frequently, such cases are discussed as topics at the regular meetings of the BfR Committee for the Assessment of Poisonings. A category-based comparison of cases with the statistics of causes of death established by the German Federal Statistical Office has shown significant differences in the numbers of cases of poisoning: The 1 903 deaths due to poisoning by toxicants under § 16 e ChemG recorded at the Federal Statistical Office are opposed by no more than about 50 deaths documented by German poison information centres and only seven deaths among the cases reported to BfR. Since the German poison information centres, BfR and the National Committee for the Assessment of Poisonings have a good idea of the poisoning situation in Germany the figures stated by the Federal Statistical Office are not plausible and should become the subject of an expert discussion.

There may be problems when encoding death certificates, above all in cases where there is even the slightest suspicion of poisoning. According to the results of the MA thesis, the number of deaths due to poisoning by chemical substances is overestimated in the statistics published by the Federal Statistical Office.

Comments

For the first time on the basis of substantiated figures, the MA thesis has provided evidence of the importance of the cases of poisoning reported by physicians under § 16 e ChemG. The analyses were based on a uniform categorization system which served to encode and compare the cases of poisoning recorded. This categorization system had been created in the context of the EVA research project and was developed further under the TDI research project. At present, it constitutes the most important basis for the evaluation of cases of poisoning on the national level. This new categorization system was already used for the analysis of cases published in the last annual report Cases of Poisoning Reported by Physicians in 2009.

For future annual reports and statistics on cases of poisoning, it is envisaged to use uniform categorization systems to enable a comparable statistical evaluation, if possible directly on the EU level. The development of a common categorization system and standardization of data are the most important steps on the way to a national monitoring of cases of poisoning in Germany. They represent a key area of the work of the BfR Committee for the Assessment of Poisonings.

2 Selected toxicological problems

2.1 Por Çöz

Severe chemical burns in a young child due to a Turkish household cleaner

A girl aged 2 years and 11 months had ingested Por Çöz, a rust-removing and descaling agent containing nitric acid (Fig. 3), which had been sold mainly in Turkish retail shops all over Germany. The family called the medical emergency service through the emergency response centre. The emergency physician found the child in an abnormal condition not showing any adequate neurological reactions. The child was reported to have vomited several times, with bloody vomitus at times. Due to communication problems with the parents, the initial medical history was scanty.

The child was intubated already at the scene of the accident. It was possible to obtain some bloody mucilaginous secretion through the endotracheal tube. Under artificial ventilation, the child was admitted to the hospital as an emergency case. Immediately after admission, another episode of bloody vomiting and clouding of consciousness were observed so that the child had to be transferred to the intensive care unit.

Fig. 3: The product Por Çöz

Status on admission

Dystrophic girl, psychomotor retardation, cerebral paresis as a possible sequela of kernicterus, pale, hypothermic (35.3 °C), intubated and ventilated, lungs, heart and abdominal findings otherwise within normal limits, pupils mid-dilated.

Laboratory parameters Hb 8.6 g/dL, elevated leukocyte count (11 200/µL) with shift to the left, low thrombocyte count (48 600/µL), CRP 41.3 mg/L, respiratory and metabolic acidosis (pH = 7, pCO_2 74 mmHg, BE –11.8 mmol/L), initial bronchoscopy normal.

Manifestations / course

After admission, nasogastric lavage was performed because of gastrointestinal bleeding. Gastroscopy performed 24 hours later revealed considerable signs of chemical burns affecting the entire oesophagus in a circular distribution. Parts of the mucosa were found to peel off in sheets, an increased bleeding propensity was found particularly in the oesophagus. Severe chemical burns were found in the entire stomach, partly with adhering clots. Marked burns were found from the pharyngeal region to about 3 cm behind the duodenal bulb. There was no clinical evidence of burns in the deeper sections of the duodenum and small intestine.

The child was immediately put under intensive medical care and artificial respiration. Later, i.v. antibiotics and parenteral nutrition were administered. In the further course of therapy, the child suffered considerable blood loss requiring repeated transfusion with packed red blood cells and fresh plasma. Such blood loss was again and again caused by the severe and extensive damage to the mucous membranes from the pharyngeal region to the duodenum. A first follow-up gastroscopy performed four days later revealed a gastric perforation in the greater curvature near the antrum requiring partial gastrectomy. The clinical course was complicated by aspiration pneumonia which was difficult to treat. This condition had probably been caused by the repeated episodes of vomiting on the first day.

After 12 days of intensive medical and surgical therapy, it was eventually possible to stabilize the patient's condition so that she could be transferred to a paediatric surgery ward for onward treatment. Two weeks after the chemical burn incident it was possible to carefully reintroduce oral food intake, which was very well tolerated by the child. Follow-up examinations carried out on the 20th and 25th days of inpatient treatment showed normal findings, particularly an absence of stenosis in the oesophagus and gastrointestinal tract. Tracheobronchoscopy findings were normal.

After six weeks of inpatient treatment the child could be discharged and referred to outpatient paediatric care. The gastrostoma was maintained over three months, after which the wound healed without complication. Extensive follow-up examinations of the child carried out about ten months after the incident showed a favourable healing process. It has been assumed that probably no permanent impairment of the gastrointestinal tract will result from the partial removal of the stomach performed.

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

Comments
Cases of poisoning have demonstrated that nitric acid may cause severe chemical burns and also poisoning by inhalation. This has been a particular risk in accidents occurring at the workplace. In the private sphere, nitric acid has very rarely caused poisoning and chemical burns in Germany because German companies neither produce nor distribute products containing nitric acid for private household use. The product Por Çöz is produced in Turkey and exported to Germany and a number of other countries. It is known to have caused severe chemical burn accidents in Turkey.

Investigations by BfR into cleaners containing nitric acid in Germany
Case investigations were initiated immediately on the product Por Çöz containing 25 % nitric acid. It was found that the product purchased in Germany had been imported from Turkey. It had, however, neither been labelled as "Corrosive" nor equipped with a child-resistant fastening. The product had obviously been sold on a large scale in the Federal Republic of Germany. In spite of intensive investigations by authorities in several federal Länder, the importer could not be identified. The Turkish manufacturer did not provide any information on the trade routes to Germany or other EU countries.

The investigating public health laboratories of the Länder (Landesuntersuchungsämter) and federal authorities (BfR, UBA) were facing a special problem because in addition to the product involved, another one having the same product name, Por Çöz, was found to exist which had been properly labelled in German with the correct warning signs and equipped

with a child-resistant fastening. It also contained about 25 % nitric acid. The distributor of this Turkish product had complied with all safety precautions required by law. However, he was also unable to provide information with regard to the improperly labelled product that had no child-resistant fastening.

It is noteworthy that already in 2003, a similar product, Por Çöz, containing nitric acid had been the subject of activities of government authorities in the federal Land of Baden-Württemberg (Fig. 4).

Ministerium für Ländlichen Raum und Verbraucherschutz
Baden-Württemberg

DAS MINISTERIUM
- Der Minister
- Der Ministerialdirektor
- Aufgaben
- Organisation

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- Landwirtschaft
- Tiere
- Pflanzen
- Verbraucherschutz
- Lebensmittel und Ernährung
- Ländlicher Raum
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- Naturschutz
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Pressemitteilung 90/2003

Verzicht vor dem Gebrauch des Reinigungsmittels der Marke Por Çöz - Rust Dissolvant

Verätzungsgefahr durch Salpetersäure / Verbleib vor allem über türkischen Einzelhandel

Das Ministerium für Ernährung und Ländlichen Raum warnt vor dem Gebrauch des Reinigungsmittels Por Çöz. Das Reinigungsmittel Por Çöz besteht aus Salpetersäure in einer Konzentration von 25 Prozent. Beim Umgang mit dem Mittel bestehen erhebliche Gefahren durch Verätzungen von Haut und Augen sowie durch Einatmen giftiger Dämpfe.

Das Produkt stammt aus der Türkei und wird vor allem in türkischen Einzelhandelsgeschäften bundesweit verkauft. Es handelt sich um eine blaue Plastikflasche (900 ml) mit gelber Verschlusskappe (s. Hinweis). Die Kennzeichnung ist überwiegend in türkischer Sprache.

Produktname: Por Çöz Scale & Rust Dissolvant

Hersteller: Levent Kimya San. Antalya

Auf der Rückseite befinden sich auch eine deutsche und eine englische Gebrauchsanweisung sowie einige Warnhinweise, die jedoch den Verbraucher nicht ausreichend auf die Gefahren hinweisen.

Das Mittel wird als Kalk- und Rostlöser angepriesen. Es wird von verschiedenen Großhändlern aus der Türkei nach Deutschland importiert und überwiegend an türkische Einzelhandelsgeschäfte in vielen Bundesländern geliefert.

Salpetersäurehaltige Lösungen können bereits ab Konzentrationen von fünf Prozent schwere Verätzungen verursachen. Ein Einatmen der konzentrierten Dämpfe kann ebenfalls zu Verätzungen der Schleimhäute, des Atemweges sowie zu Husten oder Atemnot führen. Außerdem besteht die Gefahr, dass bei Reaktionen von salpetersäurehaltigen Lösungen mit oxidierbaren Stoffen gesundheitsschädliche nitrose Gase entstehen.

Der weitere Vertrieb des Reinigungsmittels wurde von den Lebensmittelüberwachungsbehörden untersagt. Die verantwortlichen Importeure haben das Produkt aus den Geschäften zurückgerufen. Verbraucher, die das Mittel noch in ihrem Haushalt vorrätig haben, werden zu besonderer Vorsicht aufgerufen.

Hinweis:

Abbildungen des Produktes sind im Internet unter www.mlr.baden-wuerttemberg.de bei Aktionen eingestellt.

Fig. 4: 2003 press release in Baden-Württemberg

Rapid communication of the case under the BfR product information system (PRINS)
After receipt of all product information required and the medical report from the hospital, the data on this severe case of poisoning were submitted to the responsible ministries, the Turkish manufacturer, the German distributor of the correctly labelled product and the corresponding industrial associations in the form of a rapid communication (BfR product information system, PRINS, see also Chapter 4.3.1). In this context, attention was drawn to the considerable risks (severe chemical burns and poisoning by inhalation) resulting from the use of nitric acid in consumer products and suggestions for prevention were made.

Due to the identity of names it was particularly problematic to unequivocally identify the incriminated product and its formulation. Therefore, the process of product identification is briefly described below. It may serve as an example for other cases.

As in many other cases of poisoning, only the product name, Por Çöz, was known initially. In the beginning of investigations, the original bottle and label were not considered as particularly important. In violation of the legal obligation of notification, the formulation had not been duly notified to enable its use by poison information centres and therefore, it was not available for a clinical-toxicological assessment of the case. Therefore, internet research was required for a first orientation. Soon, a safety data sheet was found for the properly classified and labelled product of the German distributor, stating the product to contain 10–25 % nitric acid. With this information to hand, the poison information centre consulted in this case was able to immediately conduct a correct assessment of the situation.

However, since the original bottle was labelled with the symbol “Irritant” only instead of “Corrosive”, there was a considerable risk initially that the situation could be misjudged by the attending physicians. Only owing to the prompt consultation of the poison information centre and the knowledge of the clinical manifestations such as bleeding, mucosal burns etc., the degree of severity of the case could be assessed most rapidly and delays in the administration of adequate treatment avoided.

Experience made by BfR and the German poison information centres has shown again and again that appropriate treatment is only possible if the product involved in the poisoning incident can be identified unequivocally based on the original package and the formulation of the product. In the above case of poisoning, it took almost two months until the product identity could be communicated to all institutions and government authorities involved and hence, could be correctly assessed although BfR, thanks to the assistance of the attending physicians who had been most cooperative, had the original bottle seized at the hospital for investigations by government authorities. In this respect, some thought should be given to improvements and simplification of administrative procedures, above all where cooperation is to extend beyond the borders of a single federal Land.

Given the vast variety of products available today, a quick product research on the internet, resulting for example in locating a variety of safety data sheets, may lead to errors in evaluation and even wrong therapies. In each case of poisoning, a poison information centre should be consulted for expert assessment. In cases of doubt, the product incriminated can be identified within a sufficiently short period and efficiently by means of digital images e.g. taken with a mobile phone camera, digicam etc. and by submitting these images to competent institutions such as BfR or one or more poison information centres.

Again and again, official investigations conducted directly on the scene or in shops selling such products are of course most success-

ful. Essential contributions to the assessment of properly or improperly labelled Por Çöz products available on the market were provided for example by authorities responsible for the control of chemicals in the federal Länder of Schleswig-Holstein, North Rhine-Westphalia and the Landesgesundheitsamt in Stuttgart (public health department of the federal Land of Baden-Württemberg).

A photograph by the Landesgesundheitsamt in Stuttgart shows cleaners containing hypochlorite and nitric acid being stored and offered in a risk-prone way in an open steel shelf (Fig. 5). This manner of storage involves the risk of chlorine gas release (due to chemical reaction of products containing hypochlorite and nitric acid stored closely to each other) and release of nitrous gases (due to a chemical reaction of cleaners containing nitric acid with the steel shelf). Brown stains resulting from chemical reactions are visible in the picture.

Fig. 5: Steel shelf in a shop (photo: Landesgesundheitsamt Stuttgart)

Activities following the rapid communication
In addition to the rapid communication of the severe case of caustic burn, BfR immediately contacted the responsible department of the Federal Environment Agency (UBA) since the Por Çöz rust remover and descaler represents a cleaning agent in the sense of the Detergents and Cleaning Agents Act (Wasch- und Reinigungsmittelgesetz – WRMG). On the legal basis of § 10 WRMG, formulations of detergents and cleaning agents are to be notified to BfR to serve as information for medical purposes. If there are reasonable grounds to assume that a certain detergent or cleaning agent poses a risk to the safety or health of humans or animals, the placing on the market of the product may be temporarily prohibited or subjected to special requirements by UBA, in agreement with BfR (§ 14 WRMG). In compliance with these provisions, UBA immediately informed the other Member States of the European Union, the Commission of the European Communities and the authorities of the federal Länder responsible for supervision of chemicals, stating the reasons behind the decision taken.

In parallel, at the meeting of federal and Länder government representatives on detergents and cleaning agents held on 14 April 2011 in Erfurt, and at the meetings of the BfR Committee of the Assessment of Poisonings on 19 and 20 April 2011, the risk of severe chemical burns due to cleaners containing nitric acid was discussed and new avenues for prevention considered.

Between 1999 and 2010, altogether 134 cases of health damage associated with the use in households of rust removers and descalers containing nitric acid were analyzed and assessed jointly with the German poison information centres for the purposes of toxicological monitoring and comparison of cases.

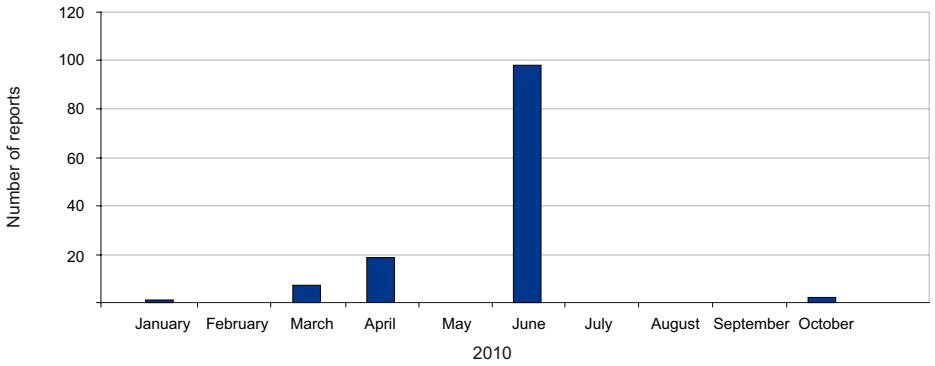


Fig. 6: BfR survey on cases of poisoning by Por Çöz in Germany. Temporal development of reports received by BfR.

So far, there have been no statistical records on cases of poisoning in the Federal Republic of Germany. Therefore, the cases had to be carefully compiled and assessed one by one in close cooperation between BfR and the German poison information centres.

As shown in Fig. 6, the processing of cases took almost the entire year of 2010. In late September 2010, two cases could be added to the case collection after risk assessment had been completed. After processing and assessment, the cases could be retrospectively assigned to the year when the accidents happened (Fig. 7).

It is clearly seen that the temporal development of figures took place in two series of cases. The first case series ending in 2003 resulted in the measures taken by the Landesgesundheitsamt of Baden-Württemberg. The second series comprising a higher number of cases eventually led to the ban on the EU level.

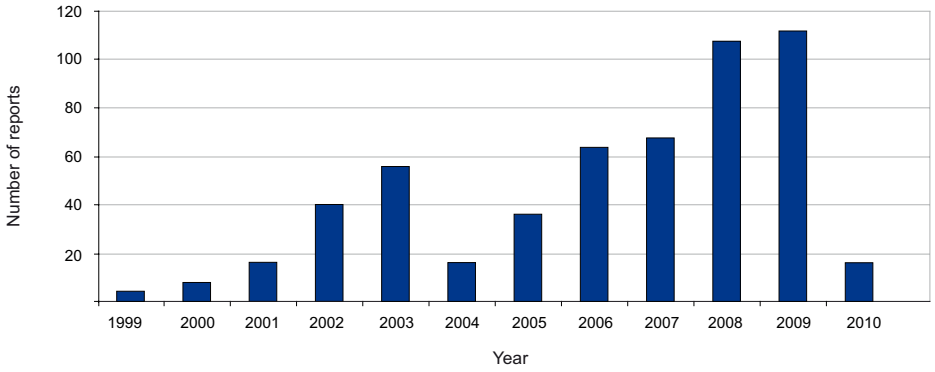


Fig. 7: Cases of poisoning by Por Çöz by year of accident

Health risks posed by cleaning products containing nitric acid (Risk assessment No. 041/2010 by BfR of 6 September 2010)

The legal terms of reference of BfR include the provision of information on possible, identified and assessed risks. An essential part of the work at BfR consists of conducting risk assessment describing the current state of scientific knowledge in a way that is transparent for all citizens. Against the background of the numerous cases reported of health impairment due to the descaler and rust remover, Por Çöz, BfR has assessed the health risk posed by the use of household cleaners containing 20–30 % nitric acid.

The use and reasonably foreseeable misuse of the descaler and rust remover containing nitric acid led to sometimes severe health impairment in consumers (Fig. 8). In the 1999–2010 period, altogether 134 cases were reported to BfR. In the majority of cases (59.1 %), chemical burns had resulted from oral intake of the product containing nitric acid. In almost one quarter of cases (23.7 %), manifestations were caused by inhalational exposure to the product.

