Determination of tolerable process chemical residues after reprocessing thermolabile endoscopes

H. Biering

The manufacturers of process chemicals and of washer-disinfectors (WDs) used to clean and disinfect thermolabile endoscopes are required to inform users about the tolerable amounts of process chemical residues. Performance qualification of the reprocessing process at the site of use should demonstrate that the amount of residues measured on the medical device is lower than the specified tolerable residual value. These investigations can be based on extraction of residues from the endoscope surfaces or, as applicable, from process challenge devices (PCDs), followed by analytical determination of the respective chemicals.
The present study explored the possibility of using PCDs. After comparing the adsorption and extraction behavioural patterns of selected process chemicals in respect of synthetic materials versus distal end pieces of endoscopes, we investigated the possibility of using these materials as PCDs. Based on our findings, we propose using a polyurethane PCD for determination of process chemical residues after reprocessing thermolabile endoscopes, and also describe the conditions for residue extraction from the PCDs.

KEY WORDS
- instrument reprocessing
- medical devices
- thermolabile endoscopes
- process chemicals
- tolerable residues
- validation

Introduction

The standard ISO 15883-1 (1) stipulates that the manufacturers of washer-disinfectors (WDs) used for automated reprocessing of reusable medical devices must specify the amount of residues than can be tolerated on the medical devices at the end of the process.
Before a medical device is first used on a patient its biological compatibility must be assessed by conducting risk assessment in accordance with the ISO 10993 (2) series of standards. A similar approach is used for toxicological assessment of any risks posed by residues of the process chemicals used to reprocess medical devices (3). Based on German guidelines, i.e. guidelines on validation of automated cleaning and thermal disinfection processes for medical devices (4), manual cleaning and manual chemical disinfection of medical devices (5) as well as automated cleaning and disinfection processes for reprocessing thermolabile endoscopes (6), the tolerable chemical residues should be determined at the time of validation of the reprocessing methods. The maximum tolerable residues limits are set by the manufacturer of the process chemicals or of the washer-disinfector.
For validation of automated cleaning and thermal disinfection processes, on using for example mildly alkaline and alkaline detergents, measurement of the electrical conductivity of the final rinse water suffices for estimation of the amount of process chemical residues on the medical devices (7, 8, 9). For validation of manual cleaning and chemical disinfection methods as well as of processes used for chemothermal reprocessing of thermolabile endoscopes, (9, 10), analytical determination of the process chemical residues on the surfaces of medical devices or, as applicable of PCDs, is recommended because of the potential toxicity of disinfectants as well as of certain ingredients of neutral detergents, in particular of non-ionic surfactants. For manual methods of medical device reprocessing, apart from thermolabile endoscopes, details of a method for extraction of the residues from the instruments will be published (11). The manufacturer must provide information on the method to be used in each case for analytic determination of the process chemicals in the extraction solution.

There are reports of process chemical residues, for example glutaraldehyde, on endoscope surfaces causing intestinal infection (12, 13). Systematic investigations of residue extraction from endoscope surfaces have been conducted in the case of glutaraldehyde. Using water heated to 40 °C, Drongelen et al. (14) extracted formaldehyde and glutaraldehyde residues from 38 endoscopes that been used for routine procedures in 13 hospitals. The extraction time was 20 min. Emmrich et al. (15) studied the effect of the pH value, temperature and water composition on glutaraldehyde extraction efficiency from PCDs, which consisted of parts of endoscope insertion tubes. On using a largely similar glutaraldehyde baseline quantity, the greatest amounts of residues were extracted from the PCD surfaces with distilled water at pH 2 and a temperature of 36 °C. On using water of standardized hardness (16) at pH 7, a virtually identical residue amount was extracted. Further testing of manually contaminated endoscopes revealed that,

PD Dr. Holger Biering, Gladiolenstr. 19, 41516 Grevenbroich, Germany
E-mail: holger.biering@web.de

when employing correction factors, it was also possible to conduct extraction at pH 7 and with a temperature of 20 °C, with corresponding extrapolation of the values. Based on these studies it was possible to devise a practical method for extraction of glutaraldehyde residues, while describing its analytical determination and evaluation, which can be used for performance qualification of endoscope reprocessing (17).

The use of PCDs as an alternative to residue extraction from endoscopes for performance qualification can be contemplated if the PCDs are subjected to the same reprocessing process as the endoscopes. An expert working group was set up to identify an appropriate PCD that could be used for determination of different types of detergent and disinfectant residues. These experts were composed of representatives of member companies of the healthcare section of the German Industrial Association for Hygiene and Surface Protection (IHO). The group is moderated and coordinated by Priv.-Doz. (Assistant Professor) Dr. Holger Biering and comprises the following experts: Dr. Richard Bloß (Bode-Chemie), Dr. Erik Brückner (Dr. Schumacher), Markus Kamer (Dr. Weigert), Dagmar Martini (Bode-Chemie), Alexander Müller (B. Braun), Dr. Andreas Otte (Ecolab), Michael Schreiner (Schülke & Mayr), Anna-Maria Sprünken (Schülke & Mayr).

