Keywords
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Occupational Exposure Limit

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Inhalative exposure to glutardialdehyde – a risk for personnel during automated endoscope reprocessing?

Summary

Background and objective: In endoscope reprocessing, different classes of active substances with specific advantages and disadvantages are used for disinfection. Aldehyde-based disinfectants are characterized by high efficacy combined with excellent material compatibility. Disadvantages include the known fixation of proteins and potential health risks when handling these active substances and, in case of glutardialdehyde (GDA), the strong odour which is perceived as unpleasant. The objective of the present study was to determine the occupational exposure to GDA vapours in the practice of automated endoscope reprocessing with a GDA-based disinfectant (0.2 % GDA in the use-solution) and to assess the risk regarding the toxicological properties of GDA.
Method: The occupational exposures of the employees involved in automated reprocessing were determined in the endoscopy units of three hospitals and in the professional endoscope reprocessing of a company. The personal measurements were carried out in accordance with the VDI's (Association of German Engineers) guideline 3862 using aldehyde collection cartridges located in the breathing zone. During the 2-hour sampling period, 60 litres of air were passed through a cartridge coated with 2.4-dinitrophenylhydrazine and analyzed by liquid chromatography. A total of 17 individual measurements were taken. In addition to the personal GDA values (air concentration in mg/m^3), room volume, type of washer disinfector, room situation (e.g., number of operating washer disinfectors, ventilation, other activities) and the personnel's exposure time in the rooms were assessed.
Results: The measured concentrations varied depending on room and working conditions. In one hospital, where the personnel remained in the reprocessing room only shortly, the GDA concentrations were below the detection limit of 0.02 mg per m^3 of air. With prolonged exposure, measured values were between 0.044 and 0.153 mg/m^3 of air. The highest values (0.1 to 0.153 mg/m^3), however, were measured in a reprocessing room, where manual instrument disinfection with another GDA-based product was performed at the same time. Overall, the measured concentrations were clearly below the occupational exposure limit of 0.21 mg/m^3 proposed by the German MAK (maximum workplace concentration) Commission. This concentration is defined as being low enough to prevent any adverse effects on health including carcinogenic effects, even in case a person is exposed repeatedly for long periods.
Conclusion: The results show that no harmful occupational exposure via the room air has to be expected in automated endoscope reprocessing with a GDA-based disinfectant (0.2 % GDA in the use-solution) when the product is used professionally. Potential olfactory annoyance can be minimized by proper workplace ventilation as well as by technical measures like installation of centralised dosing units or local exhaustion directly in the washer disinfector.

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Introduction

In automated instrument reprocessing, cleaning and disinfection are carried out in special closed washer disinfectors, while reprocessing of heat-sensitive materials like anaesthetic equipment or endoscopes is carried out as automated chemo-thermal disinfection at temperatures of 55–60 °C. For automated disinfection different classes of active substances are used, such as aldehydes, quaternary ammonium compounds and active oxygen-releasing agents. Aldehyde-based products are characterised by high efficacy and excellent material compatibility.

Among aldehyde-based disinfectants, glutardialdehyde (GDA) belongs to the active substances most frequently used. Al-

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though GDA in use-solutions possesses a low vapour pressure, small amounts get into the air. Hence, GDA can affect the user as vapour via the respiratory tract and through direct skin contact, which has to be minimised with appropriate protective measures.

In the past years important findings on the toxicology of GDA resulted in a more strict classification with regard to the sensitising effect and a reduction of the occupational exposure limit.

The toxic effects of GDA, both local and systemic, are based on the reactivity of the aldehyde groups with functional protein groups. The irritant effect of GDA at the portal of entry predominates in all exposure pathways. During the exposure to GDA-based products particularly symptoms like skin and eye irritations, irritations of the upper respiratory tract, headache and dizziness have been reported [1,2].

In case of contact with skin and mucous membranes, GDA has irritant to caustic effects depending on the concentration. Acute exposure to GDA vapour or aerosol irritates the eyes and the upper respiratory tract in particular. In tests with volunteers (non-smokers) the odour threshold for GDA after short exposure (15–30 seconds) at 0.001 mg/m³ (0.27 ppb) was very low. After the exposure to GDA vapours the threshold for the perception at the eye was 1.64 mg/m³ (0.394 ppm) and the threshold for the irritation of the nasal mucosa 1.96 mg/m³ (0.472 ppm). Tests with a 15-minute exposure in an exposure chamber demonstrated that mucous membrane-irritating effects have only to be expected at air concentrations above 0.42 mg/m³ (0.1 ppm) [3].