While oral intake and dermal contact can be avoided by careful handling of the household cleaner containing nitric acid and technical safety measures, health risks from exposure by inhalation are almost inevitable even if the product is used properly or in cases of foreseeable misuse. In addition, an analysis of the reports on cases of poisoning has shown an alarming exposure situation for consumers.

Nitric acid, particularly in its concentrated form, will decompose mainly by forming nitrogen dioxide and nitrogen monoxide. These gases which are referred to as nitrous gases are constantly released from the solution. Therefore, the toxic effects of nitric acid cannot be assessed by taking into account the risk of chemical burns alone. Rather, the effects of the nitrous gases being transformation products of the acid have to be

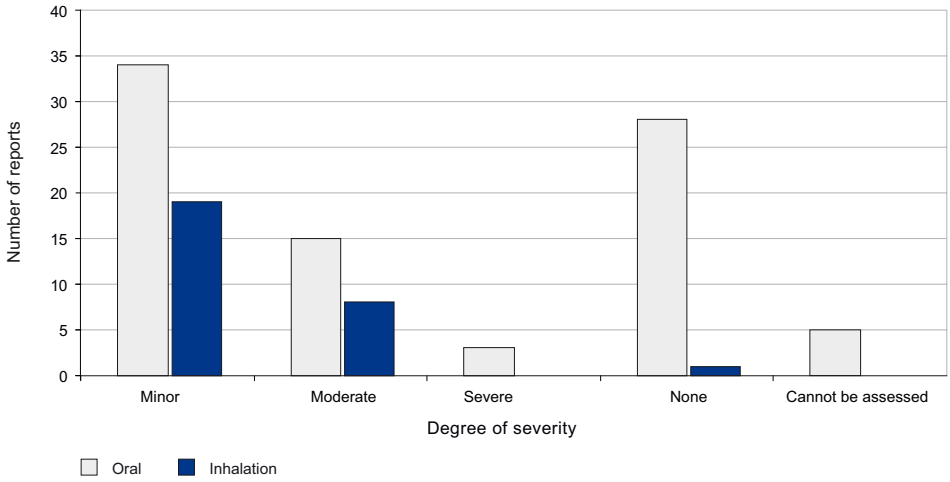


Fig. 8: Accidents caused by exposure to Por Çöz in the 1999-2010 period

included in the considerations. Depending on the concentration of the acid present and the duration of contact, nitric acid will react with surrounding materials, and nitrous gases (mostly nitrogen dioxide) are released. This chemical effect may occur particularly on contact with metals, mainly copper and silver, but also steel (e.g. metal shelves, metallic water pipes, gullies or sinks from cast steel).

Nitrogen dioxide is a gas of red-brown colour and pungent smell. The irritation threshold (for humans) in air is stated to be 20–30 mL/m³. During normal breathing, 80–90 %, and during maximal breathing, more than 90 % are absorbed through the respiratory tract. Based on model calculations, nitrogen dioxide was found to accumulate in the lower airways at the alveolar level. It is absorbed mainly in the lower respiratory tract. There is a variety of effects of nitrogen dioxide but in most cases, this gas will act as an irritant. In addition, there is a genotoxic and carcinogenic potential. In aqueous solution, the nitrogen dioxide radical may react with amines, forming genotoxic nitrosamines. Other genotoxic compounds may form by a reaction with aromatic compounds (carcinogenic nitroaromatics, nitropyrene and the polycyclic aromatic hydrocarbon pyrene). The data available from *in vivo* studies are scarce. They have suggested the presence of genotoxic effects in the rat lung. At concentrations of 4–10 mL NO_2/m³, there were indications of tumour-promoting and carcinogenic effects, respectively, in male rats. This is why nitrogen dioxide has been classified as carcinogenic by the German MAK Commission (responsible for the establishment of maximum admissible concentrations at the workplace).

Results from studies with single short-term exposure (maximum four hours) of healthy test persons to nitrogen dioxide concentrations in respiratory air have shown clear indications of pulmonary toxicity (Table 3) and damage to lower lung segments

Manifestations	Dose
Indications of inflammatory reactions	> 0.6 mL/m³
Increase in bronchial reactivity	> 1.5 mL/m³
Changes to lung function (increase in airway resistance)	> 2.0 mL/m³
Bronchitis, bronchopneumonia	25–75 mL/m³
Bronchiolitis and focal pneumonitis	50–100 mL/m³
Lethal obliterative fibrous bronchiolitis	150–200 mL/m³
Lethal pulmonary oedema and asphyxia (methaemoglobinaemia)	> 300 mL/m³

After Greim[3]

Table 3: Effects of nitrogen dioxide in respiratory air: Findings in humans

No adequate data are available that would permit assessment of inhalational exposure during the use of a household cleaner containing nitric acid. Therefore, the possible indoor air concentrations of nitric acid were determined based on three model exposure scenarios under certain assumptions, without calculating the nitrogen dioxide concentrations. Using a special software for exposure assessment (Cons Expo 4.1, RIVM, 2008), it was examined to which extent the indoor air concentration of nitric acid was influenced by application of a relevant quantity (assumed variables: nitric acid concentration 30 %, room size 30 m³, surface treated 1 m², quantity applied 10 g, air exchange rate 0.2/min). The air exchange rate was found to have only little influence on the indoor air concentration.

[3] *Greim H (Hrsg). Gesundheitsschädliche Arbeitsstoffe, Toxikologisch-arbeitsmedizinische Begründungen von MAK-Werten, Loseblattsammlung, 39. Lfg. Deutsche Forschungsgemeinschaft, VCH Verlag Weinheim, 2004.*

On 28 September 2010, based on the assessment of health risks posed by the use of cleaning products containing 20–30 % of nitric acid, BfR recommended that due to the risk of chemical burns, of inhalation of dangerous vapours and the carcinogenicity of the nitrous gases formed, cleaning products containing nitric acid should not be offered for sale to private consumers. The placing on the market of cleaning products containing 20–30 % of nitric acid has been restricted preferentially under § 14 para 2 WRMG due to the urgency of such action.

Regulatory measures with regard to Por Çöz as a cleaning agent containing nitric acid
On 29 October 2010, based on the cases of poisoning by Por Çöz and the BfR risk assessment of nitric acid, UBA informed the EU Commission and the other Member States about the temporary ban on the placing on the German market of the cleaning agent Por Çöz. It was possible to provide the EU with unequivocal evidence of a risk for human safety and health posed by nitric acid in accordance with Article 15 of the Detergents Regulation. As a result, the EU Commission has banned the placing of this product on the market for one year and considers a permanent restriction in the future of the use of nitric acid in consumer goods.

Moreover, based on the knowledge gained from the series of cases involving Por Çöz, BfR has submitted, in the context of the REACH substance evaluation, a CLH report (Proposal for Harmonised Classification and Labelling) to the European Chemicals Agency (ECHA), to achieve an unequivocal labelling and classification of nitric acid on the European level taking into account also its inhalation toxicity in the future.

2.2 "Herbal blends"

For several years now, an increasing number of cases of poisoning have been reported that had been caused by a new fashionable drug named *Spice*. It is a fact that, meanwhile countless products have become available which are referred to as "herbal blends" or "herbal incense blends" under many fun-oriented brand names such as *Spice, Smoke, Monkees go bananas, Lava red, Sweed, DJ Feel the vibe, Maya etc.* (see Fig. 9).

Fig. 9: "Herbal blend"

According to the labelling on the package, these products contain blends of different plants in dried form such as *Canavalia maritima* (Aubl.) Petit-Thouars (syn. C. *rosea* [SW.] DC.) (beach bean), *Pedicularis densiflora* Benth. ex Hook. (Indian warrior), *Leonotis leonurus* (L.) R. Br. (lion's ear, lion's tail, wild dagga), *Zornia latifolia* Sm. (false Marijuana, fake cannabis), *Leonurus sibiricus* L. (honeyweed, Siberian motherworth), among others. Some of these plants are said to have cannabis-like effects and are indeed consumed as cannabis substitutes in their countries of origin, mostly by smoking. However, analysis of some of these "herbal incense blends" revealed that often, none or only some of the plants listed were actually contained in the mixture. Nevertheless, a cannabis-like narcotic effect is observed, in some cases resulting in manifestations of poisoning. Analyses revealed

that in the cases examined, the *Spice* products were mixed with synthetic chemical substances (synthetic cannabinoids) that act on the body in a way similar to that of natural cannabinoids.

Fig. 10: Cannabis plant

Natural cannabinoids are transformation products of terpenophenolic compounds which are contained in the cannabis plants comprising the species, *Cannabis sativa* and *Cannabis indica* (Fig. 10). From the female plants, the resin (hashish) and the shoot tips (in a dried state referred to as marijuana) are obtained. The ingredient determining the value is delta-9-tetrahydrocannabinol (Δ^9-THC). The use of cannabis for medical purposes has a long tradition: In China, it goes back to the 3rd millennium B.C. Dronabinol, a cannabinoid administered today for medical purposes, is produced in a partly synthetic way. The latter, being the active substance contained in the formulation, and nabilone, a fully synthetic THC analogue, being an imported proprietary medicinal product, are used in Germany. Indications include anorexia (absence of appetite) and cachexia (emaciation) in AIDS patients and administration as an antiemetic in patients undergoing cancer therapy. Other fields of application such as glaucoma, ulcerative colitis, Crohn's disease and multiple sclerosis are presently being discussed and in part, examined as a subject of clinical studies. In Germany, the cannabis plant and plant parts as well as marijuana, hashish and Δ^9-THC/dronabinol/nabilone are regulated by the Narcotics Act (Betäubungsmittelgesetz).

The effects of cannabinoids are mediated through cannabinoid receptors composing the endogenous cannabinoid system of the body together with the body's own ligands such as anandamide. Depending on the dose, the action mediated by the cannabinoid receptor type 1 (CB1) receptors found predominantly in central and peripheral nerve cells will result in effects similar to inebriation such as mood elevation, euphoria and others, but also effects desired for therapeutic purposes such as analgesia, stimulation of appetite and antiemesis. Undesirable initial side effects may include tachycardia, mydriasis, and increase in blood pressure. Later on, nausea, vomiting, dry cough, anxiety, ataxia, tremor, cardiac dysregulation and peripheral circulatory disturbances may be experienced. Cannabinoid receptor type 2 (CB2) receptors are found in immune cells. They are presumed to have immunomodulating functions.

In the cases of poisoning by "herbal blends" reported to BfR, the manifestations observed ranged from dry mouth, mydriasis and somnolence to dizziness, tachycardia, nausea and vomiting to clouding of consciousness, electrolyte imbalance and convulsions of cerebral origin. In the majority of these cases, the typical symptomatology of a pronounced THC/cannabis poisoning was observed (see above). All patients were admitted to hospital and kept under observation.

The ways how and the places where these products are produced have so far remained largely unknown. Obviously, the drugs containing cannabinoids are mixed with synthetic cannabinoids. To this purpose, the latter are presumably dissolved in an organic solvent to be subsequently sprayed onto the dried plant material. In contrast to their declaration, the "herbal blends" or "incense blends" are, as a rule, not used as incense but smoked as joints or by means of water pipes, sometimes also mixed with tobacco, and

sometimes ingested as an infusion. In Europe, such products are predominantly sold via the internet, but also in head shops, smart shops, sex shops and at petrol stations. They are offered as "incenses" or "natural cannabis substitutes" containing a legal and thus apparently harmless mixture of herbs. Synthetic cannabinoids pose a risk because there has hardly been any research into their potential action, and their pharmacological potential is assumed to exceed that of THC by far. In contrast to THC, some substances are full CB1 receptor agonists (higher binding affinity), are potential carcinogens and have longer half-life periods. These properties involve a risk of fatal overdosage.

Although the action of synthetic cannabinoids resembles that of THC, their structure clearly differs from that of natural cannabinoids in most cases. A distinction is made between different series of substances: THC analogues (structurally related to THC), e.g. HU-210, the CP series (developed by Pfizer in search for new analgesics) including CP 59,540, CP 47,497 and homologues; the substances first synthesized by J. W. Huffman of the series named after him JWH, e.g. JWH-015, JWH-018, JWH-073, JWH-250, JWH-398, and the substances developed by Sterling/Winthrop such as WIN-55212-2, substances of the AM (Alexandros Makriyannis) series such as AM-2201, and RCS substances.

However, what makes these products so interesting? Many consumers are interested in the supposedly biological and in addition "legal" narcotic substances. They want to try something new, being inter alia inspired by media reports on the new herbal fashion drugs. Moreover, in contrast to marijuana or hashish, rapid drug testing may fail to detect their use. Meanwhile, awareness of the problem has resulted in banning of these substances in many countries. In Germany, JWH-018, JWH-019, JWH-073, CP 47,497 and homologues were included in the listing of Annex II to the Narcotics Act in 2009. Already since 2008, the European Monitoring Centre for Drugs and Drug Addiction has operated a programme for the monitoring of *Spice* products. After the publication by J. W. Huffman et al.[4] on pathways of synthesis of a number of these substances, it appears to be easy to synthesize derivatives with similar effects in order to circumvent current legal regulations. In the case of such flexible opponents, legal measures will therefore always come too late, and the problem of poisoning due to these products will not lose its topicality.

"Herbal blends": Cases of minor health impairment

Case No. 1
A young male stated to have smoked a "herbal incense blend" with abusive intent. As a result, he developed mild toxic symptoms and was admitted to hospital.

Manifestations/course
The patient was admitted to hospital with manifestations of nausea, somnolence and mydriasis and kept under observation. No complications were observed so that he could be discharged.

Case No. 2
A young female reported to have smoked a substance declared as harmless. Because her general condition deteriorated, she sought help at a hospital.

[4] *Huffman JW, Mabon R, Wu MJ, Lu J, Hart R, Hurst DP, Reggio PH, Wiley JL, Martin BR. 3-Indolyl-1-naphthylmethanes: New Cannabimimetic Indoles Provide Evidence for Aromatic Stacking Interactions with the CB1 Cannabinoid Receptor. Bioorganic & Medicinal Chemistry 2003; 11: 539–549.*

Manifestations/course
She was admitted to hospital with nausea, vomiting, abdominal cramps and disturbances of consciousness. After these manifestations had receded she could be discharged.

Case No. 3
A young male stated to have smoked a joint and a "herbal blend" one day before. On the same day of his report he stated to have only smoked the "herbal blend" and as a result, experienced health complaints.

Manifestations/course
He was admitted to a hospital for inpatient treatment where he developed tachycardia and hyperventilation. He was kept under observation and later could be discharged in the absence of complications.

Case No. 4
A young female had smoked an "incense preparation" purchased at a head shop. Later, she presented at the emergency ward of a hospital.

Manifestations/course
At the hospital, she experienced hallucinations in addition to agitation. As these manifestations did not deteriorate, the patient could be discharged.

Case No. 5
After having spent a night at a hospital, a male adolescent, obviously a body builder, reported to have consumed a "herbal blend" on the evening before.

Manifestations/course
At the hospital, the patient appeared bradyphrenic, and the analysis of blood levels revealed electrolyte imbalance, thrombocytopenia and leukocytosis. In this context, however, a possible association of findings with a probable consumption of "restoration supplements" should be taken into account. Regrettably, unambiguous elucidation was impossible in this respect. The young male could be discharged in the absence of further complaints.

Case No. 6
A male adolescent had smoked a "herbal blend" in a pipe and was admitted to hospital due to health complaints.

Manifestations/course
The patient developed somnolence and mydriasis. No deterioration was observed, and he could be discharged.

Case No. 7
A female adolescent had smoked a "herbal blend" on the evening before the day when she developed manifestations of disease.

Manifestations/course
The patient complained of tachycardia, nausea, visual disturbance in the form of double vision, dizziness and headache. At the hospital she was found to be free from manifestations. She stayed at the hospital for one night and was kept under observation. No complications were observed so that she could be discharged on the next day.

Case No. 8
A young male stated to have smoked a "herbal blend" during the day. He was unable to remember the precise time when this took place. In the evening, he developed complaints.

Manifestations/course
At the hospital, the patient developed tachycardia and conjunctivitis and appeared bradyphrenic. He could be discharged later without having developed further manifestations.

Case No. 9
A young male had consumed alcohol and the contents of a "sachet" purchased via the internet. This "sachet" was presented by him to the emergency physician at the hospital.

Manifestations/course
At the hospital, the patient showed tachycardia, dizziness, unrest and mydriasis. He was treated by administration of diazepam. As a result, tachycardia receded soon. He stayed at the hospital for one night without developing any further manifestations.

Assessment of cases No. 1–9
Based on the information given on the temporal and spatial relationship between exposure and the occurrence of the manifestations observed, and in the absence of other causes, a causal relationship has been rated as possible.

Case No. 10
A young female had smoked a "herbal blend" labelled as Car Perfume with abusive intent. This resulted in vomiting, dizziness and anxiety attacks so that she had to be admitted to hospital for inpatient treatment.

Manifestations/course
At the hospital, the patient did no longer show any manifestations so that she could be discharged.

Case No. 11
An adolescent was admitted to hospital for detoxification after excessive alcohol consumption.

Manifestations/course
On the next day, at the hospital, he reported to have consumed a "herbal blend" by inhalation on the afternoon of the day preceding his hospitalization. He stated to have not noticed any changes of his condition at that time. At the hospital he showed a typical symptomatology of alcohol intoxication including drowsiness. No deterioration was observed and no further symptoms developed so that he could be discharged.

Assessment of cases No. 10 and 11
Based on the information given on the temporal and spatial relationship between exposure and the occurrence of the manifestations observed, and in the absence of other causes, a causal relationship has been rated as probable.

"Herbal blends":
Cases of moderate health impairment

Case No. 12
A young male had smoked 0.5 g of a "herbal blend" and subsequently developed symptoms persisting for more than two hours. Therefore he presented at a hospital and brought the "sachet" with him.

Manifestations/course
The patient complained of tachycardia, tinnitus, episodes of sweating, a dry mouth and recurrent vomiting. All symptoms soon receded and no further complications developed during his stay at the hospital.

Case No. 13
An adolescent had consumed a "herbal blend" with abusive intent. He suffered a convulsive seizure and was admitted to a hospital.

Manifestations/course
At the hospital, the patient woke up and became responsive, and he reported to have consumed a cannabis-like "herbal blend". He remained at the hospital for observation, however, without developing further symptoms.

Case No. 14
A young male had smoked a "herbal blend" and subsequently suffered a convulsive seizure.

