

Health risks of nitric acid-containing cleaning products

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German poison treatment and information centres have reported cases of what was, in some instances, serious health damage caused by handling specific nitric acid-containing cleaning products in the home. The cases notified to the poison treatment and information centres show that not only adults but also children were affected. Against this backdrop and based on the scientific findings available up to now, the Federal Institute for Risk Assessment (BfR) has undertaken an assessment of the health risk linked to the use of household cleaning products containing 20-30% nitric acid. The Institute has come to the conclusion that products of this kind are not suitable for use in the home and urgently advises against their utilisation. Furthermore, BfR recommends measures to restrict the placing of these nitric acid-containing consumer products on the market.

1 Subject matter of the assessment

The German poison treatment and information centres have notified the Federal Institute for Risk Assessment (BfR) of 134 cases of what were partially severe health impairments following contact with a specific limestone solvent and rust remover. The safety data sheet on this product indicates nitric acid as a dangerous ingredient with a content of 20-30%. The product is in some cases sold without any effective child-resistant closure and with incorrect labelling. Against the backdrop of the numerous cases of health impairments notified, the Federal Institute for Risk Assessment (BfR) has, based on the scientific findings available up to now, undertaken an assessment of the health risk linked to the use of household cleaning products with 20-30% nitric acid.

2 Result

The 20-30% level of nitric acid in cleaning products, which are sold to consumers, entails a disproportionately high health risk for consumers. The risk results from the toxic effects of nitric acid and the nitrous gases released from it. BfR recommends limiting the placing on the market of cleaning products of this kind.

3 Reasons

3.1 Source of danger

3.1.1 Nitric acid (HNO₃)

Nitric acid (HNO₃) is an oxidising mineral acid, which has a highly corrosive effect on the skin, eyes and mucosa in the case of direct contact. Extensive yellow colouring of the affected skin and mucosa (xanthoprotein reaction) is a characteristic feature of this acid. Already after short exposure to the eye, undiluted nitric acid causes corneal ulcers and necrosis with permanent impairment of vision down to blindness. Oxidation can lead to clouding of the eye lens.

In the case of oral intake HNO₃ also has a corrosive effect on the gastrointestinal tract and can produce symptoms ranging from nausea, vomiting (bloody), haemorrhagic gastritis, strong retrosternal burning down to corrosion (first to third degree), formation of necrosis, shock, glottis oedemas with respiratory insufficiency, perforation, methaemoglobinaemia, haemolysis and metabolic acidosis. The lowest fatal dose in the case of oral exposure for

humans is 430 mg/kg body weight. Longer exposure to lower concentrations can lead to a yellowing of the teeth.

The inhalation of HNO_3 vapours leads in the respiratory tract to mucosal irritations, bronchial catarrh, pulmonary inflammation and necrosis of the alveolar epithelium. Because of the high lipid solubility even a low level of irritation of the upper respiratory tract is observed while the the alveolar-capillary boundary membrane is frequently affected. After a typical latency period of 3 up to 30 hours, this can result in toxic pulmonary oedema. Inhalational exposure to released HNO_3 vapours in concentrations of 160 ml/m^3 caused irritation of the nasal mucosa and the mucosa of the respiratory tract in experimental animals and led to bronchial catarrh, bronchospasms, pulmonary inflammation (chemical pneumonitis) down to corrosion of the pulmonary alveoli with the formation of oedema and emphysema. All symptoms can occur with a delay of up to 30 hours, the pulmonary oedema with a delay of up to 72 hours after exposure. These effects were also observed in individuals after accidents. Already concentrations of around 12 ml/m^3 (33.7 mg/m^3) lead in humans to major mucosal irritation of the upper respiratory tract and the lungs.

Technical nitric acid usually contains 56-68% HNO_3 . In particular concentrated nitric acid disintegrates through the formation mainly of nitrogen dioxide (NO_2) and nitric oxide (NO) which are released from the solution. So-called white fuming nitric acid (WFNA) contains 0.1-0.4%, red fuming nitric acid (RFNA) 8-17% of dissolved NO_2 . Hence the toxic effects of nitric acid cannot be assessed in isolation but must be considered in conjunction with these conversion products, the nitrous gases which are either spontaneously formed in the reaction of nitric acid involving the slow release of nitrogen dioxide (NO_2) and oxygen or in contact with metals with no passivation (above all copper and silver) or alkaline solutions.