Skin contact with GDA can lead to sensitisation and to allergic reactions after repeated contact. The threshold for eliciting skin-sensitising effects of GDA is approx. 0.5 % [4]. In addition, vaporous GDA can cause asthmatic reactions in sensitive persons, either as result of an unspecific bronchial hyperreactivity or as respiratory allergy. In spite of available case reports, the respiratory tract-sensitising effect is not definitely proven, even though there are precise indications of specific immunological mechanisms being involved. In view of the large number of exposed persons and the comparatively low number of case studies, GDA is evaluated as inhalation allergen with low potency [5].

Until 2004, the exposure limit for GDA at workplaces was 0.42 mg/m³ (0.1 ppm) in accordance with the German Technical Rule for Hazardous Substances (TRGS 900), although the MAK Commission (German commission for determining the maximum concentrations at the workplace) proposed to lower the limit value to 0.21 mg/m³ (0.05 ppm) with a short-term exposure limit (15 min. mean value) of 0.42 mg/m³ (0.1 ppm) and a momentary value (value that must never be exceeded) of 0.83 mg/m³ (0.2 ppm) already in 2002 [6]. With the revised Ordinance on Hazardous Substances from the 1st January, 2005 there will only be health-based occupational exposure limits (OELs). The OEL for GDA is currently adapted by the Committee on Hazardous Substances on the basis of the MAK Commission proposal. Also in other countries, the occupational exposure limits for GDA have been lowered successively (Table 1).

In 2005, the MAK Commission classified GDA in category 4 of the cancer-producing (carcinogenic) substances. This classification bases upon animal inhalation studies where epithelium lesions in the nasal mucosa were observed due to the irritant effect of GDA. These long-term studies in rats and mice, however, did not result in tumours. Category 4 applies for carcinogenic substances for which genotoxic effects play no or only a subordinate role. This means that these substances are not expected to have a significant contribution to human cancer risk as long as the MAK value is followed. This statement of the MAK Commission applies for the proposed occupational exposure limit of 0.21 mg/m³ (0.05 ppm): For this limit, irritations of the respiratory tract and, therefore, cell-damaging effects with subsequent regenerative growth as precondition for a possible carcinogenic effect can be excluded [7,8].

Numerous studies on the developmental toxicity in different species did not observe any toxic effects in offspring at doses that did not cause maternal toxicity. Hence, the MAK Commission classified GDA in Pregnancy Risk Group C. This means that, as long as the MAK value is observed, a risk of foetal damages does not have to be feared [8].

The objective of the present study was to determine GDA concentrations in the inhaled air during automated endoscope reprocessing in nonventilated and ventilated rooms as well as to assess the risk on the basis of the current standard of knowledge on the toxicological properties of this active substance.

*Table 1: Occupational exposure limits in different countries [5]. * Proposal of the MAK Commission in 2002.*

Country	Occupational exposure limit (mg/m³) for GDA
Germany	0.21* 0.42* (15 min mean value) 0.83* (momentary value which should not be exceeded)
The Netherlands	0.25
UK	0.2
Denmark	0.8
Sweden	0.8
USA	0.2

Materials and Methods

Sampling and analysis

Personal sampling was carried out with an aldehyde collection cartridge in accordance with VDI guideline 3862, part 3 [9]. The cartridge was attached to the personnel's clothing at the height of the collar. During the 2-hour sampling period, 60 litres of air were passed through the cartridge (Personal Air Sampler Gilian Gil Air 5 from Sensidyne). The resulting volume flow rate of 0.5 L/min was within the range recommended for exposure monitoring. The limit of detection was 0.02 mg/m³.

Temperature and humidity were determined continuously during the entire measurement period.

The collection cartridge contained acidified 2.4-dinitrophenylhydrazine (DNPH) as adsorber material. The deter-

Table 2: Reprocessing rooms and operational circumstances during GDA measurements.