Manifestations/course
He presented at a hospital where no further manifestations were found. Since the patient had a history of repeated convulsive seizures he was admitted as an inpatient and kept under observation. No complications were observed so that he could be discharged.

Assessment of cases No. 12–14
Based on the information given on the temporal and spatial relationship between exposure and the occurrence of the manifestations observed, and in the absence of other causes, a causal relationship has been rated as possible.

Comments
So far, BfR has received reports on 15 cases due to an abuse of synthetic cannabinoids. Of these, 11 were classified as "minor", three as "moderate" and one as "cannot be assessed". The consumption of such substances has been observed among the age groups of adolescents and young adults.

The cases described have shown a wide range of manifestations. These include, among others, unrest, tinnitus, headache, episodes of sweating, dry mouth, dizziness, nausea, vomiting, abdominal cramps, conjunctivitis, visual disturbance, mydriasis, disturbances of consciousness, anxiety attacks, tachycardia, hyperventilation, electrolyte imbalance and convulsive seizures. Such variety of adverse effects has to be attributed to the composition of the respective "herbal blend" involved and will also depend on the structure of the synthetic cannabinoids consumed (see introduction to this Chapter). For example, "herbal blends" containing JWH-18 may cause a variety of symptoms, but nervous or muscular symptoms or hypokaliaemia cannot be attributed to this synthetic cannabinoid. Only a combination of e.g. JWH-18, JWH-122 and JWH-150 will result in the entire range of symptoms to develop. In the majority of cases, manifestations observed after the consumption of "herbal blends" resembled those typical of cannabis intoxication. However, convulsive seizures and the decrease in potassium levels mentioned have not been reported so far after THC consumption and therefore, should be rated as obvious warning signals.

The cases described have also illustrated the delayed onset and the duration of effects of the "herbal blends" consumed by smoking. However, the manifestations receded after 4 to 14 hours. Altogether, the composition of synthetic cannabinoids has to be characterized as very heterogeneous. Therefore, a differentiated analysis is of essential importance. Other factors to be considered include possible synergistic effects in combination with other substances such as medicinal products or "natural" cannabis. Further research is required in this field.

Due to particular difficulties regarding the procedure to detect such "herbal blends", progress in passing the relevant legislation has been rather hesitant. This is why consumers face a double risk: Although such "herbal blends" appear to be licit drugs, consumers buying them not only bear the risk of poisoning but also of coming into conflict with the law.

2.3 Amanitas (*Amanita spp.*)

Every year, with the onset of the mushroom season in late summer, cases of poisoning occur because inedible or poisonous mushrooms are mistaken for edible ones. In this respect, representatives of the genus, Amanita Pers. are of particular importance. The species to be mentioned first is *Amanita phalloides* (Vaill. ex Fr.) Link, commonly known as the death cap (Fig. 11). This species alone accounts for 80–90 % of all fatal mushroom poisonings in central Europe.

characteristics. However, they are found less often in central Europe. Well-known amanitas found quite frequently include *Amanita pantherina* (DC.) Krombh, commonly known as the panther cap (Fig. 12), and *Amanita muscaria var. muscaria* (L.) Hook., commonly known as the fly agaric (Fig. 13). Manifestations of poisoning by these two species are similar, albeit more pronounced for the panther cap. Poisoning by these mushrooms will not be fatal, as a rule.

Fig. 11: Death cap (Amanita phalloides)

Fig. 12: Panther cap (Amanita pantherina)

In 2010 alone, BfR received 12 reports on death cap poisoning. Six of these had to be classified as severe. Due to this fact, the problem of poisoning by death caps and other amanitas has been discussed in this report as a special topic.

In addition to the death cap, also other representatives of the Amanita genus have played a role in terms of poisoning incidents, although to a lesser extent, either due to a less frequent occurrence or lower toxicity. *Amanita verna* (Bull.) Lam., commonly known as the fool's mushroom, which possibly is just another variety of the death cap, as well as *Amanita virosa* (Fr.) Bertill, commonly known as the destroying angel, correspond to the death cap in their toxicological

Fig. 13: Fly agaric (Amanita muscaria)

Amanita citrina (Schaeff.) Pers., commonly known as the false death cap (Fig. 14) is poisonous only if eaten raw. In 2010, BfR received reports on one mild case of poisoning by *Amanita pantherina* and another one involving *Amanita strobiliformis* (Paulet ex Vittad.) Bertill.

Fig. 14: False death cap (Amanita citrina)

The cap of *Amanita phalloides* is 5–15 cm in diameter. In a dry state, the skin has a silky shine and is easily peeled. The colour may vary, ranging from yellow-green over various shades of green to olive, also whitish pale with increasing age. When young, the fruiting body is enveloped in a veil (membrane).

The stipe of adult specimens is 5–15 cm long, up to 2.5 cm thick and white with a scattering of greenish scales. The stipe has a bulbous base which is enclosed in a white volva. This volva and the white collar found in the upper third of the stipe are important features to reliably distinguish the mushroom from edible or less poisonous mushrooms.

The gills, the spore powder and the flesh of the fruiting body are white, the smell is sweet resembling that of artificial honey, and the taste has been described as nutty.

This fungus preferentially grows in deciduous or mixed deciduous woodlands as a mycorrhizal fungus associated with oaks and other deciduous trees. The death cap is only remotely similar to a number of other mushrooms some of which are edible, like the field mushroom (*Agaricus campestris*), the man on horseback or yellow knight (*Tricholoma equestre*/*Tricholoma flavovirens*) or the greasy green brittlegill (*Russula heterophylla*). Nevertheless, it has been ingested in mushroom meals again and again, sometimes with deadly consequences.

Of the toxic substances found in amanitas the most important ones are the amatoxins. Already amounts as low as 5–7 mg, corresponding to less than 50 g of fresh mushrooms, may be fatal in adults. Children may die from quantities of only 1/20 of the lethal dose for adults. BfR was informed about a case in a young child who died after ingestion of a piece of fresh dead cup having the size of a small finger nail. The component most relevant in toxicological terms is amanitin, a cyclic octapeptide acting as an RNA polymerase inhibitor in the liver cells. It inhibits the formation of messenger RNA and thus, protein synthesis, eventually leading to the death of liver cells. A major part of amanitin is excreted into the bile, and a certain part also eliminated via the renal route. Another part, however, is re-transported to the liver by an enterohepatic circulation, meaning an additional increase in and prolongation of the hepatotoxic effects.

The poisoning symptomatology also referred to as the phalloides syndrome is characterized by a quadriphasic course (Table 4). After an initial asymptomatic latency phase, first complaints will be experienced including vomiting and cholera-like diarrhoea over a period of 11–24 hours (gastrointestinal phase). This is typically followed by a phase of apparent wellbeing with receding symptomatology. However, already two to three days later, liver cell necrosis may set in. After about five days without treatment, during the hepatorenal phase, death will occur as a

consequence of liver dystrophy, hepatic coma and/or the loss of renal function, in most cases becoming manifest as multiple organ failure.

The most reliable criteria for diagnosis include the determination of transaminase levels and prothrombin time (Quick's value) in the blood and amanitin detection in the blood and/or urine. To confirm the diagnosis, also the analysis of leftovers of the mushroom meal or mushrooms by a mycologist and the detection of spores in gastric contents or stools play an important role.

Among the therapeutic measures to be taken, primary detoxification by means of activated charcoal as well as compensation for the loss of fluid by electrolyte infusions are of paramount importance. In cases of minor vomiting and/or bowel movements, gastric evacuation by gastric lavage or forced diarrhoea by means of sodium sulphate or lactulose may be important. As a supporting measure, a duodenal tube may be inserted for continuous suction of bile and thus, removal of amatoxins. As an antihepatotoxic therapy of choice, administration of silibinin, being an ingredient of the milk thistle, *Silybum marianum* (L.) Gaertn., or milk thistle extract has become established. Intravenous administration is carried out by two-hour infusions four times a day with a daily dose of 20 mg/kg body weight. On the one hand, this will result in a stabilization of cell membranes and thus, reduce the penetration of poison into the liver cells, which in turn will interrupt the enterohepatic circulation of amatoxins. On the other, the formation of ribosomal RNA is stimulated. This will increase the synthesis capacity of the liver cells. Such treatment should be initiated as soon as possible also in cases of suspected poisoning since pathological changes in laboratory parameters may set in with a delay. As a supporting measure to prevent or treat hepatic coma, the administration of high doses of acetylcysteine (ACC) has been tried and tested. In cases of irreversible liver damage, liver transplantation should be considered early enough as a measure of last resort. The administration of milk thistle preparations has resulted in a considerable increase in survival rates. At the same time, the number of liver transplantations required due to complete hepatic failure after amanita poisoning has dropped markedly.

Phase	Time of onset/duration	Manifestations
I: Latency phase	5–24 hours (–48 hours)	None
II: Gastrointestinal phase	After 6–60 hours; duration 11–24 hours	Vomiting, diarrhoea, exsiccosis, drop in blood pressure, abdominal pain
III: Quiescent phase	After 24–72 hours; duration 2–24 hours	Swelling of the liver, onset of necrosis and of renal insufficiency
IV: Hepatorenal phase	After 5–7 days	Hyperbilirubinaemia, pressure sensitivity of the liver, icterus, coagulation disorders, liver dystrophy, hepatic coma, renal failure, circulatory failure

Table 4: Phases of the phalloides syndrome after Scholer, Regeniter [5]

[5] *Scholer A, Regeniter A. Intoxikationen mit Amanitinen (Knollenblätterpilz). Toxichem + Krimtech 2000: 67(3); 98–104.*

2.3.1 Amanitas (*Amanita spp.*): Cases of minor health impairment

Case No. 1
An elderly female had collected and consumed mushrooms and afterwards, developed nausea, abdominal cramps and vomiting.

Manifestations/course
At the emergency unit, the patient was immediately administered charcoal, Glauber's salt and silibinin. On admission to the normal ward of the hospital, the patient was asymptomatic and remained so for the entire duration of her stay. Silibinin therapy by the i.v. route was continued and could be terminated after five days. Clinical chemistry revealed elevated bilirubin levels of max. 1.5 mg/dL (reference range: <1 mg/dL), elevated transaminase levels of GPT max. 215 U/L (reference range: < 34 U/L), GOT max. 204 U/L (reference range: < 35 U/L) and elevated gamma GT of max. 262 U/L (reference range: < 38 U/L). Quick's value was not reduced at any time. Neither physical examination nor sonography resulted in any pathological findings that might have been caused by amanita poisoning. After six days, the patient could be discharged and referred to outpatient treatment, which included follow-up analysis of liver parameters.

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

Cases No. 2 and 3
A pair of friends had collected mushrooms in September. Both had ingested a small piece of a mushroom resembling a button mushroom. About 45 minutes later, they experienced a burning sensation in the oesophageal and gastric regions lasting for 5 minutes.

Except for these, no other complaints were reported. They sought medical assistance at a hospital.

Manifestations/course
On admission to the first hospital, the immunological test for alpha-amanitine was positive, and a single dose of 50 mg charcoal was administered. The patients were transferred to a transplantation hospital and kept under observation. On admission, both were found in a very good general condition, awake, completely capable of orientation and showing adequate reactions. Also in the further course, they remained asymptomatic and did not develop any nausea, vomiting or diarrhoea. Due to the confirmed alpha-amanitin poisoning, either of them was administered a total dose of 350 mg silibinin i.v. Clinical chemistry revealed only a slight increase in bilirubin levels in the patients (female: max. 2.1 mg/dL, male: max. 1.5 mg/dL). After one night spent at the transplantation hospital, the patients could be discharged and referred to outpatient treatment including further follow-up examinations.

Case No. 4
An elderly male had collected and prepared some mushrooms for himself. He ingested an amount of ca. four tablespoons of the meal. On the next morning he developed massive watery diarrhoea. Therefore, he presented to an emergency department.

Manifestations/course
Blood analysis revealed elevated transaminase levels (max. GPT 134 U/L). A tentative diagnosis of amanita poisoning was made immediately. As a prophylactic measure, the patient was administered a single dose of charcoal and 350 mg of silibinin i.v. The tentative diagnosis was confirmed by toxicological urine analysis for amanitin. The patient was admitted to the intensive care unit of a transplantation hospital.

He was administered high doses of ACC, glucose infusions, vitamin K and silibinin i.v. As a result of such treatment, transaminase levels returned to normal and the watery diarrhoea stopped. Coagulation remained stable at any time. Both ACC and silibinin administration were discontinued during inpatient treatment. The patient could be discharged in an asymptomatic state and was referred to outpatient care. Follow-up examinations included analysis of transaminase levels and abdominal examination by sonography.

Case No. 5
A young female had collected mushrooms in late summer. In the evening she prepared a soup using about one kg of mushrooms of which she ate about one helping (soup plate). On the next morning, she developed nausea, vomiting and diarrhoea. Therefore, she sought medical attendance at a hospital.

Manifestations/course
Because of the elevated transaminase levels, the patient was immediately administered 400 mg silibinin and in addition, lactulose, paromomycin and an infusion therapy. Amanitin was detected in the urine by toxicological analysis. Due to a further increase in transaminase levels (GPT max. 188 U/L, GOT max. 84 U/L), the patient was transferred to a transplantation hospital. On admission to the latter, she was in a stable condition. Silibinin therapy as well as the additional administration of vitamin K, glucose and ACC were continued. As a result, transaminase levels became markedly reduced, and also nausea and abdominal cramps were no longer observed. The coagulation status did not show any pathological changes at any time. After five days, the patient could be discharged and referred to outpatient treatment.

Assessment of cases No. 2–5
Based on the information given on the temporal and spatial relationship between exposure and the occurrence of the manifestations observed, and in the absence of other causes, a causal relationship has been rated as confirmed in the cases described.

2.3.2 Amanitas (*Amanita spp.*): Case of moderate health impairment

Case No. 6
On a late summer evening, an elderly female had prepared a meal of mushrooms she had collected for herself. She ate about half a tablespoon of this meal. On the morning of the next day, she developed acute diarrhoea and vomiting. As late as two days afterwards, the patient presented to a hospital.

Manifestations/course
At this time, markedly elevated transaminase levels were found. The patient was administered silibinin every 8 hours and a dose of 10 million IU penicillin. Her condition deteriorated further, and in addition, a clouding of consciousness set in. Therefore, she was transferred to the intensive care unit of a transplantation hospital.

The patient mainly complained of colicky abdominal pain and diarrhoea, which, however, receded under administration of silibinin, ACC and volume replenishment. Also her elevated transaminase (GPT max. 926 U/L and GOT max. 1 079 U/L) and bilirubin levels (max. 1.6 mg/dL) showed a decreasing tendency, and her reduced Quick's value of min. 51 % (reference range 70–130 %) returned to normal so that she could be transferred to a normal ward. As a secondary finding, the patient developed an uncomplicated urinary tract infection requiring administration of ciprofloxacin. Altogether, her general condition improved so that she could be transferred to a hospital close to her place of residence.

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

2.3.3 Amanitas (*Amanita spp.*): Cases of severe health impairment

Case No. 7
On the day following consumption of a mushroom meal, a young female had developed vomiting, abdominal cramps and diarrhoea (up to 14 stool discharges). Therefore, she presented to a hospital.

Manifestations/course
At the hospital, elevated transaminase levels were found and one single dose each of silibinin and charcoal was administered. Subsequently, the patient was transferred to the intensive care unit of a transplantation hospital. There she developed a massive increase in transaminase levels (GPT max. 5 647 U/L, GOT max. 5 893 U/L) and a drop in Quick's value to 37 %. Under i.v. silibinin and ACC administration as well as volume replenishment, the laboratory parameters and symptomatology showed an improvement. The patient could be transferred to the normal ward. However, intermittent abdominal colicky pain and diarrhoea (2–3 discharges a day) persisted. In the further course of inpatient treatment, the diarrhoea stopped and pain symptomatology receded. Liver sonography revealed a normal status, and silibinin administration could be discontinued. After eight days, the young female could be discharged in a good general condition and referred to outpatient follow-up care.

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

Case No. 8
In late summer, an elderly male had prepared a supper from mushrooms he had collected himself. He ate ca. six tablespoons of the dish accompanied by three beers. On the next morning, he developed acute diarrhoea and vomiting. Two days later, he presented at a hospital.

Manifestations/course
At the time of his admission, the patient's transaminase levels were markedly elevated, and death cap poisoning was diagnosed. The patient was administered silibinin every eight hours and 10 Million IU penicillin. His condition deteriorated further, and in addition, clouding of consciousness set in. Therefore, he was transferred to the intensive care unit of a specialized hospital.

The patient's history of chronic alcohol abuse resulted in a protracted course, and transaminase levels continued to increase (GPT max. 3 990 U/L, GOT max. 4 775 U/L). Bilirubin levels increased up to 8.7 mg/dL, and coagulation parameters showed abnormal values with a 33 % Quick's value and 46.4 sec. PTT (partial thromboplastin time, reference range: 26–40 sec.). However, these parameters returned to normal under the therapy comprising the administration of silibinin, ACC and volume replenishment. On the morning of the fifth day of inpatient treatment, the patient complained of angina pectoris symptoms such as a sensation of chest tightness and cardiac pain also radiating into his left arm. Cardiac catheter examination revealed third-degree coronary heart disease, which required coronary balloon angioplasty to widen the coronary blood vessels. There were no more complications during the postoperative course so that the patient could be transferred from the intensive care unit to a normal ward. On admission he was found awake and capable of orientation, slightly bradyphrenic and in a moderate general and nutritional condition.

Silibinin administration could be discontinued soon. However, the patient developed a urinary tract infection associated with increasing inflammatory parameters requiring another targeted administration of the antibiotic, ciprofloxacin. The patient could be transferred to a hospital close to his place of residence while continuing the antibiotic treatment, cardiac medication and ornithine aspartate therapy which had been initiated earlier due to a tentative diagnosis of alcohol-related hepatic encephalopathy associated with elevated ammonia levels.

Case No. 9
A young male had prepared a soup from mushrooms he had collected himself. He consumed about 1–2 bowls of this soup together with two bottles of beer. On the next morning, he developed nausea, vomiting and diarrhoea. Therefore, he presented at a hospital.

Manifestations/course
At the hospital, transaminase levels were found to be elevated and therefore, 400 mg silibinin, lactulose, paromomycin and plasma substitute were administered immediately. The toxicological testing for amanitin was positive. Because transaminase levels continued to increase it was decided to transfer the patient to the intensive care unit of a transplantation hospital. The maximum transaminase levels (GPT 2 626 U/L, GOT 1 255 U/L) decreased under continued silibinin and ACC administration and vitamin K glucose infusions so that the young male could be transferred to a normal ward. Coagulation levels did not show any changes at any time. Sonographic findings of the liver and liver vessels were normal. After having spent six days at the transplantation hospital the patient could be discharged in a good general condition and referred to outpatient follow-up care.