The first task undertaken in this study was to investigate under standard conditions the adsorption and extraction profiles, with respect to various synthetic materials, of the various ingredients of the process chemicals used to reprocess thermolabile endoscopes. To that effect, selected formulations with a broad spectrum of ingredients were studied. Based on the findings, PCDs and methods for extraction of process chemicals from the PCD surfaces were proposed as a potential method for residue determination in performance qualification of reprocessing processes for thermolabile endoscopes.

Materials and Methods

Products tested

The following process chemicals used for cleaning and/or disinfection of thermolabile endoscopes were tested:

- Product A: Liquid disinfectant, contains 10 – 25% glutaraldehyde, solubilizer and water, density: 1.04 g/cm^3, colour: light yellow, pH value: 2.5, use concentration: 1.0 vol. %.
- Product B: Liquid disinfectant, contains 5 – 15% glutaraldehyde and water, density: 1.03 g/cm^3, colour: light yellow, pH value: 3.5, use concentration: 1.0 vol. %.
- Product C: Liquid detergent disinfectant, contains <10% quaternary ammonium compound (Quats), <10% diamine, non-ionic surfactants, solubilizer, chelating agents and water, density: 1.1 g/cm^3, colour: green, pH value: approx. 7.5, use concentration: 1.0 vol. %.
- Product D: Liquid detergent disinfectant, contains <10% quaternary ammonium compound (Quats), <5% biguanide derivative, non-ionic surfactants, solubilizer and water, density: 1.005 g/cm^3, colour: green, pH value: approx. 9.0, use concentration: 1.0 vol. %.
- Product E: Liquid disinfectant, contains 1 – 5% peracetic acid, 8 – 35% hydrogen peroxide, <10% acetic acid and water, density: 1.12 g/cm^3, colour: colourless – light yellow, pH value: 1.0, use concentration: 4.5 vol. %.
- Product F: Granulated detergent disinfectant, contains > 30% oxygen-based bleaching agents, phosphates and non-ionic surfactants, bulk density: 0.80 kg/l, colour: white, pH value (solution 2.O wt.%): 7.6, use concentration: 2.0 wt.%.
- Product G: Liquid detergent disinfectant, contains 15 – 25% coco propylene diamine, non-ionic surfactants, solubilizer, chelating agents and water, density: 0.98 g/cm^3, colour: cyan, pH value: approx. 10.0, use concentration: 1.0 vol. %.
- Product H: Liquid detergent, contains 5 – 15% fatty alcohol alkoxylate (non-ionic surfactant), solubilizer and water, density: 1.0 g/cm^3, colour: blue, pH value: approx. 7.0, use concentration: 1.0 vol. %.

Materials tested

The following materials were used as PCDs in the extraction tests:

- Test pad measuring 60 × 40 × 4 mm and composed of silicone rubber, surface area: 56 cm^2,
- Test pad measuring 60 × 40 × 4 mm composed of chloroprene, surface area: 56 cm^2,
- Test pad measuring 60 × 40 × 3 mm composed of polyurethane, surface area: 54 cm^2,
- Test pad measuring 60 × 40 × 4 mm composed of ethylene propylene diene monomer (EPDM), surface area: 56 cm^2,
- Distal end manufactured by Pentax, surface area: 56 – 58 cm^2.

Experiments with PCDs

The PCDs were immersed in the use-concentration solutions of the process chemicals, as listed above, for 1 h or 2 h at room temperature (20 °C to 25 °C) while ensuring that all surfaces were fully wetted. Tests were carried out in duplicate for each PCD/test product combination. After removing the PCDs from the solution the chemical solution was allowed to drip off and then the PCDs were placed vertically for 15 s on paper tiles. Next, the moist PCDs were left to dry off for one hour in the air.

The process chemical residues on the PCD surfaces were extracted by immersing the PCDs in a defined volume of demineralized water (10 ml to 50 ml). Samples were taken from the extraction solution at specified intervals and the concentrations determined.

