

# Health risks of surface disinfection with special consideration of quaternary ammonium compounds (QAC)

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**No microbicidal agent is without toxicological risks, but depending of the structure distinct differences exist**

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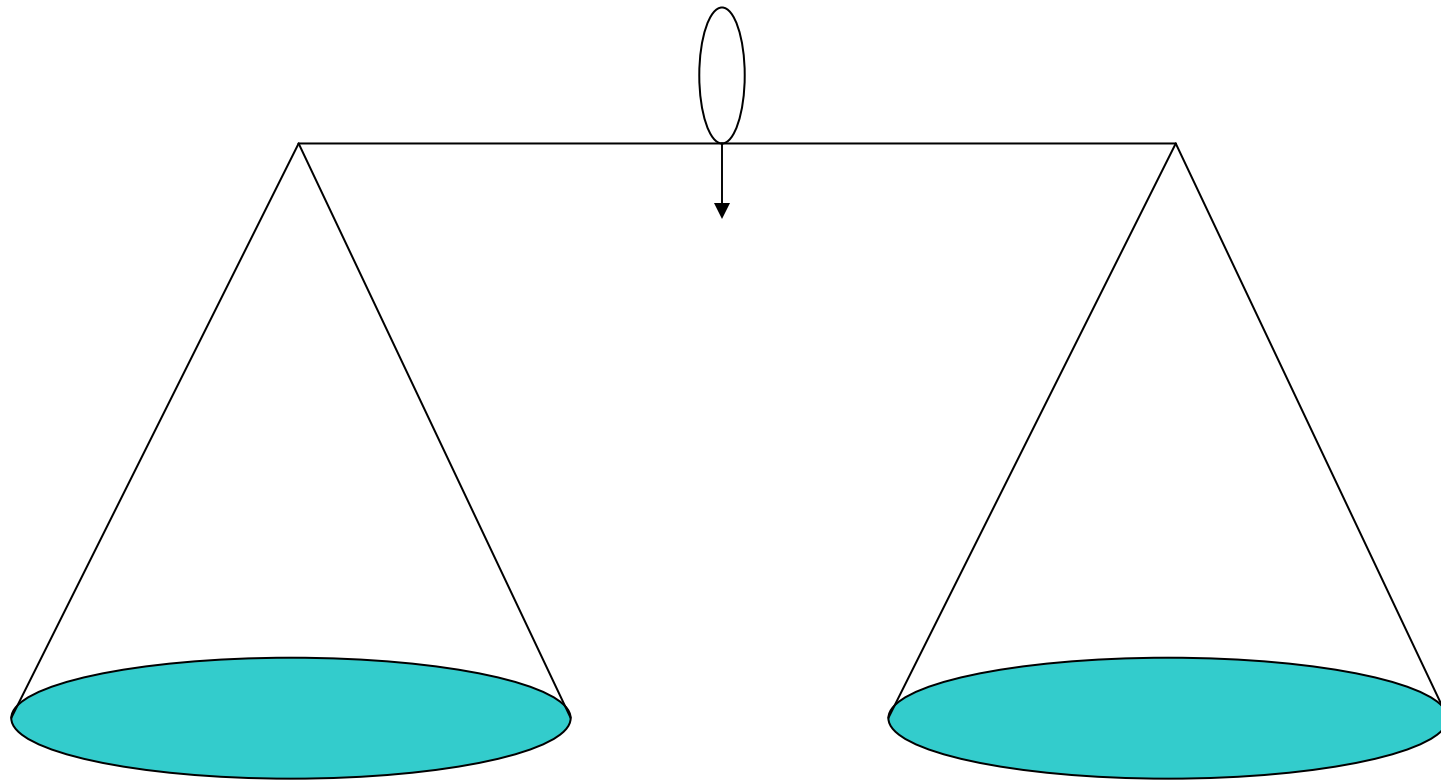
- **Because of their antimicrobial action, the use of disinfectants requires a careful risk benefit assessment to minimize potential side effects in humans as well as in the environment**
- **This is valid in particular for their application within household setting**