Case No. 10
A female had collected and eaten mushrooms. On the next day, she had developed shivers, nausea, vomiting and diarrhoea. Due to a tentative diagnosis of death cap poisoning, she was brought to the intensive care unit of a transplantation hospital by emergency ambulance.

Manifestations/course
On admission to the intensive care unit, the patient was found awake, in a stable cardiopulmonary condition and reacted in an adequate way. Amanita poisoning was confirmed by toxicological examination detecting amanitin in the urine. The therapy included administration of charcoal, Glauber's salt, silibinin, ACC and glucose infusion, as well as a symptomatic treatment of the patient's abdominal complaints. When her complaints had receded, the patient could be transferred to the normal ward. When transaminase levels (GPT max. 2 784 U/L, GOT max. 1 044 U/L) had decreased and the Quick's value (min. 49 %) had increased, the i.v. administration of silibinin and ACC was discontinued. Hypokaliaemia (3.0 mmol/L) had been caused most probably by protracted hypovolaemia as a result of vomiting and diarrhoea. A silibinin-induced hypokaliaemia could not be confirmed. A return to normal values could soon be achieved by oral potassium substitution. After 10 days of inpatient treatment, the patient could be discharged in a good general condition and referred to outpatient care.

Case No. 11
A female had ingested death caps with suicidal intent. She developed diarrhoea and was admitted to an emergency ward for internal medicine.

Manifestations/course
From the emergency ward, she was transferred to the intensive care unit of a transplantation

hospital. Urine testing for amanitin was positive. The Quick's value dropped to 39 %, and transaminase levels increased to GPT max. 6 953 U/L and GOT max. 6 228 U/L. The patient was administered one course of dialysis due to incipient perirenal failure, which was associated with her history of concomitant lupus erythematosus involving the heart, CNS and kidneys. Owing to continued silibinin therapy, the transaminase levels decreased rapidly, the Quick's value increased and diarrhoea receded. As a result, the patient could be transferred to a normal ward. Ten days later, the silibinin therapy she received at this ward could be discontinued. Abdominal sonography revealed a pronounced steatosis of the liver, which required outpatient follow-up examination of liver parameters. Initial pollakisuria (frequent urination of small amounts) associated with urinary tract infection receded after administration of ciprofloxacin. After eleven days, the patient could be discharged in a stable general condition and referred to outpatient care.

Assessment of cases No. 8–11
Based on the information given on the temporal and spatial relationship between exposure and the occurrence of the manifestations observed, and in the absence of other causes, a causal relationship has been rated as confirmed in the cases described.

Case No. 12
An elderly woman had collected mushrooms and consumed a meal prepared from these in the evening. During the following night, she developed vomiting and diarrhoea. She was admitted to the monitoring ward of a hospital.

Manifestations/course
At this ward, silibinin administration was initiated immediately after consultation of a poison information centre. The clinical manifestations receded noticeably. However, no urine could be collected for toxicological confirmation. Clinical chemistry revealed a massive increase in transaminase levels and a decrease in Quick's value. Therefore, the patient was transferred to a transplantation hospital one day later with a tentative diagnosis of amanita poisoning. There, the patient died from amanita poisoning as the suspected cause of death. The exact cause of death has remained unknown to BfR.

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

Comments
In the twelve cases of amanita poisoning reported to BfR, the laboratory parameters relevant in terms of toxicology have been obvious. In the cases described, the criteria for a reliable diagnosis mentioned in the introduction to this Chapter were fulfilled. The determination of transaminase levels and prothrombin time (Quick's value) always revealed typical changes. These also represent the most important laboratory parameters to be considered for a decision about the necessity of a liver transplantation.

In addition, special studies after Ganzert et al.[6] have shown the combination of prothrombin time and creatinine levels in the serum considering certain limit values over a defined period to provide better evidence for the purpose of a reliable indication for liver transplantation. In this retrospective study carried out in 2005, laboratory-specific parameters were measured and compared in 198 patients suffering from amanita poisoning. The main result of the study was that a combination of prothrombin index and serum creatinine was significantly more powerful as a predictor of a possible fatal outcome

[6] *Ganzert M, Felgenhauer N, Zilker T. Indication of liver transplantation following amatoxin intoxication. J Hepatol. 2005; 42: 202–209.*

than were other parameters such as bilirubin and GPT levels. The recommendation derived from this study is as follows: The indication of liver transplantation should be considered as confirmed if between the third and tenth day after the ingestion of poisonous mushrooms the prothrombin value is lower than 25% and the serum creatinine level higher than 106 µmol/L. Patients in whom the above mentioned limits for both parameters had been exceeded died.

Amatoxins can be detected by different methods. The best-known and most widely used methods are briefly described below. The probably most prominent test is referred to as the Wieland test (also known as Wieland-Meixner or Meixner test). Of the mushroom material to be tested, a small amount of juice is squeezed onto the unprinted margin of a newspaper (it is important for the paper to contain wood). When the spot formed in this way has become dry, 1–2 drops of 10–20% hydrochloric acid are placed on it. In the presence of more than 0.02 mg amatoxin per mL, a bluish-pink colour will appear after 5–10 minutes. This test uses the known formation of pigments by indole compounds reacting with aromatic aldehydes. The pigments are liberated due to the reaction of the concentrated hydrochloric acid with the lignin contained in the newsprint. It has to be taken into account, however, that mushrooms may contain also other indole compounds in addition to amatoxins and phallotoxins. Therefore, false-positive test results may be obtained from harmless mushrooms. Conversely, a missing coloration must not be interpreted as the tested mushroom species being non-poisonous. The value proper of this test method is to enable a simple identification of mushrooms so far unknown to contain amatoxin and a rapid testing for orientation about a risk of amanita poisoning. It is applicable only where there are leftovers of the fresh mushrooms available. Such test should always be followed by a more detailed chromatographic or biochemical analysis to confirm or disprove the information obtained initially.

An immunological method frequently used to detect toxins is the radioimmunoassay (RIA). This test is based on the immunological properties of the amatoxins and phallotoxins.

To this purpose, iodine nuclide (^{125}I) is added to the patient sera to be tested. The specific antibodies contained in the sera will then bind to the labelled antigen. Subsequently, the antigen-antibody complexes formed are precipitated by chemical reactions. When the chemical equilibrium is achieved, radiolabelled amanitin will accumulate in the test solution, its amount depending on the concentration of toxins in the analyte solution. Finally, radioactivity is measured by means of a scintillation counter. The intensity of radioactive radiation measured will be proportionate to the concentration of the specific mycotoxins in the patient's serum. The detection limit is as low as 3 ng/mL of analyte solution.

Another method, which above all is less time-consuming than the RIA, is offered by the enzyme-linked immunosorbent assay (ELISA). This test is carried out without using radionuclides, and first results are obtained already within one hour. ELISA is based on the specific recognition reaction between the antigen and antibody, coupling it to an enzyme-controlled colour reaction. This test method is referred to as a sandwich assay: Initially, the test substance sample (e.g. patient's serum) is applied onto a carrier material already coated with the specific antibodies. After rinsing, antibody is added which is specific to the same substance but in addition, coupled with an enzyme. If the substance in question is present in the sample, an antibody-antigen-antibody "sandwich" is produced. The last step after rinsing will result in an enzyme-linked colour reaction. Upon adding a precursor, which as a substrate for the enzyme reacts to form a colorant, the colour of the substrate will change if the substance to be detected is present. Hence, a change in colour is only observed if the enzyme is retained in the sandwich, i.e. in the presence of the toxin to be detected.

In addition, there are several instrumental-analytical detection methods, e.g. chromatographic techniques such as high-performance (or pressure) liquid chromatography (HPLC) and a combination of liquid chromatography and mass spectrometry, referred to as liquid chromatography-mass spectrometry (LC-MS) or high-performance (or pressure) liquid chromatography-mass spectrometry (HPLC-MS).

3 Case reports

3.1 Magic Nano impregnation spray

Severe inhalation poisoning associated with pulmonary oedema after exposure to impregnation spray

In 2010, a female used a surface impregnation spray she had bought in 2006. Soon after she had applied the spray, she developed acute dyspnoea and fever so that she had to be admitted to a hospital.

Manifestations/course

On admission, the blood oxygen saturation level was 70 % only. The patient developed the clinical picture of pneumonitis with incipient toxic pulmonary oedema. Under conditions of a permanent readiness for intubation, the patient received a conservative therapy including administration of glucocorticoid and furosemide. As a prophylactic antibiotic therapy, ceftriaxon was administered for seven days. After this treatment, the patient was free from residual manifestations and could be discharged.

Evaluation of the case described

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

Comments

The case described has shown in an impressive way that severe poisoning accidents may occur even four years after the harmful effects of the Magic Nano impregnation sprays on human health had become known. In 2006, two surface-sealing sprays had been placed on the market by a major chain of discount shops, accompanied by an advertising campaign. Within 24 hours after the first cases of health impairment had become known, these products were removed from the shelves upon intervention by BfR jointly with poison information centres. During the period between 27 March and ca. 10 April 2006, partially severe health impairments such as cough, dyspnoea and in single cases, toxic lung oedema were experienced by ca. 170 consumers. To date, BfR has received 195 reports on these sprays demonstrating undesirable health effects in consumers due to inhalation. The pattern of manifestations resembled the series of cases experienced in the past which occurred after the use of impregnation sprays in 1982/83 (Germany) and 2002 (Switzerland and the Netherlands). Extensive research into the formulations of the new surface sealant sprays revealed a great similarity of the chemical spectrum of the relevant components with that of the impregnation sprays. Hence, the symptomatology seen after inhalational exposure corresponded to that of the known “impregnation agent syndrome”. However, it was found that, in contrast to the claims made by the advertising campaign, no “nano particles” were contained in the products. The term “nano” was meant to refer to the ultrafine water and dirt repelling film formed in a chemical reaction of silanes, which constituted the active ingredients. Silicon is the basic atom of silanes. As a result of an atomic bond between silicon and carbon, organosilanes may form, which are used to functionalize surfaces as mentioned above (bridge molecule between organic and inorganic chemistry). In sprays, a droplet size of less than 100 micrometres may be achieved due to the action of propellants. Due to such small droplet size, the components of the product may reach the alveolar region of the lungs causing an accumulation of fluid, which in turn will result in an impairment of the oxygen and moisture exchange.

Nanotechnology is regarded as a technology of future, i.e. the 21st century, with a broad range of applications such as scratch-resistant car paints, dirt-repellent textiles or control of diseases. However, as for all new technologies, research is still required to identify the risks and consequences that may arise from its use.

Together with the Federal Institute for Occupational Safety and Health (BauA/FIOSH) and the Federal Environment Agency (UBA), BfR developed a research strategy for the identification of potential risks from nanotechnology in August 2006. This research strategy has been aimed at developing methods to measure and characterize nanoparticles, compiling information on exposure as well as toxicological and ecotoxicological effects and promoting the development of a risk-based test and assessment strategy. Presently, estimates of exposure to nanomaterials still show considerable uncertainties because on the whole, the available data appear to be deficient. Sufficient information is lacking with regard to the identity, dissemination and use of nanomaterials, standardized measurement methods and strategies.

Possible sources of an exposure of consumers may be packaging materials for foods, cosmetics, food supplements, cleaning agents, lacquers, paints etc.

On principle, exposure to nanomaterials may take place by the dermal, oral and inhalational routes. For example, dermal exposure may occur through the use of cosmetics, but also by wearing textiles treated with substances containing nanoparticles. Oral exposure may take place by the consumption of foods containing nanomaterials. Also nanomaterials migrating from packaging materials to foods may lead to oral exposure. Exposure by inhalation may result for example from the use of aerosol sprays in the household.

From the angle of consumer health protection, knowledge about the presence of nanomaterials in household products is therefore of major interest. Hence, a sufficient documentation and labelling of the use of nanomaterials in consumer products by the manufacturers is a necessity.

3.2 Drain cleaner

Severe health impairment following ingestion of a drain cleaner

In May 2010, BfR received a report from a university hospital on a severe case of health impairment in a three-year-old child. The girl had suffered severe alkaline burns in the oral, laryngeal, pharyngeal, oesophageal and gastric regions after ingestion of a drain cleaner containing sodium hydroxide.

At about 9 pm, the three-year-old girl had ingested an unknown amount of alkaline solution from an almost empty bottle. Her acute reactions after ingestion have remained unknown to BfR. The young child was brought to the university hospital by emergency ambulance on the same evening.

Manifestations/course

On admission, a poison information centre was consulted immediately. The instructions for treatment given by this centre included oral administration of a defoamer and small amounts of fluid for drinking, i.v. administration of omeprazol and endoscopic examination.

On admission, the child was found awake, in an agitated state and crying with spontaneous movements of all extremities. Gross findings included chemical burns in the oral region, a white coating on the mucosa, bloody tonsils and swollen lips. Both lung fields were equally aerated and without crepitation. The cardiac sound was found to be pure and rhythmical, the abdomen soft with recognizable peristalsis.

An initial gastroscopy revealed second degree chemical burns, fibrinous deposits and superficial ulceration on an intensely reddened mucosa in the entire oesophagus. No deeper ulceration was found. In the region of the cardia, reddish-streaky ulceration and erosions were seen, in part covered with fibrinous deposits. The duodenum was found to be normal. Findings made by an ENT specialist consultant included fibrinous and necrotic mucosae in the regions of the tonsils and the posterior pharyngeal wall associated with a severe oedematous swelling. Also the lower pharyngeal and laryngeal regions exhibited pronounced signs of chemical burns and oedemas. Therefore, it was decided to intubate the child. Intensive medical care was required which included antibiotic therapy, artificial respiration over a total of 281 hours, and intensive sedation. On the third day of inpatient treatment, gastroscopy revealed oesophageal stenosis at ca. 13 cm distance from the row of teeth, and a markedly swollen larynx. A central venous catheter was inserted for parenteral nutrition. This led to the development of a small thrombus in the region of the right jugular vein where the catheter had been placed. Therefore, i.v. heparinization was initiated. In the further course, the alkaline burns together with the intensive sedation resulted in intestinal paralysis associated with vomiting and absence of peristalsis. Therefore, a gastric tube was inserted. An improvement of intestinal motility could soon be achieved by an adjustment of the sedation. A follow-up gastroscopy performed on day 13 after admission revealed a marked improvement of findings so that the young child could be extubated. On day 17, also the thrombus receded, and on day 21, heparin administration was discontinued. After 24 days of inpatient treatment, the young child was transferred to a rehabilitation facility with a pronounced transitory psychotic syndrome, completely enteral nutrition and normal defecation.

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

Comments
Solid sodium hydroxide is an essential component of drain cleaners. In powdery drain cleaners, sodium hydroxide (also referred to as caustic soda) is contained in its solid form. Sodium hydroxide will dissolve in the drain water, forming sodium hydroxide solution. Liquid drain cleaners consist of sodium hydroxide solution. In the drain, the latter will react with organic dirt (substances that may cause drain clogging). However, the strongly alkaline sodium hydroxide will also react with metals such as aluminium or zinc, releasing hydrogen. This gas helps to break up drain clogging. This is why some aluminium is often added to drain cleaners. During this reaction, heat is developed in addition, which will cause greasy substances to melt and thus accelerate the cleaning process.

Sodium hydroxide has very strong irritant and corrosive effects on the eyes, skin and mucous membranes. Typical swelling and liquefaction of tissues may be caused already by concentrations as low as 1 %. Higher concentrations will result in deep necrosis referred to as colliquative necrosis. Due to cell lysis, the outer layers of the skin are rapidly penetrated, resulting in deep chemical burns characterized by greasy and hyaline damage to the mucous membranes of the oral and pharyngeal regions and the tongue. Possible risks also include that of gastric perforation and a disturbance of the acid-base balance. In addition, inhalation of sodium hydroxide applied by spraying may cause severe chemical burns of the respiratory tract and pulmonary oedema. The corrosive effect of sodium hydroxide is most intense due to its strong tissue-liquefying property.

Anyone having ingested a corrosive agent should immediately drink water or another fluid available, except alcohol and milk. The corrosive effect will set in within 20 seconds. Large amounts of corrosive agents ingested can be removed by suction using a gastric tube in the case of solutions, and by lavage in the case of granular matter. Vomiting must never be induced after ingestion of corrosive substances since this could cause additional damage to the sensitive mucous membranes of the gastrointestinal tract and also the lungs could become affected due to aspiration. If nevertheless vomiting occurs, aspiration of vomitus into the trachea must be prevented by a head-down position of the patient in order to avoid severe lung damage. Further measures according to the scheme for treatment of chemical burns include pain management, circulatory assistance, administration of glucocorticoids, oesophagoscopy, and hospitalization. For a detailed discussion of the issue of chemical burns, reference is made to the Cases of Poisoning Reported by Physicians 2005 annual report.

By 31 December 2010, BfR had received 238 reports on cases of poisoning by drain cleaners. Of these, 48 cases referred to children under 14 years of age, including 44 in which young children under the age of three had been affected. Three of these reports were classified as severe cases of poisoning. The substances toxicologically relevant in these cases were potassium and sodium hydroxide. All of these severe cases occurred in children under the age of three. This has clearly shown children of this age group to be at an increased risk. For a safe handling of such products, other types of packaging would be of great benefit. This could be achieved for example by packaging of portions in sachets difficult to open for children and by refraining from the use of liquid preparations, which are easy to swallow.

3.3 Manure gases

Severe inhalation trauma associated with manure gases

At a family farm, a severe accident due to accumulation of manure gases happened because a number of standard preventive measures had been ignored when discharging liquid manure from the pigsties. On the day of the accident, removal by pumping and disposal of liquid swine manure from the pit had been envisaged to take place. Therefore, the manure from some other pigsties was to be discharged into the pit before. To achieve a fast discharge of liquid manure, several drain plugs were opened at the same time. After the discharge of manure had been completed, manure gases were sucked back by the still running ventilation fan through the open drains into the building with all windows and doors being closed. When the 33-year-old farmer wanted to close the drains with the plugs, he inhaled the gases. As a result, he was no longer able to leave the building and temporarily lost consciousness. Also some pigs fainted. After introduction of fresh air, the farmer and the pigs regained consciousness. Afterwards, the patient vomited repeatedly. He was brought to a hospital and admitted for inpatient monitoring.