Analytical methods for concentration determination

A lead substance whose concentration was representative of the residual amounts of the respective product was defined for each test product. The following analytical methods were applied in the participating laboratories to determine the concentration in the extraction solution of the lead substance used to represent the process chemicals:

- Product A – HPLC (high performance liquid chromatography) – lead substance: glutaraldehyde
- Product B – HPLC (high performance liquid chromatography) – lead substance: glutaraldehyde
- Product C – Hach-Lange test LCK333 – lead substance: non-ionic surfactant
- Product D – HPLC (high performance liquid chromatography) – lead substance: quaternary ammonium compound
- Product E – Merckoquant peracetic acid test 5 ppm to 50 ppm – lead substance: peracetic acid
- Product F – Hach-Lange test LCK333 – lead substance: non-ionic surfactant
- Product G – HPLC (high performance liquid chromatography) – lead substance: alkylamine
- Product H – Hach-Lange Test LCK333 – lead substance: non-ionic surfactant

Results

Selecting suitable PCDs – Determination of extraction time

In preliminary tests suitable analytical methods were identified for determination of the anticipated small quantities of these substances in the extraction solutions. Using distal end pieces of endoscopes as PCDs, the relationship between the extracted residual amount and the time was investigated for the test products. The findings demonstrated that for the vast majority of the process chemicals studied (products A to H), the amount of substance extracted continued to rise during a 24 h extraction time, then remaining to a large extent constant (Fig. 1). Already after 1 h, the extracted amount was already between 50% and 70% of the value reached after 24 h for the majority of products (Table 1: products C,D,F,G,H). If the guide value used for analytical determination is based on a decomposing substance (product E), the extraction time should not exceed 1 h. The decline in the extracted amount for product A when using longer extraction times was interpreted as adsorption/reaction and/or penetration of the analytical lead substance (glutaraldehyde) on or into the PCD material after prolonged exposure times (14). A shorter extraction time of 1 h proved to be advantageous.

Selecting suitable PCDs – Determination of a suitable material

To select a suitable material for use as a PCD the adsorption and extraction profiles of the test products in respect of various synthetic materials were compared with those of a distal end piece of an endoscope. Further tests were conducted to identify whether the material type had any impact on the analytical method. Problems were encountered in the case of the chloroprene PCDs due to interaction with product E, giving rise to yellow discoloration of the disinfectant and extraction solution. Problems also arose when carrying out the analytical procedure with the EPDM-based PCDs for determination of the lead substances for the products G and F (Table 2). Polyurethane and silicone rubber proved to be suitable materials for use as PCDs, with comparable or higher process chemical residual amounts extracted from the PCD surfaces compared with distal end pieces of endoscopes (Table 2).

Table 1: Amount of process chemicals extracted from distal end pieces of endoscopes used as a PCD after an extraction time of 1 h and 24 h

Process chemical	Extracted amount			
	1h		24h	
	µg/cuff	µ/cm²	µg/cuff	µ/cm²
Product A	130.0	2.28	40.0	0.70
Product B	6.8	0.12	38.19	0.67
Product C	36.6	0.64	52.7	0.92
Product D	30.0	0.53	40.0	0.70
Product E	60.0	1.05	n.d.[1]	n.d.[1]
Product F	49.6	0.87	91.2	1.6
Product G	60.0[2]	1.05[2]	90.0[2]	1.58[2]
Product H	23.0	0.40	48.0	0.84

Legend:
1: n.d. – not determined
2: Modification of the experimental procedure: After removal from the test solution and before drying, the PCDs were lightly sprayed using a spray bottle.

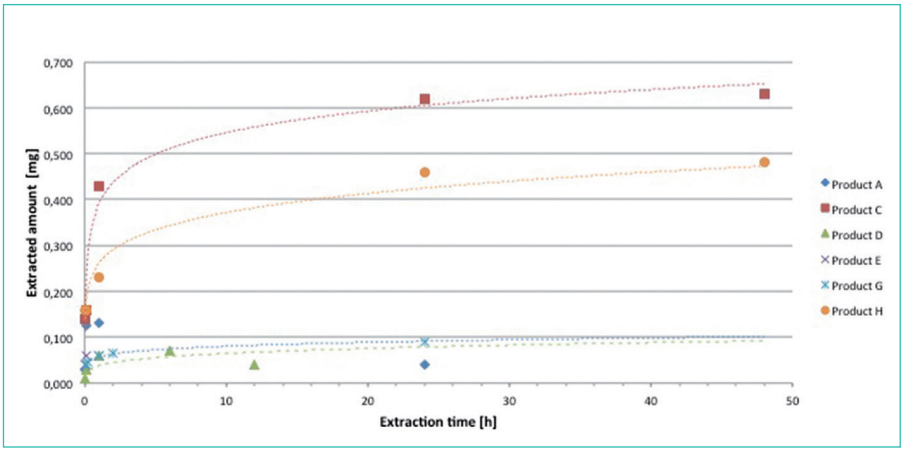

Fig. 1: Amount of process chemicals extracted in mg per endoscope cuff in relation to the extraction time

Discussion

The IHO Working Group set itself the task of investigating tolerable process chemical residues when reprocessing thermolabile endoscopes by using PCDs under conditions that could then be used for performance qualification at the user's site.