Measurement location	Measure-ment	Type and number of washer disinfectors	Ventilation	Room size	Other cleaning and disin-fection mesures
Hospital A	A1	Olympus ETD 2 plus (n = 2)	No ventilation	36 m³	No manual instrument disinfection
	A2				
	A3				
	A4				
Hospital B	B1	Olympus ETD 2 plus (n = 3, davon 1 außer Be-trieb)	Ventilation via open door and small ventilation flap	38 m³	Manual instrument disinfection with GDA-free product
	B2				
	B3				
	B4				
Hospital C	C1	BHT Innova E 3 (n = 2)	Room with balanced ventilation, washers with ventilation	30 m³	Manual instrument disinfection with GDA-based product, handling at open disinfection bath
	C2				
	C3				
	C4				
Company	U1	HAMO T 21 (n = 3)	open window, ventilation system	82 m³ unclean room, 91 m³ clean room	No manual instrument disinfection
	U2		open window, ventilation system		
	U3		open window ventilation system turned off		
	U4		open window ventilation system turned off		
	U5		open window, ventilation system		

mination was carried out according to the DNPH method: Carbonyl compounds quantitatively react with 2.4-dinitrophenylhydrazine to the corresponding hydrazones in the presence of acid. The transformation is described in the chemical equation in figure 1.

The single components were desorbed through extracting the filter with acetonitrile in the ultrasonic bath. Afterwards they were analysed by means of high performance liquid chromatography (HPLC) and UV detection (photo diode array detector).

The amount of GDA was determined in relation to the 60 litres of air passed through the cartridge during the two hours and was expressed as GDA concentration in mg/m³ of air.

Operating conditions during the measurements

In the investigated hospitals, the size of the endoscope reprocessing rooms ranged between 30–38 m³; the rooms were equipped with 2–3 endoscope washer disinfectors according to DIN EN ISO 15883-4 (EWD). The industrial company's relatively large professional endoscope reprocessing area was subdivided into a clean (91 m³) and an unclean room (82 m³), both separated by a total of 3 EWDs.

Measurements were taken under realistic worst-case conditions. The reprocessing rooms of the endoscopy units in the hospitals were not equipped with ventilation systems. During normal operation, ventilation was provided via windows and/or doors or via small ventilation flaps. In hospital C, the EWDs were equipped with an offtake to the outside. The ventilation in the industrial company's reprocessing rooms was provided via ventilation systems and open windows; measurements were taken with both turned-on and turned-off ventilation system.

Endoscope reprocessing was carried out by nursing staff. The individual employee's exposure time varied between 5–120 minutes during the respective 2-hour measurement period. In all three hospitals 1–4 reprocessing procedures and in the industrial company 6 automated reprocessing procedures were carried out within each measurement period. Due to the higher number of automated reprocessing procedures and the significantly higher disinfectant consumption the measurements in the industrial company also included two canister exchanges. During the second canister exchange (measurement 5) a small amount of product concentrate was spilled and immediately removed with water.

Room temperature and humidity were continuously measured during sampling. Temperatures ranged between 20 and 27°C, humidity was between 23 and 63 %.

Operating conditions and duration of stay in the reprocessing rooms are summarised in tables 2 and 4.

Used product

For disinfection a 1 % solution of a product containing 20 % GDA (Korsolex® Endo Disinfectant; BODE Chemie Hamburg) was used in amounts of 120–350 ml per cycle. In two hospitals, manual endoscope reprocessing was carried out at the same time; in one case a GDA-based product was used (Korsolex® extra; BODE Chemie Hamburg). The labelling of the

product used for automated reprocessing is specified in table 3.

Table 3: Labelling of the used disinfectant depending on the dilution

Disinfectant	Labelling
Concentrate with 20 % GDA	C; R 10-20/22-34-37-42/43 R 10 Flammable R 20/22 Harmful by inhalation and if swallowed R 34 Causes burns R 37 Irritating to respiratory system R 42/43 May cause sensitisation by inhalation and skin contact
1 % use-solution with 0.2 % GDA	Labelling as hazardous substance not necessary

Results

The personal measurements during automated endoscope reprocessing with a GDA-based instrument disinfectant (use-solution with 0.2 % GDA) resulted in a mean GDA concentration of 0.065 mg/m³ (± 0,046 mg/m³). The highest concentration (0.153 mg/m³) was measured in one room, where parallel manual instrument reprocessing with another GDA-based product (hospital C) posed an additional exposure source.

Measurements with a short exposure time yielded GDA concentrations below the limit of detection (0.02 mg/m³). During predominant stay in the reprocessing rooms all values were far below the previous occupational exposure limit (OEL) of 0.42 mg/m³ as well as clearly below the OEL proposed by the MAK Commission (0.21 mg/m³), which was reached up to 21–73 % (Table 4, Figure 2).