Manifestations/course

On admission, the patient was conscious and capable of temporal and local orientation. He showed signs of hyperventilation while his circulation was stable. Examinations did not find any lung crepitation, which could have indicated water retention. After one day of inpatient monitoring, the patient was discharged and fit to return to work.

Evaluation of the case described

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

Comments
Manure gases are produced during the breakdown of metabolizable substrates (e.g. proteins) by bacteria, which may accumulate in great numbers in liquid biological waste. The metabolic end products formed include a number of gases such as hydrogen sulphide, ammonia, methane and carbon dioxide. These gases are dissolved in the liquid phase of the manure and become released only if the manure is set in motion by mixing, pumping or flushing.

Hydrogen sulphide is an extremely toxic gas having an unpleasant smell. Its presence can be clearly perceived at levels as low as 0.3 ppm due to a penetrating odour resembling that of rotten eggs. At low concentrations (10–100 ppm), hydrogen sulphide acts as an irritant to the mucous membranes of the eyes and airways. At levels exceeding 100 ppm, the olfactory receptors become paralyzed so that the characteristic odour is no longer perceived. Inhalation of hydrogen sulphide in concentrations above 150 ppm will cause headache and dizziness. Concentrations of 500 ppm and above will lead to convulsions and loss of consciousness. Concentrations of about 1 000 ppm are life-threatening for humans already on exposure over a few minutes.

Other gases dissolved in manure include ammonia, methane and carbon dioxide, which, however, are less harmful.

Ammonia becomes life-threatening only at high concentrations. Due to the moisture on the mucous membranes, ammonia has a corrosive effect on the respiratory tract which may lead to laryngeal or pulmonary oedema and eventually, respiratory arrest. Absorption into the blood may result in CNS disturbances and eventually, coma and death. Carbon dioxide may accumulate in waste pits because it is heavier than oxygen. Oxygen displacement from the respiratory air may result in suffocation.

Methane, which is also produced during manure gasification, is non-toxic.

In contact with oxygen (under high pressure), the three manure gases, hydrogen sulphide, methane and ammonia are highly explosive. This is why special caution should be exercised when handling open flames, and spark formation must be avoided.

The above accident, which was due to manure gases, in particular hydrogen sulphide, could happen primarily because a number of standard preventive measures had been ignored. The reasons why a considerable accumulation of manure gases in the pigsties could occur included the following:
The ventilation of the animal quarters had not been switched off. The doors had been locked. Several effluent drains had been opened simultaneously. The drains were not closed immediately after the discharge of manure. The manure mixer had been in operation too long. In addition, the weather conditions prevailing at that time were hot and humid with a low air exchange. As a result of these circumstances, manure gases were sucked back into the building. No operating instructions were available, and no risk assessment had been performed because the family farm did not employ non-family persons. On principle, the persons involved were aware of the harmful effects of liquid manure. When working on and in effluent and liquid manure pits, special precautionary measures have to be taken. These include wearing a respiratory mask, direct securing of the working person, e.g. by wearing a safety harness or having other persons standing by for assistance when performing such operations.

Almost every year, BfR has received reports on severe accidents involving the inhalation of manure or wastewater gases containing hydrogen sulphide. A considerable number of these accidents had a fatal outcome or led to late sequelae.

3.4 Phosphoric acid dental etchant gel

Severe eye injury due to dental etchant gel
During the filling of a syringe with phosphoric acid etchant gel, the right eye of a 39-year-old dental nurse was hit by splashes of this gel. Immediately afterwards, the eye was thoroughly rinsed with water. Then, the patient was given emergency medical care by a local ophthalmologist. Having suffered 3rd and 4th-degree chemical burns of her right eye, she was brought to an ophthalmological hospital by emergency transport.

Manifestations/course
During the emergency transport to the ophthalmological hospital, rinsing of the eye with isotonic solution was continued. On admission to the hospital, visual acuity in the right eye was sc 1/40 LT and that of the unaffected left eye, sc 1.0. Taking into account the stage of the injury, therapy was administered according to Reim's scheme, a treatment algorithm for severe chemical and thermal burns of the eye. Still on the day of admission, conjunctival slit and necrectomy were performed under local anaesthesia. Four days after admission, excision of necrotic tissue was carried out again, followed by tenonplasty and amniotic membrane transplantation to cover the defect. After three weeks of inpatient stay, the patient was discharged and referred to onward outpatient treatment. Findings on discharge included a large corneal lesion, corneal oedema, lens opacity and mydriasis associated with a minimum of visual acuity.

After careful consideration the patient and the attending ophthalmologists decided to forego, for cosmetic reasons, a possible residual function of the eye and perform a plastic reconstruction of the eye. Therefore, the eyeball was removed (evisceration) and a provisional prosthesis implanted about four weeks after the accident. The extremely comprehensive surgical measures did not involve any technical problems. Also in the first period of the postoperative course, no complications occurred. In the subsequent course, however, the patient developed a cicatrical shrinkage of tissue and poor eyelid closure. This led to desiccation, wound discharge and malposition of eyelashes requiring subsequent operations. The last information on the further course is dated about two months after the accident. The onward treatment was aimed at the restoration of eyelid closure and adjustment of the prosthesis by an ocularist.

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

Comments
In the mid-1990ies, the use of composite resins as restorative materials in dentistry was introduced as a standard. Since then, these materials have been increasingly used.

To enhance adhesion, both the enamel and the dentin at the site of the carious lesion to be filled must be treated by application of an etchant gel containing 30–50 % of phosphoric acid prior to the application of composite resin fillings. A residence time of 15 seconds after application of the etchant gel is followed by rinsing and thorough drying of the area to be treated. Adhesive systems containing both etching and bonding components may be used to replace etching and rinsing as separate steps. In the case described above, the required quantity of etchant gel had been prepared and obtained from a dosing cartridge by the dental nurse (see Figs. 15 to 20). For reasons of risk prevention, the use of ready-for-use syringes containing only a few millilitres of the material should be preferred. However, these are expensive. Another hazardous procedure is the application of the etchant gel to the tooth. Both the dentist and dental nurse should wear protective clothing such as gown, gloves and eye protection, the latter being a must.

Fig. 15: Protective packaging containing syringes filled by the pharmacy

Fig. 18: During this procedure, some air will inevitably become entrapped

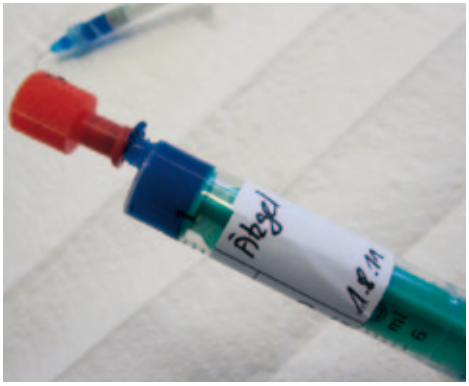


Fig. 16: The material obtained from the pharmacy has to be portioned first

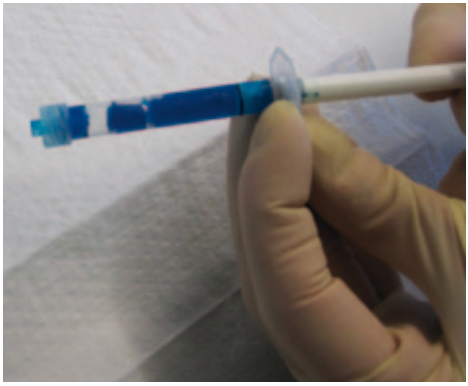


Fig. 19: Trapped air has to be removed

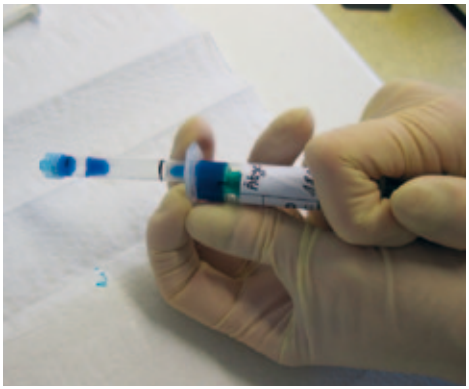


Fig. 17: Skill and strength are required for filling the material into the application syringes

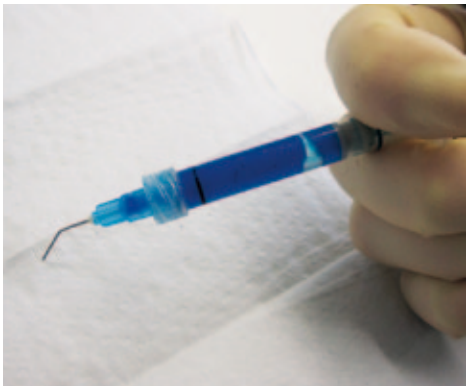


Fig. 20: Now, the application syringe is ready for use

In cases of chemical burns of the eye, the latter should be rinsed intensively for at least 10 minutes, ideally under running water. Loose foreign bodies may be removed carefully. After first aid measures having been taken, patients should present to an ophthalmologist for further treatment. The issue of chemical burns of the eyes was discussed in detail in the 2005 and 2009 annual reports, Cases of Poisoning Reported by Physicians. In 2010, BfR received a total of 19 reports on accidents involving the eyes from phosphoric acid or products containing phosphoric acid. During the last ten years, BfR has received reports on 126 cases of eye injury due to dental etchant gel.

3.5 Sac spider bite

Minor health impairment after sac spider bite
On a late-summer evening, a female living in south Germany had been hanging her laundry out to dry on the balcony when suddenly, she experienced a sting on her left ring finger. Afterwards, she discovered a spider in a basin on the wall. She developed a burning and tingling sensation and numbness of the finger reaching up to her armpit. For these reasons, she sought help at a hospital.

Manifestations/course
Except for a mild reddening on the distal phalanx of her left ring finger, the examination performed at the hospital on admission did not reveal any abnormal findings or motor disturbances. However, tingling paraesthesia on fingertips and numbness ascending to the armpit were still present. Physical findings and vital parameters measured were normal. No poison detection was carried out. The patient was given advice and information and could be discharged and referred to her family doctor on the same day.

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

Comments
In the case described, unequivocal identification of the sac spider was impossible. This is why this case has been rated as that of a suspected sac spider bite.

The long-legged sac spiders (Miturgidae family) belong to the order of Araneae (true spiders). They are represented by 378 species belonging to 29 genera. The best known representative of the sac spiders is *Cheiracanthium punctorium* (Villers), the yellow sac spider. It is mainly found in south and central Europe. The yellow sac spider (see Fig. 21) and the water spider, *Argyroneta aquatica* (Clerck), are the only poisonous spider species in Germany whose bite may cause health complaints in humans. The yellow

Fig. 21: Yellow sac spider (Cheiracanthium punctorium)

sac spider is a nocturnal animal. The poisonous bite of both males and females may penetrate human skin. Such bite will initially cause pain and a burning sensation, often followed by a variety of clinical manifestations.

In cases of spider or insect bites it is always problematic to define the species to which the injury is to be attributed because these animals will quickly escape after the bite. Therefore, a confirmed diagnosis of sac spider bite can be made in extremely rare cases only where the spider could be unequivocally identified.

The initial burning pain experienced around the bite wound will extend into the entire extremity within the next minutes, but this may also take hours. In the majority of cases, the patients affected will experience pain and pressure sensitivity in the neighbouring lymph nodes. In rare cases only, severe courses have been observed characterized by paralytic manifestations, shivers, dizziness, vomiting, mild fever or circulatory failure. In most cases, the manifestations will have receded completely after 24 to 30 hours. There have been no reports on cases of permanent damage to health or deaths so far. Children and susceptible adults affected by such bites should be kept under medical observation. However, symptomatic treatment will be sufficient.

The widely shared opinion stating that yellow sac spider bites may lead to small-scale necrosis has not been adequately confirmed by scientific evidence. A literature study conducted in 2006 by Vetter et al.[7], which reviewed in a critical way all cases of poisoning by yellow sac spider bites, found that in one case only, the spider bite had resulted in a bean-sized necrosis on the site of the bite. Statements were also made as to the frequency of such bites. However, these data are difficult to confirm: In the majority of cases it had remained unclear whether the patient affected had indeed been bitten by a yellow bag spider because, as mentioned above, the animal was not available for identification or had escaped before it could be spotted. The literature study could confirm no more then 12 cases of poisoning by yellow bag spider bites to have occurred in Europe in the 1876–2006 period. BfR has not received any confirmed case report.

[7] *Vetter RS, Isbister GK, Bush SP, Boutin LJ.Verified bites by yellow sac spiders (genus Cheiracanthium) in the United States and Australia: where is the necrosis? Am J Trop Med Hyg. 2006 Jun; 74(6):1043–8. Review.*

3.6 Poisonous snake bite

Cases of minor health impairment after poisonous snake bite

Case No. 1
An elderly male had been walking through grassland in a local recreational area in late spring. In the early afternoon, he was bitten into the third toe of his left foot by a snake he was unable to identify. Subsequently, he developed increasing swelling, pain and reddening on the site of the injury. Therefore he presented at a hospital without delay.

Manifestations/course
On admission, he was found in a good general and nutritional condition and completely capable of orientation. In addition to a reddened face, marked pasty swelling was seen in the regions of his left forefoot and the lower third of his lower leg. On the back of the third toe left, a tiny bite mark was seen. Blood circulation and sensitivity in this area were normal. A general symptomatology was missing altogether, and the swelling was not found to increase. It had receded and reached a moderate degree. Administration of an antiserum was omitted. Clinical chemistry revealed an increase in leukocyte count to 17.0 G/L (reference range 4.0–9.0 G/L), an elevated D-dimer level of 918 µg/L FEU (reference range < 500 µg/L FEU) and a mild increase in the MCV level to 93 fL (reference range 82–92 fl). A poison test conducted was negative. The patient was given symptomatic treatment. This included bedding of the extremity affected in a Braun's splint, administration of compresses and cooling. In addition, the

patient was administered diclofenac by the oral route as an antiphlogistic and analgesic therapy. Since the patient was not in a position to provide reliable information on his vaccination status he was also given a tetanus vaccination. After five days, the patient could be discharged and referred to outpatient treatment by his family doctor after being comprehensively informed about the observance of rest, cooling and elevation of the extremity.

Fig. 22: Common European adder (Vipera berus)

Case No. 2

An elderly male being on a hike in the mountains in summer had been resting in a rest place. When he wanted to support himself with his right arm behind his back, he was bitten into the third finger of his right hand by a black snake of about 30–40 cm length. Subsequently, a moderate burning pain developed. Due to an increasing swelling, the patient removed a ring from his finger. About one hour later, he developed nausea and vomiting. An emergency ambulance was called and because of the symptomatology described, he was admitted to the nearest hospital.

Manifestations/course

At the hospital he was administered infusions and a tetanus vaccination. An i.v. antibiotic treatment was initiated consisting of amoxicillin and metronidazole. Due to increasing swelling, he sought outpatient treatment two days later at a university hospital. There, the patient was found in a good general and nutritional condition and completely capable of orientation. The region around the bite wound as well as the back of his hand, his forearm and upper arm up to the armpit still showed a marked swelling with haemorrhagic discoloration in the regions of the ulnar side of the bend of the elbow and of the armpit. Circulation, sensitivity and motor activity were found to be intact. Due to the absence of pressure pain, no presentation to the surgical department was required. Also, antiserum therapy was omitted because of the long latency period. Clinical chemistry revealed elevated leukocyte counts of 11.47 G/L (reference range 4.0–9.0 G/L), an MCH of 33 pg (reference range 27–32 pg), an MCV of 95 fL (reference range 82–92 fL), a urea nitrogen level of 23 mg/dL (reference range 7–18 mg/L) and a CRP of 1.8 mg/dL (reference range <0.5 mg/dL). Testing to detect the poison was negative. Also in this case, symptomatic treatment was performed and a forearm splint used to provide for consequent rest of the arm affected. In addition, the patient was informed that elevation of his arm would accelerate the healing process. The antibiotic treatment could be discontinued because of the minor-degree rise in inflammation parameters found. The patient was only administered diclofenac and pantoprazole. For prevention of thrombosis, the patient was prescribed heparin to be administered once a day. He was discharged from the university hospital on the same day and presented to his family doctor.

Evaluation of the cases described

Based on the information given on the temporal and spatial relationship between exposure and the occurrence of the manifestations observed,

and in the absence of other causes, a causal relationship has been rated as probable.

Comments
The subject of the wildlife European snakes of the genus *Viperidae* was already discussed in the context of the 2004 annual report, Cases of Poisoning Reported by Physicians. Due to repeated, albeit mild cases of poisoning, the problem is briefly described in the present report. Both the geographic and temporal circumstances have suggested *Vipera berus* (Linnaeus), the common European adder or viper, to have been involved in the two cases described above. It should be noted, however, that *Vipera berus* was not unequivocally identified in neither of these cases. The adder will only bite when alarmed, e.g. by being touched or stepped on inadvertently. The venom yield of these snakes is quite limited, i.e. 10–18 mg (dry weight). This is why, as a rule, bites may be dangerous only for children and elderly persons. After a bite, a widespread swelling associated with reddening will develop around the bite wound (two symmetrical punctures at a distance of ca. 1–1.5 cm) within an hour. Other local reactions such as oedema, pain, blue-red discoloration of the skin, haematoma, blistering, necrosis and swelling of lymph nodes may occur, possibly followed by systemic reactions. These include anxiety, dizziness, vertigo, headache, weakness, sweating, vomiting and diarrhoea. Haemorrhages and coagulopathy associated with bleeding and thrombosis will be the most prominent manifestations in cases of poisoning involving vipers. These may be followed by hypotension and shock and may lead to acute renal failure.

Since the venom of this snake may also affect nerve tissue and cells, dyspnoea, heart complaints and paralysis may develop. This symptomatology has been observed in extremely rare cases only. 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. Other therapeutic measures will depend on the manifestations. Antisera should be administered in the event of a massive local reaction associated with considerable systemic effects.

In Germany, injuries from adder bites have occurred again and again in recent decades. Since 1959, only one death has been recorded after an adder bite: In 2004, an elderly female suffered a bite from *Vipera berus* on the island of Rügen and died shortly afterwards. In this case, death occurred only a few minutes after the bite. The woman had been discharged from hospital shortly before the incident and was still in a weak general condition. Due to these circumstances, it has to be rated as improbable that death occurred exclusively due to the venom. According to data recorded by the poison information centre (Informationszentrale gegen Vergiftungen) at Bonn University Hospital, there had been only 64 cases of hospitalization due to adder bites in Germany in the period from 1972 to 1995. In 42 of these cases, only mild manifestations were developed by the patients. BfR has so far received ten reports on cases of adder bites. In five each of these cases, the degree of severity was classified as minor and moderate, respectively.