3.1.2 Nitrogen dioxide (NO_2)

Nitrogen dioxide (NO_2 , CAS No. 10102-43-9) is a red brown, pungent gas which is in equilibrium with the colourless nitrogen oxide (N_2O_4)¹. Depending on the test conditions the perception threshold is 0.1 up to $0.2 \text{ ml NO}_2/\text{m}^3$. However, perception of the odour is reduced if the concentration is increased gradually. In the case of people with normal breathing between 80 and 90% and in the case of maximum respiration, more than 90% is absorbed by the respiratory tract. Model calculations have shown that NO_2 is mainly absorbed in the lower respiratory tract whereby NO_2 accumulates in particular in the interlinking space between the air conducting and respiratory airways^{2,3}. Between 20 and 30 ml/m^3 are indicated as the threshold for humans for NO_2 in the air⁴.

The effects of NO_2 are diverse, though only the most important modes of action are regarded here. Nitrous acid (HNO_2), nitric acid and nitric oxide (NO) form in the respiratory tract and can lead, in an acute situation, to irritative effects. Furthermore, the uncharged free radical $\bullet\text{NO}_2$, a medium strong oxidising agent, reacts with a number of biomolecules (e.g. DNA and nucleosides, proteins, lipids), initiates radical reactions and produces reactive oxygen species⁵. In this way NO_2 releases hydrogen from organic molecules whilst forming nitrous acid and a radical molecule, a reaction which can lead, for instance, to the destruction of the membrane lipids through lipid peroxidation. The NO_2 radical can react in an aqueous solution with amines and form genotoxic nitrosamines^{6,7}. Other genotoxic compounds can be formed through a reaction with aromatic compounds (carcinogenic nitroaromatics, nitropyrene from NO_2 and the polycyclic aromatic hydrocarbon pyrene). NO_2 has proven to be both clastogenic and mutagenic *in vitro* as well^{8,9}. Only very few data are available from *in vivo* experiments. They point to genotoxic effects in the rat lung. Valid long-term studies on carcinogenicity are not available. Indications of tumor promoting or carcinogenic effects of NO_2 are

revealed in male rats from concentrations of 4-10 ml NO₂/m³. NO₂ is classified by the German MAK Committee (committee on maximum concentrations at the workplace) as a category 3B carcinogen¹⁰.

No robust data are available on the developmental toxic effects that go beyond the risks resulting from an increase in the methaemoglobin concentration (1% increase at 1 ml/ NO₂/m³). The available experiments on developmental toxicity point to developmental toxic effects in the case of maternal exposure to NO₂ concentrations in the range of 0.5 ml NO₂/m³ air and below. Because of their limitations, these studies do not, however, suffice for definitive assessment¹¹.

Furthermore, NO₂ can intervene in cellular communication by influencing the intracellular concentration of NO (after disproportionation to nitrate and NO)¹²⁻¹⁴. NO plays an important role in various cellular signal transduction pathways. The complex processes steered by NO include, for example, inflammation, stress, apoptosis and necrosis. Released NO leads to an acute toxic effect which is based above all on the reaction with haemoglobin under formation of methaemoglobinaemia¹⁵ and is only based to a limited degree on the release of oxygen from haemoglobin-NO-haemoglobin-O₂-conjugates. Moreover, exposure to NO₂ changes in experimental animals the number and the function of neuroendocrine pulmonary cells (APUD cells). These cells are involved in pulmonary blood pressure regulation by excreting vasoactive substances¹⁶.

Through reactions of the NO₂ radicals with components of the alveoli fluid and the epithelial cells, tissue damage is caused in the terminal respiratory tract. Pneumocytes (type I) and cilia-bearing epithelial cells are damaged and replaced by less sensitive cells like type II pneumocytes and Clara cells. Signs of inflammation and reduced viral immune resistance are also observed. After long-term exposure there may be emphysema-like changes.