Discussion

As GDA is widely used as an active substance for disinfectants, many workplace measurements in hospitals exist. However, there are only few GDA measurements during automated instrument reprocessing.

The Institution for Statutory Accident Insurance and Prevention in Health and Welfare Services (BGW, Berufsgenossenschaft für Gesundheitsdienst und Wohlfahrtspflege) took 2-hour GDA measurements in endoscopy units of hospitals during endoscope reprocessing. The 24 stationary measurements in reprocessing rooms equipped with washer disinfectors exhausted the occupational exposure limit of 0.42 mg/m³ (0,1 ppm) valid at that time to a maximum of 10 %. 14 additional stationary measurements at potential emission sources exhausted the limit value to a maximum of 25 % when taken directly at the washer [10].

In a Swedish hospital, short-term measurements (15 min.) taken during automated instrument reprocessing (cold sterilisation, 2 % GDA) yielded concentrations of 0.01–0.18 mg/m³ – the highest GDA concentration was measured during preparation and application of the use-solution in a room with poor ventilation [1].

In English hospitals, stationary measurements (5–38 min.) during automated endoscope reprocessing (cold sterilisation, 2 % GDA) taken in the height of the head above the washer disinfector determined average GDA concentrations of 0.008 mg/m³ and 0.053 mg/m³ depending on the type of washer disinfector; the maximum concentration was 0.21 mg/m³. The maximum GDA concentration of the personal measurements (4–26 min.) was 0.11 mg/m³ [11].

In Australian hospitals, personal short-term measurements (1–15 min.) during automated instrument reprocessing yielded GDA concentrations of 0.034–0.21 mg/m³ (0.008–0.05 ppm) with a geometric mean of 0.1 mg/m³ (0.024 ppm); the type of automated reprocessing was not described in detail [12].

Personal ultra-short-term GDA measurements (5 sec. to 12.25 min.) with a directly displaying method were performed in Australian hospitals. The peak concentration during automated instrument reprocessing (not described in detail) was 0.34 mg/m³ (0.08 ppm). Measurements were only taken on one person while other persons carried out manual instrument reprocessing, probably with a GDA-based product. This method allows the determination of peak exposures, but is judged as uncertain due to the poor specificity of the method (e.g. sensitive to alcohols) [13, 5].

In 6 Japanese hospitals, both stationary and personal measurements were taken during semi-automated instrument disinfection with 2–3.5 % GDA. The geometric means of the stationary measurements were 0.005–0.08 mg/m³. The highest concentration (0.23 mg/m³) was measured close to a disinfection bath with a GDA-based product next to 3 washer disinfectors. Personal measurements were taken during exchanging the disinfectant solution for automated reprocessing, an activity of approx. 15 minutes duration. These yielded GDA concentrations of up to 0.4 mg/m³ (0.094 ppm). All measurements were carried out in nonventilated rooms [2].

Already in 1992, BODE Chemie initiated GDA measurements in the endoscope reprocessing of one hospital, which used the same product for automated reprocessing as in the present study (20 % GDA in 1 % use-solution). At that time, the objective of the study was to determine the exposure to GDA during operation of an EWD in a room with turned-off technical ventilation. The stationary measurements were performed as long-term measurement (34–35 min.) during

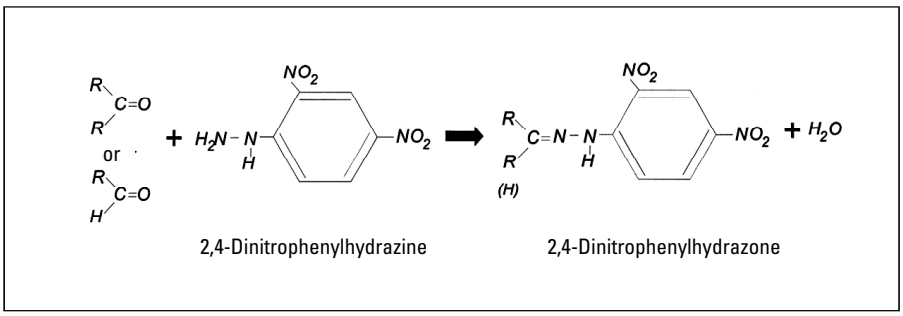

Figure 1: Reaction of carbonyl compounds with DNPH.