Like all European snakes, *Vipera berus* is a strictly protected species within the European Union. Capture or killing of these animals is prohibited.

4 Results of reports by physicians

4.1 Evaluation of reports

During the period from 1 August 1990, i.e. the beginning of the compulsory reporting, to 31 December 2010, altogether 64 440 reports on cases of health impairment, poisoning or suspected cases of poisoning were received by BfR. In 2010, the reporting year considered, 3 939 reports were received from Berufsgenossenschaften (BG – the professional insurance bodies) hospitals and medical practitioners (Fig. 23).

The share of reports submitted by hospitals and medical practitioners has remained low. Owing to intensive information activities, however, this share of reports has slowly increased again in 2010. Evaluations by the poison information centres have shown that the number of health impairments after absorption of or contact with chemical products, household chemicals, plant protection and pest control products and all other reportable product groups has remained high and does not correspond to the number of reports received by BfR.

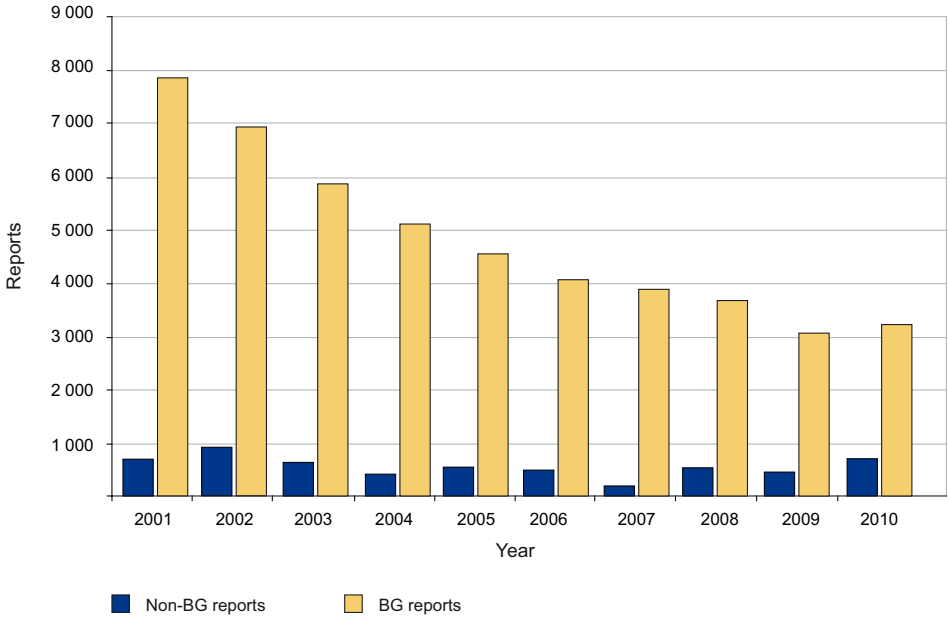


Fig. 23: Reports on cases of health impairment, poisoning or suspected cases of poisoning received by BfR in the 2001–2010 period; BG=Berufsgenossenschaften (professional insurance bodies)

4.2 Reports on cases of poisoning in 2010

4.2.1 Origin

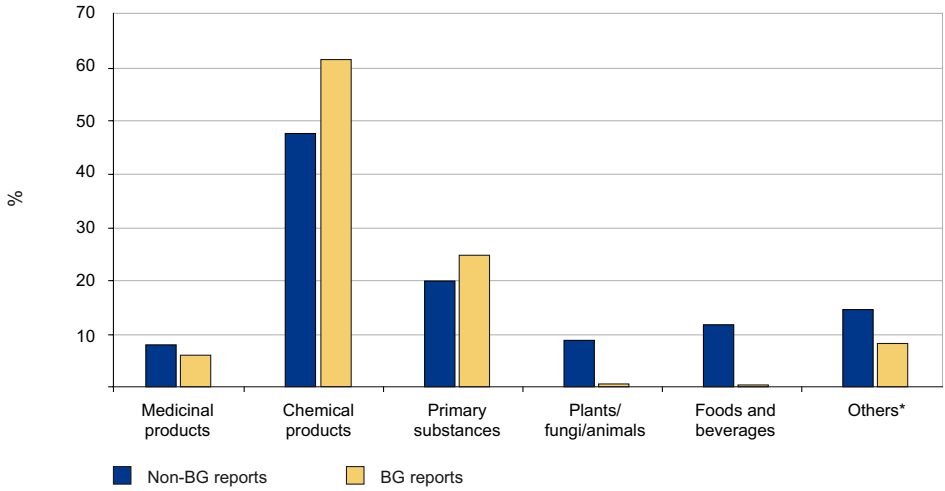
In 2010, 3 245 cases (82 %) were reported by the Berufsgenossenschaften. 694 reports (18 %) were essentially submitted by hospitals, medical practitioners and poison information centres.

4.2.2 Spectrum of cases reported

Again, reports related to chemical products ranked first in the reporting year (see Fig. 24 and Table 5). At a clear distance, the next group in ranking is that of primary substances. With regard to health impairments due to plants, fungi, animals, foods and beverages the number of cases reported by the Berufsgenossenschaften was clearly different from that reported by hospitals and medical practitioners. The number of such cases reported to BfR by hospitals and medical practitioners was markedly higher. Next in the ranking are health impairments caused by medicinal products that were reported although these are not subject to compulsory reporting under § 16 e ChemG.

For a detailed list in tabular form of toxicants reported to BfR since the beginning of compulsory reporting in 1990, see Annex (Chapter 5.3.1). In this table, the cases have been classified by product application groups (assignment of toxicants according to their intended use).

In order to enable a harmonized evaluation of cases recorded by the German poison information centres, the Society of Clinical Toxicology (Gesellschaft für Klinische Toxikologie e. V.) has developed a categorization system which, similar to the BfR system of application groups, is based on the intended use of the products. Therefore, the cases reported to BfR in 2010 were evaluated also according to this categorization system. The respective list is given in Annex 5.3.2.



**Others: Pesticides, cosmetics, veterinary medicines, agrochemicals, narcotic drugs, warfare/anti-riot agents, industrial accidents, miscellaneous*

Fig. 24: Spectrum of cases reported (BG reports 100 % = 3 245; non-BG reports 100 % = 694)

	BG reports (3 245 cases)	Non-BG reports (694 cases)
Chemical products	2 018	335
Primary substances	811	137
Medicinal products	204	55
Pesticides	80	18
Cosmetics/personal hygiene products	43	16
Foods and beverages	17	84
Agrochemicals	11	2
Industrial accidents	0	15
Veterinary medicines	3	1
Warfare/anti-riot agents	10	0
Plants	4	25
Animals	1	6
Drugs of abuse	0	48
Fungi	3	39
Miscellaneous	123	4

Table 5: Spectrum of reports (repeat listing of toxicants per case possible)

4.2.3 Circumstances of poisoning

The reports submitted by the Berufsgenossenschaften referred to occupational accidents. Among the reports submitted by hospitals and medical practitioners cases of accidental poisoning predominated (56 %), followed by exposure due to confusion (14 %) and exposure during proper use (8 %). Suicidal action was reported in 6 % of cases. 13 % of cases were associated with abuse of substances. In the remaining cases, the circumstances of exposure have remained unknown.

4.2.4 Age structure and sex distribution

The shares of male and female cases in BG and non-BG reports in 2010 have been listed in Table 6. 95 % of all cases reported referred to adults.

About 0.5 % of cases of poisoning reported by the Berufsgenossenschaften referred to children. These cases were attributed to accidents in kindergartens or schools. 99.5 % of cases reported by BGs referred to adults.

Also among the reports received from hospitals and medical practitioners, the share of cases in adults predominated (71 %), while that of children was 28 %. In 0.7 % of cases, the age was not stated.

	BG reports (100 % = 3 245 reports)	Non-BG reports (100 % = 694 reports)
Male	54 % (1 768 cases)	43 % (298 cases)
Female	33 % (1 067 cases)	34 % (237 cases)
Unknown	13 % (410 cases)	23 % (159 cases)

Table 6: Sex distribution

4.2.5 Degree of severity of health impairment

Also in 2010, 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. Cases of moderate and severe health impairment were more often reported by medical practitioners or physicians working in hospitals (Table 7).

The product groups involved most frequently with regard to the degree of severity of health effects have been listed in Table 8 for the cases reported by the Berufsgenossenschaften, and in Table 9 for the cases reported by hospitals and medical practitioners. The spectrum of toxicants reported differs because of differences in the availability of toxicants in the private sphere and at the workplace, among other reasons.

	BG reports (100 % = 3 245 reports)		Non-BG reports (100 % = 694 reports)	
None	4.7 %	(153 cases)	14.4 %	(100 cases)
Minor	82.9 %	(2 691 cases)	57.8 %	(401 cases)
Moderate	6.3 %	(206 cases)	18.2 %	(126 cases)
Severe	0.1 %	(2 cases)	5.2 %	(36 cases)
Cannot be assessed	5.9 %	(193 cases)	4.5 %	(11 cases)

Table 7: Degree of severity of health impairment

Product group	Health impairment		
	Minor (2 691 cases)	Moderate (206 cases)	Severe (2 cases)
Cleaning agents, total	667	58	
Drain cleaners	10	2	
All-purpose cleaners	47	2	
Oven and grill cleaners	18	3	
Dishwasher detergents	19	2	
Industrial cleaners	64	13	
Milking machine cleaners	47	3	
Sanitary cleaners	37		
Primary substances	636	71	
Disinfectants	281	11	
Medicinal products/medical devices	179	3	1
Paints and related materials	102	4	
Waste gases	88	4	
Building materials	75	14	
Pesticides	71	4	
Accumulators	56	4	
Galvanizing agents	2		1

Table 8: Product groups involved most frequently, by degree of severity of health impairment (BG reports, repeat listing of toxicants per case possible)

Product group	Health impairment		
	Minor (401 cases)	Moderate (123 cases)	Severe (39 cases)
Primary substances	83	30	10
Cleaning agents, total	100	37	5
Drain cleaners	2	2	1
All-purpose cleaners	6	2	
Oven and grill cleaners	1		
Descaling agents	72	23	3
Dishwasher detergents	1	1	
Glass cleaners			1
Sanitary cleaners	3	2	
Disinfectants	6	1	1
Medicinal products	21	14	6
Paints and related materials	7	1	
Waste gases	36	11	7
Glues	1		
Textile, auxiliary products	1	1	1
Foods and beverages	44	30	6
Fungi	27	4	7
Drugs of abuse	19	22	5
Plants	12	3	1

Table 9: Product groups involved most frequently, by degree of severity of health impairment (Non-BG reports, repeat listing of toxicants per case possible)

The relatively higher share of BG reports on cleaning agents as compared to cases of health impairment reported by hospitals and medical practitioners has to be attributed mainly to cases involving industrial and milking machine cleaners. As expected, BG reports were dominated by occupation-specific risk factors (Table 8). As in previous years, the non-BG reports showed a relatively high share of poisonings caused by cleaning agents (Table 9).

	BG reports (100 % = 3 245 reports)		Non-BG reports (100 % = 694 reports)	
Complete recovery	95.6 %	(3 102 cases)	62.5 %	(433 cases)
Late sequelae (confirmed or probable)	0.1 %	(5 cases)	1.5 %	(10 cases)
Death	0 %	(0 cases)	1.6 %	(11 cases)
Unknown	4.3 %	(138 cases)	34.5 %	(240 cases)

Table 10: Outcome of cases

4.2.6 Outcome of cases

Altogether eleven deaths were reported to the BfR in 2010. A summary is provided below:

- Two adults died as a result of inhalation of flue and fire gases during apartment fires.
- Four cases referred to carbon monoxide poisoning due to the use of charcoal grills in indoor environments. Three of these were confirmed suicides. In one case, the circumstances have remained unknown. This issue was discussed in detail already in the context of the 2008 annual report.
- One adult died after having inhaled hydrocyanic acid with a suicidal intent. To this purpose, he had used potassium ferrocyanide and potassium carbonate which he had processed according to instructions found on the internet.
- A forensic medical institution submitted two reports on cases of severe chemical burns caused by alkali ingestion. Two of these cases referred to combined suicides. In one of these cases, tablet ingestion had been involved in addition. In the other, the person affected had exhibited considerable cut injuries and in addition, had jumped from a great height.
- An elderly female died after death cap ingestion. However, the causal relationship has not been elucidated in this case. The exact cause of death has remained unknown to BfR.
- Likewise, the causal relationship has remained unclear in a case of death after ingestion of ragwort (*Senecio jacobaea*, syn. *Jacobaea vulgaris*). The elderly male was reported to have ingested a low quantity of ragwort over a short period of time, as he had allegedly done occasionally as a young man. He eventually died from multiple organ failure.

4.3 The product information system, PRINS

In order to protect consumers from health risks posed by chemicals and chemical products, the reports by physicians in cases of poisoning legally required under the Chemicals Act (§ 16 e para 2) are regularly evaluated in the sense of toxicological monitoring. Since 1994, the reporting physicians, the responsible ministries and the scientific community have been informed by annual reports on analyses of these reports and the corresponding results. In the context of these reports the term, poisoning, is used to designate any health impairment associated with chemicals, i.e. not only severe or life-threatening conditions but also undesirable health effects of products such as allergic symptoms and allergies.

Since 1998, manufacturers and distributors of chemical products such as household chemicals and DIY products, cosmetics, plant protection and pest control products and products for commercial use have been informed about selected and defined cases of health impair-

ment associated with their products that have become known to BfR through case reports by physicians. For this purpose, the formal product information system (PRINS) was established. In the event of reported severe health impairment, rapid communications are provided for in these cases, depending on the urgency of measures to be taken. By such approach, industry is enabled to immediately fulfil their obligations with regard to product safety. All other reports are summarized and sent to the recipients mentioned above at annual intervals.

4.3.1 Rapid communications

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

Criteria for a rapid communication include
- severe symptomatology,
- no suicide or abuse,
- no improper use.

In the period between 1 January 1998 and 31 December 2010, 31 rapid communications were prepared. A synoptic view of the last five years is given in Table 11.

Year	Product	Toxicologically relevant substance	Person exposed	Outcome	Proposal by BfR (P) and results (R)
2006	Detergent	Surfactants	Elderly female	Death	None
2007	Impregnation spray for tents	Cannot be identified	Adult female	Pulmonary oedema	P: Investigation
2008	Manual dishwashing detergent	Surfactants	Elderly female	Foam aspiration, death	P: Information
2008	Shoe impregnation spray	Cannot be identified	Adult male	Pulmonary oedema	P: Investigation
2009	Baby powder	Talc	Infant	Aspiration pneumonia, respiratory insufficiency	P: Information R: Distributed
2010	Descaler and rust remover	Nitric acid	Young child	Severe chemical burns, haematemesis, aspiration, gastric perforation	P: Measures to reduce the share of nitric acid in the product, control
2010	Drain cleaner	Sodium hydroxide	Young child	Severe chemical burns, respiratory insufficiency	None

Table 11: Rapid communications 1 January 2006–31 December 2010

In the reporting year of 2010, two rapid communications were distributed.

An almost three-years-old girl had ingested an unknown amount of a Turkish descaler and rust remover product containing nitric acid. She suffered extensive and severe chemical burns in the oral, laryngeal, pharyngeal, oesophageal and gastric/duodenal regions. After 12 days of intensive medical treatment including respiration, blood transfusion and emergency surgery, the child was transferred to a paediatric surgery ward for onward treatment. This case has been described in detail in Chapter 2.1.

In the second case, a three-year-old girl had ingested a liquid drain cleaner containing sodium hydroxide. She suffered extensive and severe alkaline burns in the oral, laryngeal, pharyngeal, oesophageal and gastric regions. The child developed glottic oedema associated with acute respiratory insufficiency. Artificial respiration was required over 281 hours. Due to oesophageal stenosis, a central venous catheter was inserted for nutrition. In the subsequent course, the child developed a catheter-related thrombosis in her right inner jugular vein. As a result of the alkali ingestion and intensive sedation, the patient developed intestinal paralysis and a pronounced transitory psychotic syndrome The course became complicated due to the long-term sedation required. After 24 days of intensive medical treatment, the child was transferred to a paediatric rehabilitation centre. For more details please refer to the case report provided in Chapter 3.2.

For explanations of individual cases up to 2009, reference is made to the previous annual reports.

4.3.2 Summary reports

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

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

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

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

By means of the BfR summary reports, manufacturers and distributors are informed about possible risks associated with the handling of their products. In single cases, they will not be satisfied by such summarized information and seek contact with the BfR in writing or by telephone in order to obtain more detailed information on a specific case of poisoning.

After evaluation of the total of 3 939 reports on cases of poisoning received by the BfR in 2010, 333 of these resulted in summary reports to the corresponding manufacturers according to the criteria mentioned above. In some cases, the report mentioned several products to have been involved as toxicants. Therefore, the total number of products listed is higher than that of the corresponding reports on cases of poisoning (see Table 12). These reports referred to a total of 345 products from 145 different manufacturers.

Table 12 provides a synoptic view of product application groups to which the summary reports on frequently listed products can be assigned.

As in the previous years, the majority of reports referred to accidents involving chemical products (total 310) with cleaning products stated most frequently (158). Also the numbers of reports referring to disinfectants (83) and those involving milking machine cleaners (26) and industrial cleaners (24) have remained high in this group.

First level Second level • Third level	**No. of cases**
Agrochemicals	**3**
Chemical products	**310**
Paints and related materials	8
• Primers	5
Building materials, auxiliary products	6
Building materials	4
Disinfectants	83
Deodorants for technical use	4
Glues	7
Cleaning products	158
• Drain cleaners	5
• All-purpose cleaners	14
• Oven cleansers	4
• Descaling agents	5
• Stain removers	3
• Floor polishes	3
• Washing-up detergents (manual use)	4
• Dishwasher detergents	10
• Industrial cleaners	24
• Milking machine cleaners	26
• Metal cleaners	3
• Sanitary cleaners	11
• Detergents, auxiliary products	4
Lubricants	3
Water treatment products	4
Cosmetics/personal hygiene products	**3**
Pesticides	**26**
Fungicides	4
Herbicides	11
Insecticides	7
• Pyrethroids	4

Table 12: Product groups frequently involved in 2010 summary reports (minimum three listings per product group)

The 333 cases leading to summary reports to manufacturers referred to health impairments characterized by the following degrees of severity (Table 13).