3.2 Hazard

3.2.1 Nitric acid (HNO₃)

Up to 2007 there was a provisional MAK (maximum workplace concentration) value of 2 ml nitric acid/m³ (5 mg/m³) based on data from a self-conducted experiment in 1907¹⁷. This provisional MAK value was shelved by the DFG (German Research Foundation) as neither longer term, robust experiences in humans nor inhalation studies in animals were available which might serve as the basis of a MAK value^{10,11}. Nitric acid is assigned to section IIB of the MAK and BAT (biological tolerance values for working materials) values list ("substances for which no MAK values can be established at the present time"). In line with the second list of indicative occupational exposure limit values in implementation of Directive 98/24/EG¹⁸, there is a short-term limit value of 1 ppm (2.6 mg nitric acid/m³) for a duration of 15 minutes¹⁹. It is based on a study in 5 volunteers in whom no effects were observed after 10 minute-exposure to 1.6 ml/m³²⁰. Tissue damage caused by nitric acid leads to acute necrotic inflammatory changes which can contribute above all in the case of chronic exposure to the formation of tumours. The assessment of possible genotoxic, carcinogenic and reprotoxic effects was not undertaken by the MAK Commission because of the unavailability of animal experiments¹¹.

Red fuming nitric acid is highly oxidising and creates a red-brown atmosphere of nitrogen oxide gases above all NO₂. The 4-hour LC₂₀ value is given as ≤ 8 ppm²¹. For the more diluted white fuming nitric acid a 30-minute LC₅₀ value of 310-334 ppm is given^{21,24}. Converted to a 4 hour LC₅₀ this would lead to an LC₅₀ value of approximately 40 ppm. An assessment

was undertaken in a similar way within the framework of an expert group for various special agencies of the United Nations²². For acute inhalational toxicity of nitric acid in dilutions down to below 70%, the GHS category 1²³ was established, i.e. a LC₅₀ value (4 hours) of 0.5 mg/l or less than 100 ppm. Based on the European Regulation (EC) No. 1272/2008 this would lead in the case of aqueous mixtures of nitric acid of 20% or more to classifications of acute toxicity in the range of categories of 1 up to 3 and the attributed labelling “hazard” and the health hazards “fatal if inhaled” (H330) and “toxic if inhaled” (H331) and the symbol “skull and cross bones”.

The existing legal attribution of these health hazards to nitric acid shows that so far only the potential harmful effects on skin and eyes have been dealt with this classification. The classification and labelling of nitric acid in terms of toxicity following one-off exposure through inhalation have not been undertaken up to now.

3.2.1 Nitrogen dioxide (NO₂)

Table 1 presents results from human studies in healthy volunteers after short, one-off exposure (maximum 4 hours) to NO₂ concentrations in the respiratory air.

Table 1 Observations in humans¹⁰

Symptom	Dose
Indications of inflammatory reactions	>0.6 ml/m ³
Elevated bronchial reactivity	>1.5 ml/m ³
Changes in pulmonary function (elevated respiratory system resistance)	>2.0 ml/m ³
Bronchitis, bronchopneumonia	25-75 ml/m ³
Bronchiolitis and focal pneumonitis	50-100 ml/m ³
Lethal bronchiolitis fibrosa obliterans	150-200 ml/m ³
Lethal pulmonary oedema and asphyxia (methaemoglobinaemia)	>300 ml/m ³

In an animal experiment Gray *et al.* determined for red fuming (NO₂ level 8-17%) and white fuming (NO₂ content 0.1-0.4%) nitric acid and for pure NO₂ in male rats LC₅₀ values for 30 minute exposure of 174 ppm (pure NO₂), 138 ppm (RFNA measured as NO₂) and 244 ppm (WFNA measured as NO₂)²⁴. Bearing in mind the molecular weight and the percentage increases of NO₂ in RFNA and WFNA, MISH indicates total gas and vapour concentrations as 310 ppm and 344 ppm respectively²⁵. After conversion to a 4-hour exposure value this leads to an LC₅₀ value for pure NO₂ gas of 43.5 ppm/4 h. ISO 10298:2010 indicates an LC₅₀/1 h of 115 ppm for nitrogen dioxide. After conversion to a 4-hour exposure value this leads to an LC₅₀ value for NO₂ gas of 57.5 ppm/4 h. Further results of animal experiments with acute exposure to nitrogen oxide are presented in Table 2.