**Always, the following premises need to be considered when disinfectants are used:**

- **Is there a justifiable indication?**
- **Is the selection of the active compound based on the expected antimicrobial spectrum?**
- **Is the active compound selected characterised by the most suitable biocompatibility index**

# Criteria for the choice of an active compound

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**toxicity of the disinfectant**

**infection risk**

**risk benefit balance**



# Non-critical antimicrobial agents

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## **Alcohol-based compounds**

- **Compounds of first choice for hand disinfection and skin antisepsis, but also for small inanimate surfaces**
- **Their spectrum includes bacteria, fungi, enveloped viruses and for special formulations also non-enveloped viruses**
- **Even at repeated dermal and inhalative exposition no critical blood levels are reached ( $\leq 0.02$  ‰)**

**Kramer, Below, Bieber et al. Quantity of ethanol absorption after excessive hand disinfection using three commercially available hand rubs is minimal and below toxic levels for humans. BMC Infect Dis 2007, 7 p117.**

**Below, Partecke, Kramer et al. Dermal and pulmonary absorption of propan-1-ol and propan-2-ol from hand rubs. Am J Infect Control 2011**



# Non-critical antimicrobial compounds

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**Oxidants (e.g. potassium peroxomonosulfate or  $H_2O_2$ ), formic acid and sodium hypochlorite (for high level disinfection)**

- **For disinfection of large surfaces**
- **Their spectrum includes vegetative bacteria, viruses and fungi as well as bacterial spores**
- **No inhalative or systemic side effects are known**



# Critical antimicrobial compounds

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**Aldehydes shall not be used on surfaces in household settings as well as in hospitals.**

## **Formaldehyde**

- high sensitisation potency
- carcinogenicity
- mutagenicity
- inhalative neurotoxic potency

## **Glutaral**

- asthma inducing potency
- mutagenic

## **Glyoxal**

- allergic
- mutagenic
- possibly teratogenic (category 3)
- classified under category 3B „possibly carcinogenic for humans“

**Kramer, Assadian. Wallhäußers Praxis der Sterilisation, Desinfektion, Antiseptik und Konservierung. Stuttgart: Thieme, 2008**




# Critical antimicrobial compounds

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**Phenolic compounds are not as critical as aldehydes, but they lost their importance for surface disinfection because of**

- **High persistence in the environment**
- **Long term health risks by inhalation including reproduction toxicity**
- **Possible sensitization**
- **Limited antimicrobial spectrum**



## Position of quaternary ammonium compounds (QACs)

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- **Contrary to aldehydes and phenolic compounds, quaternary ammonium compounds (QACs) are to be considered as safe.**
- **The consequence are a non-critical misuse of QACs for surface disinfection in health care institutions as well as increasingly in households including for decontamination of homes in situations of fungal growth, if health complaints exist.**



# Disadvantages of QACs

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- **Limited efficacy against Gram-negative bacteria and fungi, lack of activity against mycobacteria, bacteria spores and non-enveloped viruses; the insufficient antimicrobial spectrum in vitro corresponds with inadequate disinfecting efficacy in bathrooms/toilets in opposite to an active oxygen compound**  
**Dharan S, Mourouga P, Copin P, et al. Routine disinfection of patients' environmental surfaces. Myth or reality? J Hosp Inf 1999; 42 (2): 113-7.**
- **Non sufficient toxicological characteristic**  
**Kramer, Assadian. Wallhäußers Praxis der Sterilisation, Desinfektion, Antiseptik und Konservierung. Stuttgart: Thieme, 2008**
- **Developm. of cross-resistance against gentamicin + Chx**  
**Sidhu MS et al. Disinfectant and antibiotic resistance of lactic acid bacteria isolated from the food industry. Microb Drug Resist 2001;7(1)73-83.**  
**Lambert RJ. Comparative analysis of antibiotic and antimicrobial biocide susceptibility data in clinical isolates of methicillin-sensitive Staphylococcus aureus, methicillin-resistant Staphylococcus aureus and Pseudomonas aeruginosa between 1989 and 2000. J Appl Microbiol. 2004;97(4)699-711.**
- **Sporulation of C. difficile was enhanced**  
**Wilcox MH, Fawley WN. Hospital disinfectants and spore formation by Clostridium difficile. Lancet 2000; 356(9238): 1324**
- **Incompatible for natural rubber flooring**