*Table 4: Exposure periods and results of the GDA measurements. *Limit of detection = 0.02 mg/m³.*

Measurement location	Length of stay in reprocessing room during the 2-hour measurement (special activities)		Used amounts 1 % solution with 0.2 % GDA	Measured value	Exhaustion of the OEL (0.21 mg/m³)
	occasional [min]	predominant [min]	[ml]	[mg/m³]	[%]
Hospital A	A1 – 14		125	<0.02*	<10
	A2 – 8			<0.02*	<10
	A3 – 13			<0.02*	<10
	A4 – 12			<0.02*	<10
Hospital B		B1 – 115	120	0.048	23
		B2 – 105		0.059	28
		B3 – 102		0.044	21
		B4 – 105		0.071	34
Hospital C		C1 – 100	200	0.118	56
		C2 – 105		0.100	48
		C3 – 110		0.153	73
		C4 – 115		0.133	63
Company	U1 – 10		350	<0.02*	<10
		U2 – 120		0.049	23
		U3 – 110 (Canister exchange)		0.085	40
	U4 – 5			<0.02*	<10
		U5 – 110 (Canister exchange)		0.13	62
Overall evaluation Mean value ± Standard deviation				**0,065 ± 0,046**	

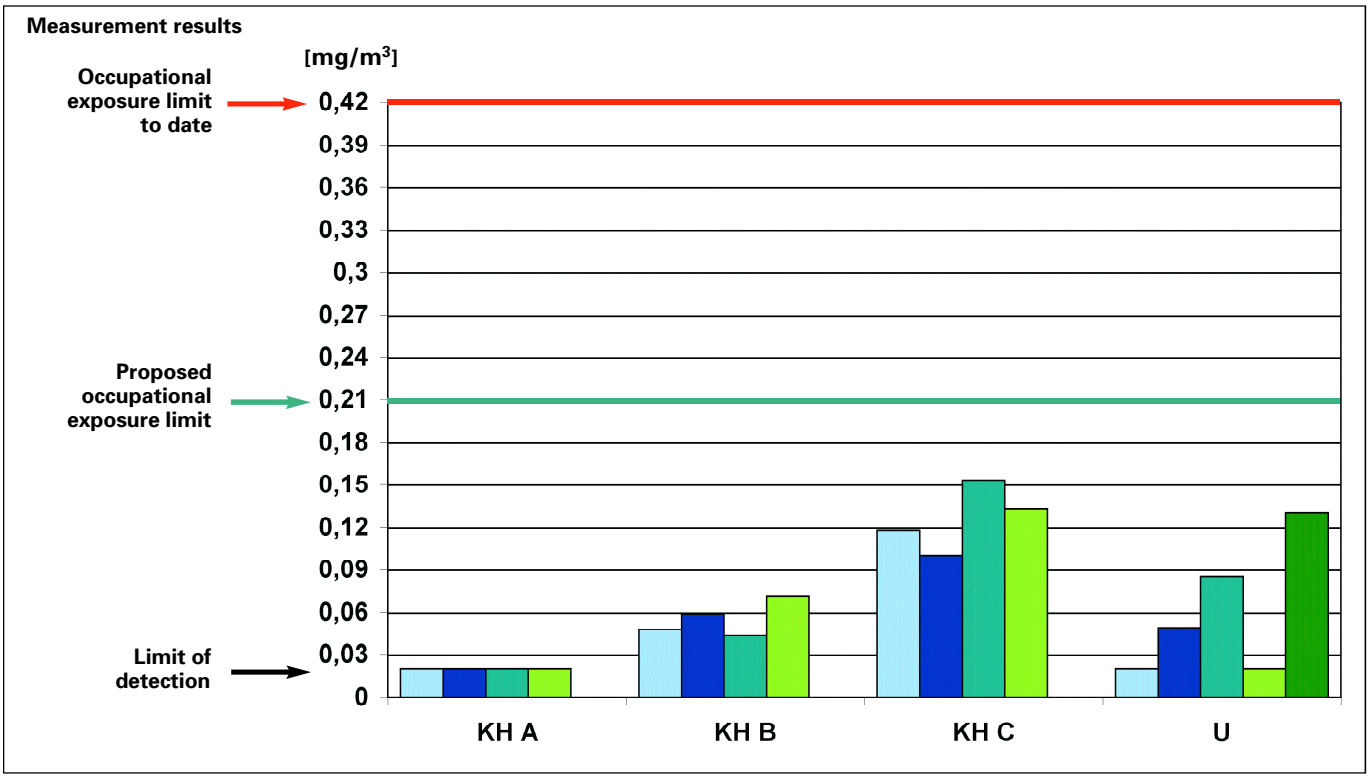

Figure 2: Measurement results of GDA concentration in the air during automated endoscope reprocessing.