Table 2: Findings from animal experiments on acute toxicity in conjunction with inhalational NO₂ exposure

Organism	LC ₅₀ (15 min.)	LC ₅₀ (60 min.)	LC ₅₀ (16 h)
Rat	200	115	39-56
Mouse	-	33-67	-
Golden Hamster	-	-	22-28
Guinea pig	-	-	50
Rabbit	315		
Dog	-	105	39-56

* Data for LC₅₀ values in [ml NO₂/m³]²

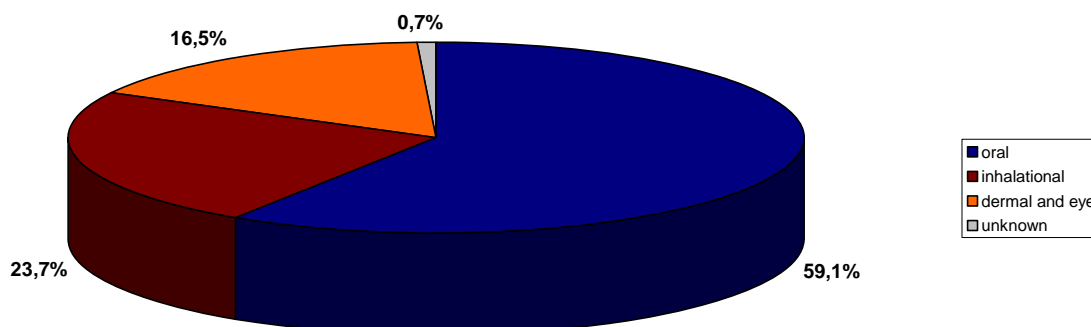
The data available so far indicate that the currently valid legal classification for pure NO₂ gas regarding toxicity following one-off exposure through inhalation is inadequate. When applying the criteria in accordance with CLP Regulation (EC) No. 1272/2008, then - based on the LC₅₀ values determined - classification appears appropriate in the highest category (category 1) of acute toxicity with the labelling “skull and cross bones”, the wording “hazard” and the hazard warning “fatal if inhaled”.

3.3 Exposure assessment for consumers

In conjunction with the use and the probable foreseeable misuse of nitric acid-containing cleaning products (20-30% nitric acid), in some instances severe health impairments were suffered by consumers. A total of 134 cases were notified to the Federal Institute for Risk Assessment (BfR) by the poison treatment and information centres between 1999 and 2010. Most of the notifications (59.1%) involved corrosion through the oral intake of nitric acid-containing products. In almost one quarter of cases (23.7%), the symptoms were caused by the inhalation of ingredients in the products.

Whereas oral intake and dermal contact can be avoided through cautious handling and technical protection, the health risks from inhalational exposure to nitric acid-containing cleaning products are almost unavoidable even in the case of correct use or foreseeable misuse. Moreover, the notifications of intoxications confirm a worrying exposure situation for consumers.

Fig.1: Case data from German poison treatment and information centres (1999-2010)



There are no adequate data available to undertake assessment of inhalational exposure during the use of nitric acid-containing household cleaning products. Hence based on exposure scenarios it was determined which indoor air concentrations of HNO_3 could be achieved based on certain assumptions. NO_2 was not included in the example calculations as no scientifically based estimate of NO_2 exposure during the use of nitric acid-containing limestone solvents and rust removers is possible on the basis of the data available. Example 1 (Fig. 2a) examined with the help of the software *Cons Expo 4.1* (RIVM, 2008) to which extent the indoor air concentration of nitric acid is influenced by the amount used (assumptions: nitric acid content: 30% room size: 30 m^3 , application area 1 m^2 , air exchange rate: 0.2/h). In example 2 (Fig. 2b) the software *Cons Expo 4.1* (RIVM, 2008) was used to model how the concentration of nitric acid in indoor air changes after application of a nitric acid-containing cleaning product (30% nitric acid) when used in rooms of different sizes ($10\text{-}30 \text{ m}^3$) with a constant air exchange rate of 0.2/h. In the third example (Fig. 2c) the software *Cons Expo 4.1* (RIVM, 2008) was used to determine the dependency of the indoor air concentration of nitric acid on the air exchange rate after using nitric acid-containing cleaning products (30% nitric acid) in a practical area between 0.2-2 per hour. This was based on a room size of 30 m^3 , an application area of 1 m^2 and an applied amount of 10 g. It is shown that the indoor air concentration is only influenced to a limited degree by the air exchange rate.