Extraction conditions

Van Drongelen et al. (14) extracted process chemical residues from endoscopes with water at a constant, high temperature (40 °C) in a flask within 20 min. As demonstrated by the study authors, that method can be implemented at the site of use but needs considerable investment in equipment. Likewise, the method proposed by Emmrich et al. (17) can be applied at the user's site but has the advantage of being able to incorporate correction factors at 20 °C. But a disadvantage is that the procedure must either be carried out under nearly sterile conditions or the test endoscopes must be reprocessed once again. Findings are available for both methods for formaldehyde and/or glutaraldehyde extraction using an extraction time of 20

Table 2: Amount of process chemicals extracted from the surface of different synthetic materials in µg/cm²

Process chemical	Extraction time [h]	Extracted amount [µg/cm²]				
		Endoscope cuff	Silicone rubber	Polyurethane	EPDM	Chloroprene
Product A	1	2.23	2.39	3.18	0.97	1.24
	24	0.71	3.44	3.05	0.91	0.43
Product B	1	0.12	1.10	<0.61	1.10	<0.61
	24	0.67	1.30	<0.61	<0.61	<0.61
Product C	24	1.70	0.82	0.36	0.71	0.53
Product D	12	0.76	1.02	0.43	2.01	0.70
Product E	1	1.06	1.84	2.13	1.50	n.c.[1]
Product F	1	0.87	0.7	3.1	n.c.[1]	0.5
	24	1.60	1.30	2.70	n.c.[1]	6.30
Product G	24	4.21	17.14	9.52	n.c.[1]	7.35
	48	6.57	21.42	10.00	n.c.[1]	7.89
Product H	24	1.30	1.15	1.51	3.43	1.55

Legend:
1: n.c. – not conducted

min. No information is available for products based on other active substances and/or ingredients.

After evaluation of the findings of the two studies (14, 15, 17) mentioned above, and bearing in mind the feasibility of carrying out the method at the site of use, in the present study we used demineralized water as extraction medium (readily available in many places) and a temperature range of 20 °C to 25 °C (room temperature) for the extraction process. Determination of the extraction temporal course revealed that the extracted amount continued to rise for the majority of the process chemicals for up to 24 h and then remained largely constant. For decomposing substances, such as peracetic acid (product E), or for substances with a high adsorbing or penetrative capacity such as glutaraldehyde (product A), extraction times of longer than one hour can produce incorrect results.

As such, the results obtained under the extraction conditions described, with demineralized water at room temperature and an extraction time of 1 h, can be deemed to be sufficiently accurate.

Selecting suitable materials for PCDs

Synthetic materials used for manufacture of reprocessable thermolabile medical devices were investigated as potential materials for PCDs. One criterion applied for evaluation was that the adsorption and extraction behavioural patterns induced by the process chemicals in respect of the materials should be similar to those exhibited by distal end pieces of endoscopes. Furthermore, the analytical procedure used for the process chemicals should not be affected by the potential PCDs and the materials should be commercially available while assuring a consistent quality.

Ethylene propylene diene monomer (EPDM) was found to exert an effect on the HPLC analytical procedure used for determination of the lead substance alkylamine in product G as well as the Hach-Lange test LCK333 analytical procedure used for determination of the non-ionic surfactant lead substance for product F (Tab. 2). Interaction of chloroprene with peracetic acid gave rise to discoloration of both the disinfectant and extraction solution in the case of product E. Both materials were therefore deemed unsuitable since the aim was to use one standard PCD model for all process chemicals.

Silicone rubber and polyurethane were found to be suitable materials. Neither of the two materials led to any problems during the analytical procedure for determination of the lead substances and the residual values obtained were on a par with those extracted from distal end pieces of endoscopes. Polyurethane PCDs proved to be particularly suitable since this material is used to produce endoscopes.

It is expected that one standard PCD model (material, dimensions) from a single procurement source will be recommended by all process chemical manufacturers for determination of process chemical residues at the time of performance qualification of reprocessing processes for cleaning and disinfection of thermolabile endoscopes. Further studies of the adsorption behaviours of process chemicals should be carried out by the manufacturers under the conditions prevailing at the respective site of use. The maximum tolerable limits for the process chemicals used in a reprocessing process as well as the analytical methods for determination of the lead substance to be employed for determination of residues are specified by the manufacturer of the process chemicals or of the washer-disinfector.

Outlook

A matter of debate is whether such PCDs can be used for performance qualification of other reprocessing processes depending on the medical devices reprocessed, the process chemicals used and the conditions prevailing at the respective site of use. These aspects will be investigated in forthcoming studies.

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Procurement source for polyurethane PCDs

The polyurethane PCDs can be sourced using the purchase order text:
PUR NA PCDs
60 × 40 × 3 mm
from the firm Buck & Sohn, Schimmelmannstr. 139, 22043 Hamburg, Germany

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Fax 0611 50593-79

info@mhp-medien.de
www.mhp-medien.de

mhp_medien