the entire washer cycle and as 5 short-term measurements (3–12 min.) during the different work steps both in front of and next to the EWD. All measured results were below the detection limit, which was 0.03–0.16 mg/m³ depending on the sampling volume, and therefore far below the occupational exposure limit of 0.84 mg/m³ (0.2 ppm) valid at that time [14].

The measured GDA concentrations correspond to the results of other studies during automated instrument reprocessing. The occupational exposure limit of 0.2 mg/m³, which is valid in most countries, was only significantly exceeded by the measurement during the exchange of the disinfectant solution in a Japanese hospital (0.4 mg/m³). The measurements were taken during semi-automated instrument reprocessing, which was performed with GDA concentrations more than ten times higher (2–3.5 %) than in automated endoscope reprocessing. The peak limit (15 min. mean value) of 0.42 mg/m³ as proposed by the MAK Commission was not exceeded during the exchange of the disinfectant solution. Also the short-term measurements in Australian hospitals were below the peak limit.

The 2-hour measurements taken in the present study describe an average concentration and cannot indicate short-term peak concentrations. In automated instrument reprocessing, higher concentrations could occur during canister exchange. Higher concentrations are not to be expected when the washer is opened after the rinse program, because the instruments are rinsed with water after disinfection. Normally, canisters are not exchanged several times a day. Hence, the determination of the short-term exposure during automated instrument reprocessing is of less importance.

There have been repeated reports about olfactory annoyances and health problems when GDA-based products are used for disinfection in hospitals. Also for these reasons other active substances such as peracetic acid and OPA (ortho-phthalaldehyde) have recently been introduced as alternatives.

GDA is an active substance that is toxicologically well-studied, which does not necessarily apply for alternatives being supposedly less harmful. So far, there are only few data on OPA (ortho-phthalaldehyde); however, structure-activity-relationships suggest a sensitising potential like with GDA [15]. In addition, anaphylactic reactions after laryngoscopies and cystoscopies that were performed with instruments disinfected with OPA have been reported [16, 17]. Peracetic acid presumably has no sensitising effect, the contact with concentrated solutions, however, can result in serious eye and skin injuries. Peracetic acid is classified in Group III B of carcinogenic substances (substances suspected of having carcinogenic potential), because there are indications of a possible carcinogenic potential, but the data are incomplete and inconsistent. Hence, final conclusions on the carcinogenic potential are not possible. Due to insufficient data, neither for peracetic acid nor for OPA occupational exposure limits have been defined so far.

The sensory irritation, particularly of eyes and upper respiratory tract, is the crucial effect when handling GDA-based products and being exposed to GDA vapours. Even in poorly ventilated workplaces, the GDA concentrations during automated endoscope reprocessing with 0.2 % GDA solution are in a range that is not expected to have any adverse health effect. For sensitive persons an olfactory perception of GDA is already possible in the ppb range. This means that the substance is already perceived in concentrations that are less than one-hundredth of the occupational exposure limit that is regarded as harmless to health.

Conclusion for clinical practice

It has been shown that, even under relatively poor ventilation conditions, no toxicologically critical air concentrations were reached during automated endoscope reprocessing with a use-solution that contains 0.2 % GDA. In this respect, there are no adverse health effects to be expected for personnel in automated reprocessing with GDA-based products in comparable use-concentrations when the product is used professionally.

To reduce possible olfactory annoyance and to prevent the occurrence of uncontrolled short-term concentration peaks, good ventilation of the workplaces has to be ensured in automated reprocessing as well. Canisters have to be exchanged very carefully; possibly spilled product residues have to be removed immediately. Due to its sensitising potential, the direct contact with GDA has to be prevented by wearing protective gloves, eye protection and suitable protective clothing. Practical examples show that the exposure of the personnel can be reduced to a minimum through technical improvements like installation of centralised dosing units or local exhaustion directly in the washer disinfector.

Conflict of interest

The authors are employees of BODE Chemie GmbH & Co. KG, Hamburg, Germany.

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