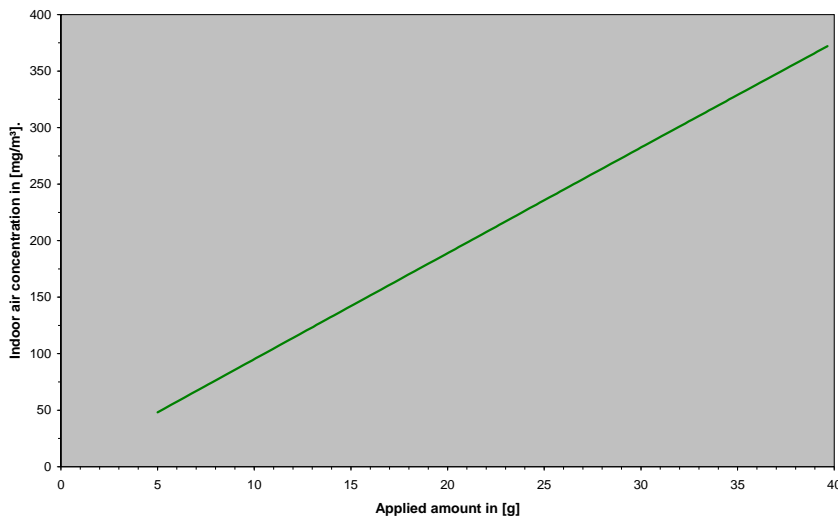


Fig. 2a:

Association between the concentration of nitric acid in the indoor air and the application amount (nitric acid-containing cleaning product with 30% nitric acid) after 30 minutes exposure. Parameters: room size= 30 m³, application area 1 m², model for release: evaporation vapour pressure 30% HNO₃= 89.6 hPa.

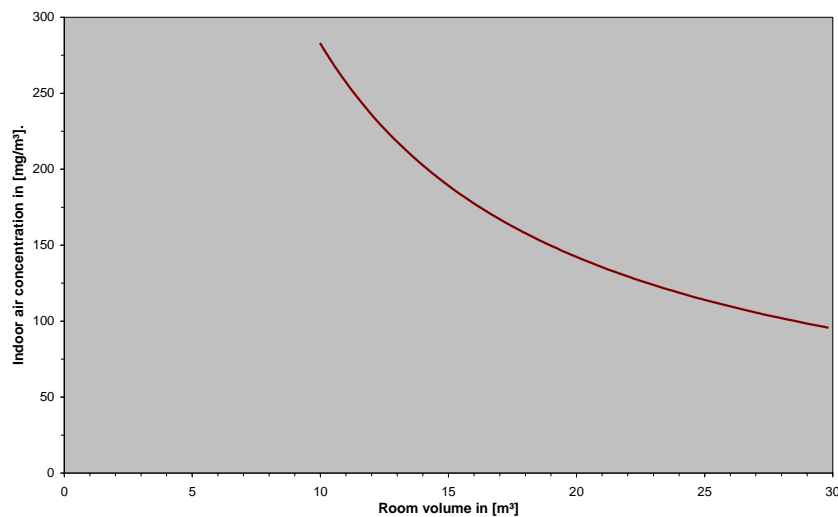


Fig. 2b:

Dependence of the concentration of nitric acid in indoor air after using nitric acid-containing cleaning products (30% nitric acid) on room volume. Parameters: application area 1 m², application amount 10 g, air exchange= 0.2/h. Model for release: evaporation vapour pressure 30% HNO₃= 89.6 hPa.

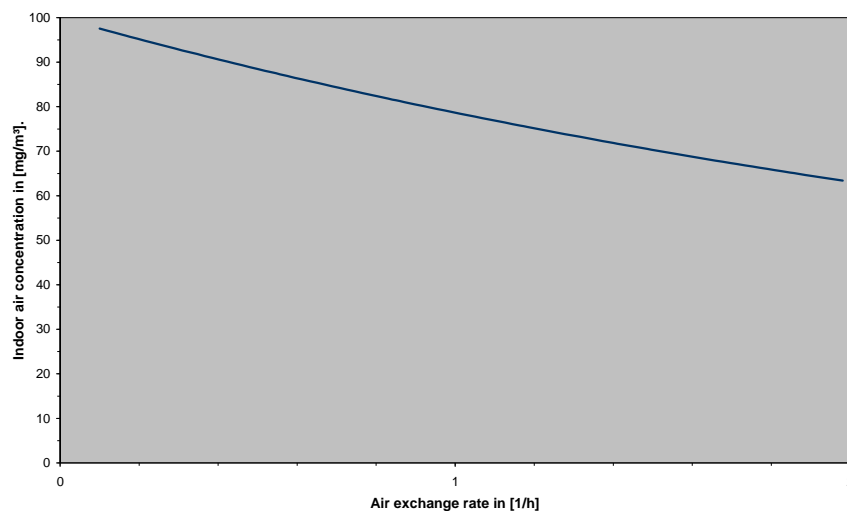


Fig. 2c:

Dependence of the indoor air concentration of nitric acid on the air exchange rate after using a nitric acid-containing cleaning product (30% nitric acid). Parameters: room size= 30 m³, application area 1 m², application amount 10 g, release model: evaporation, vapour pressure 30% HNO₃ = 89.6 hPa.

3.4 Risk characterisation

In line with the second list for indicative occupational exposure limit values in implementation of Directive 98/24/EC, there is a short-term limit value of 1 ppm (2.6 mg nitric acid/m³) referred to an exposure of 15 minutes¹⁹. The American *National Institute for Occupational Safety and Health (NIOSH)* recommended an exposure limit value (TWA) of 2 ppm/5 mg nitric acid/m³²⁶. As can be seen from Figs. 2a-c, these values can already be considerably exceeded with an application amount of 10 g cleaning product. Particularly sensitive groups in the population, who may indeed be exposed to cleaning products of this kind, like for instance older people, sick people, asthma sufferers and children, are not taken into account when establishing indicative occupational exposure limit values. The cases notified by the poison treatment and information centres show that children were affected in 42% of cases. In principle, stricter safety requirements should be imposed on consumer products than in the work environment.

The National Advisory Committee for Acute Guideline Levels for Hazardous Substances of the American National Research Council has laid down short-term values for selected substances. These AEGL values (**A**cute **E**xposure **G**uideline **L**evel) are peak concentrations of harmful substances which serve to estimate the effects of exposure of the population to chemicals in the case of accidental breakdowns but also as reference values for accidental breakdown planning and prevention. A distinction is made between 3 degrees of severity of health effects for exposure of 10, 30 and 60 minutes as well as 4 and 8 hours²⁷. As illustrated by Figs. 2a and 2b, the AEGL-3 value (30 minute value: 120 ppm/312 mg/m³) could be exceeded under the respective realistic assumptions of amounts applied from 34 g cleaning product or almost achieved when used in small rooms (<10 m³) with a low air exchange rate. The AEGL-3 is the airborne substance concentration upwards of which it is predicted that the general population may suffer life-threatening or fatal health effects. Airborne substance concentrations below the AEGL-3 but above the AEGL-2 value (30 ppm/78 mg/m³) mean levels of exposure which trigger irreversible or other serious, long-lasting health effects or can impair the ability to flee. When laying down the AEGL values one-off exposure is furthermore assumed whereas in the case of the regular use of cleaning products of this kind in the home more frequent exposure must be assumed.

In principle, the health risks associated with the use of nitric acid-containing cleaning products are to be estimated even higher as, besides the toxic properties of nitric acid itself, account must be taken of the effects of the nitrous gases including above all toxic NO₂ which may be formed spontaneously during the reaction of nitric acid or for instance in contact with surface materials of metal (above all copper and silver) or also formed when mixed with alkaline solutions. Based on the available data no scientifically robust estimation of NO₂ exposure can be undertaken in conjunction with the use of nitric acid-containing limestone solvents or rust removers. However, even small amounts of NO₂ constitute a health risk. NO₂ proved to be clastogenic and mutagenic *in vitro* and is classified by the German MAK Commission as a category 3B carcinogen. No threshold doses can be assumed for genotoxic carcinogens below which no adverse effects are to be expected anymore. In addition to the exposure which results from the use of cleaning products of this kind, the background exposure of NO₂ must be taken into account which may be higher in indoor areas than the environmental concentrations. Concentrations here may reach 0.5 ml NO₂/m³ as a 24-hour average with peak concentrations of up to 1 ml/m³²⁸.