Degree of severity of health impairment	No. of cases
Minor	286
Moderate	24
Severe	2
Cannot be assessed	21

Table 13: Degree of severity of health impairment in 2010 summary reports

Table 14 below shows the number of products in the individual product groups that were involved in cases of moderate health impairment (24 products, repeat listing per case possible). It may be concluded that an involvement in cases of moderate health impairment was seen for ca. 7 % of the total of 345 products listed in summary reports to manufacturers.

As agreed, no rapid communications were issued to the responsible persons by BfR in spite of severe health impairments reported in three cases because there was obviously no need for action by the manufacturers involved. The manufacturers were informed about the accidents afterwards in summarized form.

In the first case, Magic Nano spray had been used by a 47-year-old female for cleaning and coating of glass and ceramic surfaces. After this operation, acute dyspnoea, hypoxia and fever were experienced, and the patient developed the clinical picture of pneumonitis with toxic bilateral pulmonary oedema. The aerosol had been sold in 2006 and already recalled from the marked by the manufacturer. There was no need for a rapid communication.

Another case referred to improper use of a tissue impregnation spray in an indoor environment.

In 21 of the total number of 333 cases of poisoning where summary reports had to be sent to manufacturers, the degree of severity of health impairment could not be assessed.

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

First level Second level • Third level	No. of cases
Agrochemicals	**1**
Chemical products	**21**
Paints and related materials	1
• Primers	1
Disinfectants	1
Metallurgy, auxiliary products	1
Cleaning products	13
• Drain cleaners	1
• Dishwasher detergents	3
• Industrial cleaners	1
• Metal cleaners	1
• Furniture polishes	1
• Sanitary cleaners	1
• Shoe and leather cleaners	1
• Detergents	1
Textile, auxiliary products	1
Primary substances	**1**
Pesticides	**1**
Herbicides	1

Table 14: Cases of moderate health impairment associated with product groups involved in 2010 summary reports

5 Annex

5.1 Standards for the assessment of poisonings

5.1.1 The three-level model

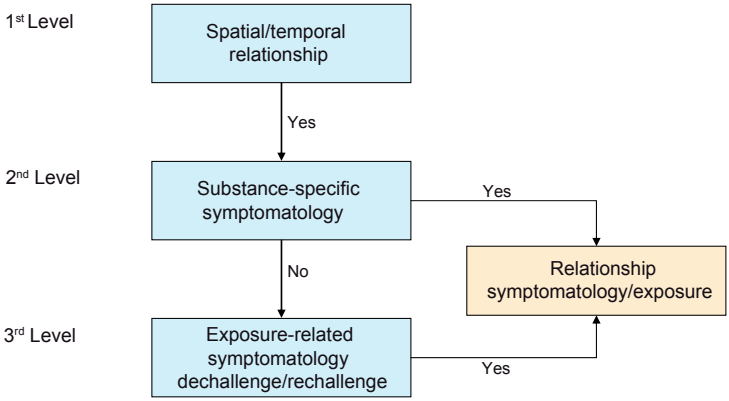


Fig. 25: The three-level model

5.1.2 Matrix to assess the degree of probability of exposure to a substance

Degree of probability of exposure		Estimation		Measurements			
		Contact with substance		Extracorporeal		Intracorporeal	
		Source(s)	Potential exposure	Single value	Represen-tative measure-ments	Single value	Exceeding of limit values
No	None	+	-	-	-	-	-
Yes	Possible/cannot be reliably excluded	+	+	+	-	-	-
	Probable	+	+	+	+	+	-
	Confirmed	+	+	+	+	+	+
?	Cannot be assessed	E.g. insufficient data, state of knowledge					

Table 15: First Step: Matrix to assess the degree of probability of exposure to a substance

5.1.3 Matrix to assess the causal relationship between health disorder/symptomatology and exposure

Relationship exposure/symptomatology		Plausible exposure to a substance	Partially specific symptoms	Specific symptoms	Specific laboratory analysis	Other diagnosis
No	None	-	-	-	-	+
Yes	Possible/ cannot be reliably excluded	+	+	-	-	+
	Probable	+	+	+	-	-
	Confirmed	+	+	+	+	-
?	Cannot be assessed	E.g. insufficient data, state of knowledge				

Table 16: Second Step: Matrix to assess the causal relationship between health disorder/symptomatology and exposure

5.2 Processing of cases of poisoning at BfR

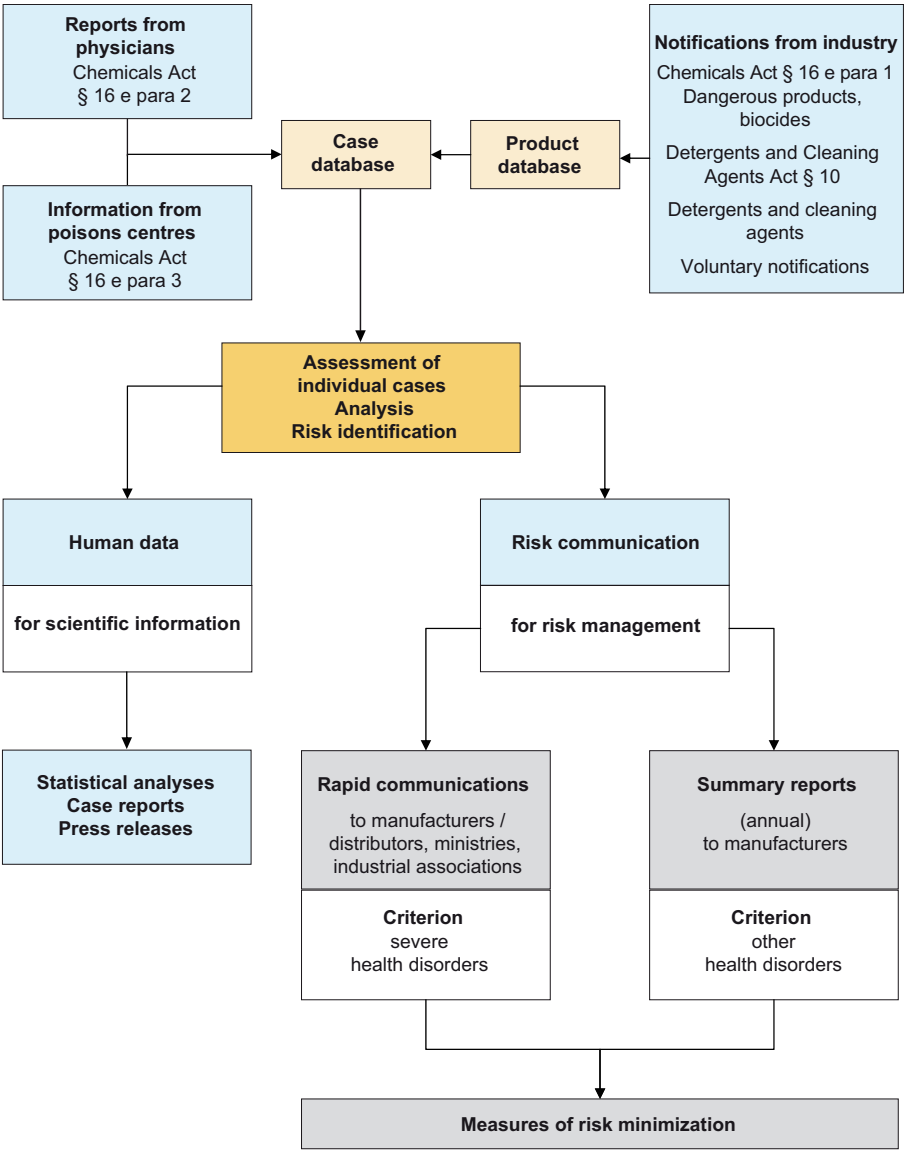


Fig. 26: Terms of reference of the Poison and Product Documentation Centre

5.3 Spectrum of reported cases of poisoning

5.3.1 Classification by BfR system of product application groups

Table 17 summarizes 63 817 reports (except for cases classified as "no relationship" between symptomatology and exposure) vs. degree of severity of health disturbance, classified by children and adults. The adult cases were in addition differentiated by exposure in the private sphere and the working environment.

The evaluation covered the period from 1 January until 31 December 2010.

Range of toxicants	Reports, total numbers					Health impairment moderate/severe				
First level Second level • Third level	Total	Children	Adults	Home	Work	Total	Children	Adults	Home	Work
Agrochemicals	**242**	**6**	**236**	**8**	**225**	**34**		**34**	**1**	**32**
Fertilizers	126	6	120	8	111	13		13	1	12
Plant care products	4		4		3	2		2		1
Growth regulators	14		14		14	3		3		3
Medicinal products	**3 280**	**770**	**2 489**	**740**	**1 512**	**509**	**119**	**386**	**245**	**49**
Medical devices	597	3	594	11	583	16	2	14	3	11
Chemical products	**34 658**	**1 913**	**32 714**	**967**	**31 629**	**3 132**	**467**	**2 654**	**359**	**2 265**
Wastes, solid	310		310		310	34		34		34
Waste gases	3 002	58	2 942	159	2 773	225	10	214	62	148
Sewage	161		161		161	19		19		19
Paints and related materials	2 438	57	2 379	87	2 283	187	12	174	25	146
• Paint removers/strippers	143		143	4	139	17		17	2	15
• Alkyd resin paints	4		4	1	2	2		2		1
• Emulsion paints	21		21		21	4		4		4
• Artist's painting materials	2	1	1		1					
• Glossy paints	506	2	504	17	487	40	1	39	3	36
• Parquetry sealers	33	4	29	21	8	3		3	1	2
• Pigments	10		10		10	2		2		2
• Primers	165	1	164	7	157	17		17	4	13
• Paint thinners/Paints and related materials	956	42	914	16	891	52	9	43	4	38
Fire lighting products	119	101	17	13	4	47	37	10	8	2

Range of toxicants	Reports, total numbers					Health impairment moderate/severe				
First level Second level • Third level	Total	Children	Adults	Home	Work	Total	Children	Adults	Home	Work
Building materials, auxiliary products	381	8	373	9	364	40	2	38	5	33
Building materials	1 805	3	1 798	17	1 780	243	1	240	1	239
Fuels, solid	3		3		3					
Fuels, solid/auxiliary products	7		7		7					
Fuels, liquid/auxiliary products	4		4		4					
Fuels, liquid	1 199	754	439	30	401	367	317	49	21	27
• Petrol	252	17	235	3	230	18	3	15	1	13
• Ethanol for technical use	66	5	61	6	53	5		5	4	1
• Lamp oil	749	727	16	13	2	324	311	12	11	1
Fuels, gaseous	51	1	50	10	39	8		8	2	6
Office materials, chemical	195	5	190	2	183	41	1	40		40
Decoration materials	54	37	17	6	11	5	3	2	2	
Dental materials	147	1	146	21	123	22		22	9	12
Disinfectants	3 874	21	3 853	35	3 815	179	1	178	18	160
Deodorants for technical use	117	73	44	6	38	5	3	2	1	1
Diagnostic agents	35	1	34		34					
Printing, auxiliary products	34		34		34	2		2		2
Insulating materials for electric equipment	2		1		1					
De-icing products	19	1	18	1	17	1		1		1
Fire extinguishing media	201	5	196	3	192	9		9		9
Flame retardants	4	1	3		3	1	1			
Galvanic cells	1 138	12	1 126	2	1 122	56	1	55		55
• Accumulators	1 086	1	1 085	1	1 082	54		54		54
• Batteries	42	2	40		40	2		2		2
• Button batteries	10	9	1	1		1	1			
Galvanizing agents, auxiliary products	33	1	32		32	9	1	8		8

Range of toxicants	Reports, total numbers					Health impairment moderate/severe				
First level Second level • Third level	Total	Children	Adults	Home	Work	Total	Children	Adults	Home	Work
Galvanizing agents	29		29	1	27	4		4	1	2
Gases for technical use	23		23		23	2		2		2
Antifreezes	47	5	42	12	29	12		12	8	3
Foundry auxiliary products	1		1		1					
Glass-working, auxiliary products	5		5		5	2		2		2
Glass-making, auxiliary products	1		1		1					
Rubber production materials	22	1	21		21	1		1		1
Semiconductor production materials	6		6		6					
Household auxiliary products, chemical-technical	5	2	3	2	1	2	1	1	1	
Hydraulic fluids	385	3	381		380	13		13		13
Ceramics, auxiliary products	16	1	15	3	12	3		3	2	1
Ceramic materials	4		4		4					
Glues	1 091	28	1 063	29	1 032	85	7	78	7	71
Plastics, starting materials	241	38	203	3	200	26		26	2	24
Plastics, formulating materials	26		26		26	3		3		3
Refrigerants	75		75	1	74	7		7	1	6
Coolants	249	20	229	2	227	16		16	1	15
Leather processing products	9	1	8	3	5	4	1	3	2	1
Luminophors	15		15	2	13					
Solvents for technical use	947	9	938	39	895	90	1	89	10	78
Soldering and welding products	105	4	101		101	8	3	5		5
Metal repair auxiliary products	1		1		1					
Metallurgy, auxiliary products	229		229	2	227	27		27	2	25

Range of toxicants	Reports, total numbers					Health impairment moderate/severe				
First level Second level • Third level	Total	Children	Adults	Home	Work	Total	Children	Adults	Home	Work
Measuring equipment, chemical-technical	31	9	21	8	12	1		1	1	
• Heating meters	16	6	9	7	2	1		1	1	
• Mercury thermometers	6	3	3	1	2					
• Thermometer fluids	7		7		6					
Microbiological auxiliary products	1		1		1					
Dairy, auxiliary products	1	1								
Paper-making, auxiliary products	13		13		13	2		2		2
Photography, auxiliary products	102		102	2	100	1		1	1	
Radioisotopes, radionuclides	6		6		6					
Cleaning products	10 760	555	10 194	390	9 743	1 004	60	938	144	776
• Drain cleaners	226	44	181	21	158	65	20	45	13	31
• All-purpose cleaners	801	53	747	33	706	53	1	51	14	35
• Oven cleaners	370	19	351	4	347	41	5	36	2	34
• Cleaners for electronic products	5	2	3		3	1		1		1
• Descaling agents	475	105	368	47	288	46	7	38	16	13
• Front wall and stone cleaners	75		75	7	68	16		16	5	11
• Stain removers	39	18	21	2	19	3	1	2		2
• Floor polishes	73	6	67	6	61	6		6	1	5
• Washing-up detergents (manual use)	143	35	108	11	96	14	1	13	7	6
• Dishwasher detergents	239	46	193	7	185	22	3	19	3	16
• Dishwasher cleaners	96	1	95		95	9	1	8		8
• Glass cleaners	158	11	147	94	52	27	1	26	24	2
• Industrial cleaners	854	5	848	5	841	89	3	85	3	81
• Rinsing additive for dishwashers	92	14	78	1	77	5	1	4		4

Range of toxicants	Reports, total numbers					Health impairment moderate/severe				
First level Second level • Third level	Total	Children	Adults	Home	Work	Total	Children	Adults	Home	Work
• Plastic cleaner	30	4	26		26					
• Coating cleaner	6		6		6					
• Milking machine cleaners	614	10	604	1	603	67	5	62		62
• Metal cleaners	290	11	279	3	273	22	1	21	2	18
• Furniture polishes	26	20	6	4	2	4	3	1	1	
• Soot removers	8	3	5		5	2		2		2
• Sanitary cleaners	415	34	381	67	309	38	1	38	22	13
• Shoe and leather cleaners	47	6	40	37	2	18	1	17	16	1
• Shampoos, technical use	1		1		1	1		1		1
• Carpet/upholstery cleansers	14	2	12	3	9	4	1	3	2	1
• Detergents, auxiliary products	57	19	37	11	22	10		9	5	4
• Detergents	159	31	128	11	117	15		15	6	9
Joke articles	5	4	1		1					
Lubricants	309	6	303	1	302	12		12	1	11
Welding fumes	395		395	3	390	36		36	1	33
Toys	18	12	6	3	3	4	3	1	1	
Dust-laying oils	2		2		2					
Textile, auxiliary products	37	3	34	13	21	14		14	9	5
Propellants/sprays	16		16		16	1		1		1
Unknown	1 339		1 339	2	1 337	79		79	1	78
Washing-active raw materials	2		2		2					
Water treatment products	60	3	57		57	2		2		2
Pet shop products	8	2	6		6					
Drugs of abuse	**99**	**1**	**95**	**84**	**2**	**54**		**54**	**48**	
Primary substances	**18 074**	**358**	**17 583**	**442**	**17 017**	**2 207**	**58**	**2 147**	**171**	**1 941**
Cosmetics/ personal hygiene products	**932**	**125**	**800**	**220**	**577**	**106**	**11**	**95**	**69**	**26**

Range of toxicants	Reports, total numbers					Health impairment moderate/severe				
First level Second level • Third level	Total	Children	Adults	Home	Work	Total	Children	Adults	Home	Work
Hair care products	278	30	248	44	203	28	4	24	17	7
• Permanent wave products	55	4	51	1	50	3		3	1	2
• Depilatory products	18	2	16	15	1	2		2	2	
• Hair conditioners	30	2	28	6	22	3		3	3	
• Hair dyes/colorants	129	6	123	13	109	14	3	11	8	3
• Hair tonics	2		2	2		1		1	1	
• Shampoos	32	15	17	4	13	2		2	1	1
Skin care products	496	73	418	111	307	49	6	43	27	16
• Bath oils/salts	41	13	28	10	18	8		8	6	2
• Tanning products	2		2	2						
• Creams/ointments	107	15	88	62	26	15		15	12	3
• Deodorants	31	6	25	2	23	2	1	1	1	
• Face tonics	1	1								
• Make-up products	8	2	6	2	4	1	1			
• Perfumes/aftershaves	49	19	30	2	28	4	1	3	1	2
• Powders	5	3	2	1	1	1	1			
• Soaps	193	5	188	7	181	10		10	2	8
• Sun blockers	9	3	5	5		3	2	1	1	
• Oils	13	3	10	4	6	2		2	2	
Oral care/dental products	75	4	69	41	28	16		16	15	1
Nail care products	72	18	54	20	32	11	1	10	9	1
Pesticides	**2 845**	**199**	**2 639**	**656**	**1 884**	**675**	**27**	**645**	**312**	**303**
Acaricides	6		6		6	1		1		1
Fungicides	188	6	180	11	165	41	1	40	4	34
Herbicides	414	11	403	29	364	66	1	65	13	48
Wood preservatives	313	26	287	178	103	133	8	125	85	35
Insecticides	1 273	113	1 156	413	672	355	15	338	207	114
• Carbamates	53	6	47	15	30	16	1	15	7	7