3.5 Discussion and recommendations

Bearing in mind the toxic properties of nitric acid outlined and the nitrous gases released from them as well as the numerous cases notified of health impairments amongst consumers when handling nitric acid-containing cleaning products, the Federal Institute for Risk Assessment (BfR) recommends measures to restrict the placing on the market of nitric acid-containing consumer products. As consumer products must comply with stricter safety requirements than products for commercial use, nitric acid-containing products should be regulated for the non-commercial area. The following options should be examined:

(1) Measures pursuant to §14 para. 2 WRMG

In order to ban the distribution of household cleaning products that contain nitric acid in the medium term in Germany, it must be examined whether the legal foundation in accordance with §14 para 2 WRMG (Detergent and Cleaning Agent Act) may suffice for a ban.

The health risk presented here in conjunction with nitric acid-containing household cleaning products justifies the assumption that a nitric acid-containing detergent and cleaning product containing 20-30% nitric acid as a dangerous ingredient, despite compliance with the provisions of Regulation (EC) No. 648/2004, constitutes a risk for the safety or health of humans or animals. This means that the Federal Environmental Agency (UBA) in agreement with the Federal Institute for Risk Assessment could prohibit the placing on the market of this detergent and cleaning agent provisionally or subject it to special conditions.

(2) Measures in response to an infringement of § 30 LFGB or § 4 GPSG

The placing on the market of cleaning products with a nitric acid content of 20-30% could constitute a violation of the ban pursuant to § 30 LFGB because of the toxic properties of nitric acid and the nitrous gases released from it. According to this provision it is prohibited to manufacture or place consumer products on the market that are likely to harm health because of their substance composition in particular through toxically active substances or impurities. When it comes to assessing the toxic properties of nitric acid-containing cleaning products account is to be taken not only of the effects of the nitric acid itself but also the effects of nitrous gases, including above all the toxic NO₂ which may be formed spontaneously during the reaction of nitric acid or for instance in contact with surface materials made of metal (above all copper and silver) or also formed when

mixed with alkaline solutions. NO₂ has proved to be clastogenic and mutagenic *in vitro* and is classified by the German MAK Commission as a category 3B carcinogen. No threshold dose can be assumed for genotoxic carcinogens below which no adverse reactions are to be expected anymore. Furthermore, the numerous cases notified by the poison treatment and information centres document the ability of nitric acid-containing cleaning products to harm the health of consumers in conjunction with correct use or unforeseen misuse.

The production or making available of nitric acid-containing cleaning products could moreover constitute a violation of § 4 para 2 GPSG whereby a product may only be placed on the market when it will not, in conjunction with correct use or unforeseen incorrect use, harm the safety or health of users or third parties.

(3) Reassessment of the harmfulness classification of nitric acid in accordance with CLP Regulation (EC) No. 1272/2008 or in accordance with the Substances Directive (67/548/EEC).

In order to make possible chemical law provisions for risk reduction, the standardised classification and labelling of nitric acid (see index No. 007-006-00-1 in Tables 3.1 and 3.2 of Annex VI of the CLP Regulation (EC) No. 1272/2008) should be widened to include the classification and labelling of acute toxic properties pursuant to Article 40 (2) of this Regulation in the classification and labelling inventory. In accordance with Article 4 (3) second para of the CLP Regulation (EC) No. 1272/2008 this must be done primarily by manufacturers or importers. They could receive corresponding official notice.

This goal could also be supported by a German application in accordance with Article 36 para 3 sentence 2 of the CLP Regulation (EC) No. 1272/2008 if reasons can be given for the need for measures on the Community level.

After widening the classification and labelling in accordance with the CLP Regulation (EC) No. 1272/2008 or the Substances Directive (67/548/EEC) on acute inhalational toxicity, aqueous mixtures of nitric acid could then come under the Chemicals Prohibition Ordinance if agreement is reached on classification of acute toxicity as T or T+ (pursuant to Substances Directive 67/548/EEC). This would then mean constraints on sale (amongst other things self-service) for consumer products that contain a specific concentration and upwards of nitric acid.

(4) Measures in accordance with Article 68 REACH Regulation (EC) 1907/2006

For a full assessment of the health risks arising from the use of nitric acid-containing products, the toxic properties of nitric acid and their proportional decomposition products, here above all NO₂, must be viewed together. As the use of consumer products, which contain 20-30% nitric acid, constitutes an unacceptable risk in the opinion of BfR, it must be examined whether a procedure for restrictions can be triggered under REACH. This would result in an amendment to Annex XVII (Restrictions on the manufacture, placing on the market and use of certain dangerous substances, preparations and articles).

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