Range of toxicants	Reports, total numbers					Health impairment moderate/severe				
First level Second level • Third level	Total	Children	Adults	Home	Work	Total	Children	Adults	Home	Work
• Phosphoric Ester	371	20	349	140	192	156	1	155	112	32
• Pyrethroids	424	50	374	130	242	90	3	87	49	37
• Chlorinated hydrocarbons	253	28	223	125	51	79	10	67	39	24
Molluscicides	12	6	5		5	1				
Repellents	14	4	10	5	5	2		2	1	1
Rodenticides	99	34	65	22	40	12	2	10	10	
• Anticoagulants	36	19	17	8	7	4		4	4	
• Phosphine derivatives	38	5	33	10	22	8	2	6	6	
Seed dressings	24	2	22		21	5		5		5
Plants	**282**	**155**	**121**	**67**	**53**	**41**	**4**	**36**	**25**	**11**
Fungi	**119**	**29**	**89**	**76**	**13**	**41**	**5**	**36**	**35**	**1**
Miscellaneous	**1 538**	**30**	**1 503**	**113**	**1 384**	**172**	**11**	**159**	**34**	**122**
Textiles	450	7	442	77	365	58	5	52	22	30
• Clothing	363	2	360	12	348	32	2	29	4	25
• Furnishing fabrics	71	5	66	60	6	24	3	21	18	3
Foods and beverages	**1 186**	**167**	**986**	**591**	**367**	**257**	**24**	**229**	**187**	**28**
Alcoholic beverages	244	14	226	135	70	88	7	80	65	4
Food additives	58	2	56	1	55	6		6		6
Food supplements	217	10	200	197	3	45	3	40	40	
Tobacco and tobacco products	148	107	40	29	2	29	3	26	21	
Industrial accidents	**2 141**	**238**	**1 875**	**480**	**1 292**	**225**	**10**	**215**	**47**	**164**
Veterinary medicines	**115**	**14**	**94**	**32**	**61**	**25**	**5**	**18**	**13**	**5**
Animals	**36**	**3**	**32**	**14**	**18**	**10**	**1**	**9**	**5**	**4**
Warfare/anti-riot agents	**119**	**16**	**102**	**10**	**91**	**6**	**2**	**4**		**4**
Pyrotechnic products	6	2	4		4	1		1		1
Tear gas	60	9	50	8	41	3	1	2		2

Table 17: Spectrum of reported cases of poisoning for the period between 1 January 1990 and 31 December 2010 vs. degree of severity of health impairment by BfR classification system for product application groups

5.3.2 Categorization by the sector system of the Society of Clinical Toxicology (Gesellschaft für Klinische Toxikologie e.V.)*

Range of toxicants	Reports, total numbers					Health impairment moderate/severe				
Level 1 Level 2 • Level 3	Total	Children	Adults	Home	Work	Total	Children	Adults	Home	Work
Products	**3 456**	**181**	**3 271**	**228**	**3 000**	**322**	**12**	**309**	**100**	**198**
Products of daily use	161	17	144	84	60	39		39	39	
• Objects of daily use (except cleaning and indoor air conditioning agents)	7	3	4		4					
• Cosmetics	56	8	48	9	39	4		4	4	
• Foods and food additives	98	2	96	78	18	37		37	37	
• Tobacco products	5	4	1	1						
Chemical/ physicochemical agents	1 644	121	1 523	56	1 428	146	10	136	25	101
• Construction materials, sealants and adhesives	170		170	1	169	20		20		20
• Paints, varnishes and dyes	121	2	119	1	117	3		3		3
• Lamp fuels, lighting, odoriferous, decorative and related chemical agents	30	8	22	7	15	1		1	1	
• Cleaning and maintenance products	1 012	106	906	50	813	111	10	101	28	61
• Chemicals for technical appliances, processes and products	287	7	280	1	277	17		17	1	16
• Products for plants and animals	10		10	2	8	1		1		1
• Chemical/ physicochemical articles -unclassified	50	1	49		49	1		1		1
Drugs of abuse	49		49	49		28		28	28	
• Centrally active sedatives	32		32	32		20		20	20	
• Hallucinogens	1		1	1		1		1	1	
• Psychostimulants	7		7	7		6		6	6	
• Drugs of abuse – unclassified	19		19	19		7		7	7	

Range of toxicants	Reports, total numbers					Health impairment moderate/severe				
Level 1 Level 2 • Level 3	Total	Children	Adults	Home	Work	Total	Children	Adults	Home	Work
Remedies	341	19	319	35	284	26	1	24	19	5
• Medicinal products (for human use)	228	18	208	30	178	19		18	17	1
• Medical devices	111	1	110	6	104	8	1	7	3	4
• Veterinary medicines	3		2		2					
Products for protection against and control of microbes and pests	404	12	392	14	372	23		23	3	17
• Biocidal material protection agents, hygiene products and disinfectants	307	9	298	6	289	16		16	2	12
• Plant protection and pest control products	101	3	98	9	86	8		8	1	6
Weapons and pyrotechnic products	16	2	14		14					
• Pyrotechnic products – civil use	1		1		1					
• Weapons and special products for military use	15	2	13		13					
Products – unclassified	957	10	946	61	884	111	1	110	35	75
• Primary substances	967	10	956	62	893	114	1	113	36	77
Natural environment	**78**	**15**	**62**	**51**	**11**	**13**		**13**	**13**	
Fungi	41	3	38	35	3	10		10	10	
• Eumycota	26	3	23	23		8		8	8	
• Fungi – unclassified	18	1	17	14	3	2		2	2	
Microbes	1		1		1					
Plants	27	12	14	10	4	2		2	2	
• Spermatophyta	27	12	14	10	4	2		2	2	
Animals	7		7	6	1	1		1	1	
• Arthropoda – Tracheata	2		2	1	1					
• Chordata – Vertebrata	3		3	3						
Natural environment – miscellaneous/unclassified	2		2		2					

Range of toxicants	Reports, total numbers					Health impairment moderate/severe				
Level 1 Level 2 • Level 3	Total	Children	Adults	Home	Work	Total	Children	Adults	Home	Work
Civilization-associated and inherited wastes	**263**	**9**	**254**	**52**	**201**	**33**		**33**	**17**	**16**
Waste products, by products and incidental products	259	9	250	52	197	32		32	17	15
• Waste products and by-products – regular	104	6	98	20	78	18		18	12	6
• Reaction products resulting from accidents/ breakdowns/fires	149	3	146	33	112	16		16	6	10
• Waste products, by-products and incidental products – unclassified	8		8		8					
Civilization-associated and inherited wastes – unclassified	4		4		4	1		1		1
Unclassified/ unknown items	208	1	207		207	14		14		14
Unknown agent	158	1	157		157	6		6		6
Unknown category	50		50		50	8		8		8

Table 18: Spectrum of cases of poisoning reported in 2010, by sectors of the categorization system of the Society of Clinical Toxicology e.V.

**Translator's note: Translation of terms to be considered as a draft, terminology should be confirmed by experts of the responsible international panels*

5.4 Reporting appeal to physicians

BUNDESINSTITUT FÜR RISIKOBEWERTUNG

Meldepflicht nach Chemikaliengesetz § 16e für Ärzte

Wer meldet?

jeder Arzt, der zur Behandlung oder Beurteilung der Folgen von Erkrankungen durch chemische Stoffe oder Produkte hinzugezogen wird

Was wird gemeldet?

gesundheitliche Beeinträchtigungen durch

- chemische Stoffe oder Produkte, die im Haushalt verwendet werden (z.B. Wasch-u. Putzmittel)
- Kosmetika
- Schädlingsbekämpfungsmittel
- Holzschutzmittel
- Pflanzen und Tiere
- beruflich verwendete Chemikalien
- gesundheitsschädigende chemische Stoffe aus der Umwelt/Störfälle

Wie wird gemeldet?

Kopie der anonymisierten Befunde/Epikrise oder Meldeformular des BfR (Kopiervorlage auf der Rückseite)

Wohin wird gemeldet?

Kontaktaufnahme:

Anschrift: Bundesinstitut für Risikobewertung
Vergiftungs- und Produktdokumentation
Max-Dohrn-Straße 8–10
10589 Berlin

Fax: 030 18412-4741

Telefon: 030 18412-0

E-Mail:

Weitere Informationen: , Stichwort Vergiftungen

5.5 Reporting form for cases of poisoning

Bundesinstitut für Risikobewertung
Dokumentations- und Bewertungsstelle
für Vergiftungen
Postfach 12 69 42

10609 Berlin

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

Mitteilung bei Vergiftungen
nach §16e Abs. 2 des Chemikaliengesetzes
Telefon: 030 18412-3460, Fax: 030 18412-3929, 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)

5.6 Reporting form for industrial accidents

BfR-Fragebogen zur Expositionsermittlung bei Stör- und Transportunfällen

Pers. Nummer

weiblich ☐ männlich ☐ Erwachsene(r) ☐ Kind ☐

Bereich I

Unmittelbar Betroffene(r)

(Bitte Eintrag in die Landkarte)

Direkt am Unfallort ☐
Nahe Unfallort ☐
☐ m

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

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

Bereich II

Nicht unmittelbar Betroffene(r)

(Bitte Eintrag in die Landkarte)

Entfernung vom Unfallort
☐ m
☐ km

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

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

Biomonitoring **Stoff:** ☐

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

5.7 List of poison information centres in Germany (status as of October 2011)

Berlin	BBGes – Giftnotruf (poison emergency telephone service) Berlin Inst. f. Toxikologie Klinische Toxikologie und Giftnotruf Berlin	Oranienburger Straße 285	13437 Berlin	Phone: +49 30/19 240 Fax: +49 30/30 686 799 mail@giftnotruf.de www.giftnotruf.de
Bonn	Informationszentrale gegen Vergiftungen Zentrum für Kinderheilkunde Universitätsklinikum Bonn	Adenauerallee 119	53113 Bonn	Phone: +49 228/19 240 and +49 228/28 733 211 Fax: +49 228/28 733 278 oder +49 228/28 733 314 gizbn@ukb.uni-bonn.de www.giftzentrale-bonn.de
Erfurt	Gemeinsames Giftinformationszentrum der Länder Mecklenburg-Vorpommern, Sachsen, Sachsen-Anhalt und Thüringen c/o Helios Klinikum Erfurt	Nordhäuser Straße 74	99089 Erfurt	Phone: +49 361/730 730 Fax: +49 361/730 7317 ggiz@ggiz-erfurt.de www.ggiz-erfurt.de
Freiburg	Vergiftungs-Informations-Zentrale Zentrum für Kinder- und Jugendmedizin Universitätsklinikum Freiburg	Mathildenstraße 1	79106 Freiburg	Phone: +49 761/19 240 Fax: +49 761/27 044 57 giftinfo@uniklinik-freiburg.de www.giftberatung.de
Göttingen	Giftinformationszentrum-Nord der Länder Bremen, Hamburg, Niedersachsen und Schleswig-Holstein (GIZ-Nord) Universitätsmedizin Göttingen Georg-August-Universität	Robert-Koch-Straße 40	37075 Göttingen	Phone: +49 551/19 240 Fax: +49 551/38 318 81 giznord@giz-nord.de www.giz-nord.de
Homburg	Informations- und Beratungszentrum für Vergiftungsfälle Klinik für Kinder- und Jugendmedizin Universitätsklinikum des Saarlandes		66421 Homburg/ Saar	Phone: +49 6841/19 240 (Emergency) +49 6841/16 283 36 (Office) Fax: +49 6841/16 211 09 giftberatung@uniklinikum-saarland.de www.uniklinikum-saarland.de/giftzentrale

Mainz	Giftinformationszentrum (GIZ) der Länder Rheinland-Pfalz und Hessen Klinische Toxikologie der Universitätsmedizin Mainz	Langenbeck-straße 1	55131 Mainz	Phone: +49 6131/19 240 +49 700-GIFTINFO Infoline: +49 6131/23 24 66 Fax: +49 6131/23 24 68 or +49 6131/28 05 56 mail@giftinfo.uni-mainz.de www.giftinfo.uni-mainz.de
Munich	Giftnotruf München Toxikologische Abteilung der II. Med. Klinik und Poliklinik, Klinikum rechts der Isar der Technischen Universität München	Ismaninger Straße 22	81675 Munich	Phone: +49 89/19 240 Fax: +49 89/41 402 467 tox@lrz.tu-muenchen.de www.toxinfo.org
Nuremberg	Giftnotrufzentrale Nürnberg Med. Klinik 1, Klinikum Nürnberg Lehrstuhl Innere Medizin – Gerontologie Universität Erlangen-Nürnberg	Prof.-Ernst-Nathan-Straße 1	90419 Nürnberg	Poison emergency hotline: +49 911/398 24 51 +49 911/398 26 65 Fax: +49 911/398 22 05 giftnotruf@klinikum-nuernberg.de

5.8 Press releases on toxicological problems issued by BfR in 2010 (Press and Public Relations Office)

Antibiotic resistances
in the food chain
18/2010, 13 December 2010

Hair straightening products with
formaldehyde are harmful
16/2010, 03 December 2010

Consumers are not at risk from
pesticide residues in redcurrants
11/2010, 02 August 2010

Information on the risks and benefits
of pesticides does not reach consumers
10/2010, 28 July 2010

Children's toys must not
cause allergies
09/2010, 07 July 2010

Nanosilver has no place in
food, textiles or cosmetics
08/2010, 10 June 2010

Carbon monoxide poisoning
on the increase indoors
03/2010, 03 February 2010

5.9 Abbreviations

Abbreviation	Meaning
µg/g	Micrograms per gram
µg/L FEU	Micrograms per litre fibrinogen equivalent units
µmol/L	Micromoles per litre
ACC	Acetylcysteine
BauA (FIOSH)	Bundesanstalt für Arbeitsschutz und Arbeitsmedizin (Federal Institute for Occupational Safety and Health)
BBGes	Berliner Betrieb für Zentrale Gesundheitliche Aufgaben
BE	Base excess
BfR	Bundesinstitut für Risikobewertung (Federal Institute for Risk Assessment)
BG	Berufsgenossenschaft (institutions for statutory accident insurance and prevention for trade and industry in Germany)
BMU	Bundesministerium für Umwelt, Naturschutz und Reaktorsicherheit (Federal Ministry for the Environment, Nature Conservation and Nuclear Safety)
CB	Cannabinoid
ChemG	Chemikaliengesetz (Chemicals Act, Germany)
CLH	Harmonised classification and labelling
CLP Regulation	Regulation (EC) No. 1272/2008 of the European Parliament and of the Council of December 2008 on classification, labelling and packaging of substances and mixtures
CP	Cyclohexylphenol
CRP	C-reactive protein
D-dimer	Fibrin degradation product
ECHA	European Chemicals Agency
EC	European Community
ECG	Electrocardiography
ELISA	Enzyme-linked immunosorbent assay
EU	European Union
e. V.	Eingetragener Verein (registered association)
EVA	Erfassung der Vergiftungsfälle und Auswertungen in den Informations- und Behandlungszentren für Vergiftungen (recording of cases of poisoning and evaluation at the poisoning information and treatmant centres in the Federal Republic of Germany)
FDA	Food and Drug Administration
fL	Femtolitre (1 fL = 1 μm^3 = 10^{-15} L)
G/L	Giga (10^9) per litre
Gamma-GT	Gamma-glutamyl transferase
GIZ	Giftinformationszentrum (poison information centres in Germany)
GOT	Glutamate oxaloacetate transaminase
GPT	Glutamate pyruvate transaminase

Hb	Haemoglobin
IU	International units
JWH	John W. Huffman
MAK	Maximale Arbeitsplatzkonzentration (maximum allowable concentration at the workplace)
MCH	Mean corpuscular/cellular haemoglobin
MCV	Mean cellular volume
mL/m³	Millilitres per cubic metre
mm Hg	Millimetres of mercury
mmol/L	Millimoles per *litre*
Nano	SI prefix meaning 10^{-9} (a billionth)
NO_2/m^3	Nitrogen dioxide per cubic metre
pCO_2	Partial pressure of carbon dioxide
PDF	Portable document format
pg	Picograms
ppm	Parts per million
PRINS	Product information system
PSS	Poisoning severity score
PTT	Partial thromboplastin time
RCS	Research chemicals
REACH	Registration, evaluation, authorisation and restriction of chemicals
RIA	Radioimmunoassay
RNA	Ribonucleic acid
TDI	Toxikologischer Dokumentations- und Informationsverbund (Toxicological Documentation and Information Network of the BMU)
UBA	Umweltbundesamt (Federal Environment Agency, Germany)
WRMG	Wasch- und Reinigungsmittelgesetz (Detergents and Cleaning Agents Act, Germany)

The Federal Institute for Risk Assessment

Do nanoparticles promote the development of allergies? Does apple juice contain harmful aluminium? The Federal Institute for Risk Assessment – in short BfR – is responsible for questions to do with the health assessment of food, consumer products and chemicals. In its work it makes an important contribution to rendering food, products and the use of chemicals safer in Germany.

BfR was established in November 2002 to strengthen consumer health protection. It is the scientific body of the Federal Republic of Germany that prepares expert reports and opinions on questions of food and feed safety and the safety of substances and products. In doing so, the Institute assumes an important task in improving consumer health protection and food safety. The activities of BfR are conducted under the responsibility of the Federal Ministry of Food, Agriculture and Consumer Protection. At the three BfR locations in Berlin, a staff of ca. 700, among them 250 scientists, is being employed to work in the field of consumer health protection. The scientific expertise needed for its assessment and research activities is provided on a non-partisan basis.

In our globalized world it is important for the institutions involved in consumer health protection to be part of international networks. BfR is the national Focal Point of the European Food Safety Agency (EFSA) and a partner of the European Chemicals Agency (ECHA). It cooperates with a number of national and international, governmental and non-governmental agencies.

BfR sees itself as the advocate of consumer health protection in a context in which many stakeholders make their voices heard. On the scientific basis of its risk assessments, it seeks to strengthen consumer health protection. To this end, the Institute offers policy advice, participates in national and international panels and disseminates consumer information. An important component in its risk assessment activities has consisted in risk communication and the various forms it can take. Risk communication has been provided by BfR by means of various projects and events.

Thanks to the high standard of its work, its scientific independence and its transparent assessments, the Institute has become a recognized player and important driver of consumer health protection on both the national and international stage. Consumers know they can trust its judgements.

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