# Prototype of QACs

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- **Benzalkonium chloride (BC)**



# Assured toxic risks of QAC

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- **Induction of anaphylactic reactions and eczema by contact as well as inhalative. In humans BC is a weak allergen.**

**Uter W, Lessmann H, Geier J, et al. Is the irritant benzalkonium chloride a contact allergen? A contribution to the ongoing debate from a clinical perspective. Contact Dermatitis 2008; 58(6) 359-63.**

**Hann S, Hughes TM, Stone NM. Flexural allergic contact dermatitis to benzalkonium chloride in antiseptic bath oil. Br J Dermatol 2007; 157(4)795-8.**

**Anderson D et al. Anaphylaxis with use of eye-drops containing benzalkonium chloride preservative. Clin Exp Optom 2009; 92(5) 444-6.**

- **Risk of irritation dermatosis**
- **Dermal absorption (~ 2%)**

**Internal information of Bode Chemie Hamburg (2002)**

- **For all QACs no hint for mutagenicity, teratogenicity and carcinogenicity**

# Assessment of toxic risks of QACs

**Biocompatibility index < 1**

**= quotient from  $IC_{50}$  and RF >lg 3 within 30 min, tested in FBS**



**more toxic than microbicidal effective**

Agent	BI [30 min]	
	L929/ <i>E. coli</i>	L929/ <i>S. aureus</i>
Octenidine	1.73	2.11
Polihexanide	1.51	1.36
Chlorhexidine digluconate	0.83	0.98
<b>Benzalkonium chloride (BC)</b>	<b>0.63</b>	<b>0.79</b>

**Müller, Kramer. Biocompatibility index of antiseptic agents by parallel assessment of antimicrobial activity and cellular cytotoxicity. J Antimicrob Chemother 2008, 61(6) 1281-7.**



# Assessment of toxic risks of QAC

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- **At rats by aerogenic exposure with 30 mg BC/m<sup>3</sup> for 6 h on 3 d (LC<sub>50</sub> ~ 53 mg/m<sup>3</sup> for 4 h) strong inflammatory irritation → classification in class I of acute inhalation toxicity**

**Swiercz et al. Pulmonary irritation after inhalation exposure to benzalkonium chloride in rats. Int J Occup Med Environ Health 2008; 21(2): 157-63.**

- **Decline of conservation of nasal cilia because of the high cytotoxicity of 0.005% BC for nasociliary epithel**

**Mickenhagen et al. The influence of different alpha-sympathomimetic drugs and benzalkoniumchlorid on the ciliary beat frequency of in vitro cultured human nasal mucosa cells. Laryngorhinootol 2008, 87(1): 30-8.**

- **600 µg BC induce broncho constriction at patients with bronchial asthma**

**Lee, Kim. Benzalkonium chloride induced bronchoconstriction in patients with stable bronchial asthma. Korean J Intern Med 2007; 22(4): 244-8.**



# Hypothesis for inhalative risks of QAC

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- **Because after each application on a surface, e.g. floor, a layer-wise „enrichment“ appear, which cannot be removed with usual cleaning methods**
- **From this surface particles may be released, which accumulate in dust with the risk of inhalation**
- **Due to the high surface activity of QAC is to be assumed that inhaled dust particles attack the surfactant layer of the lung whereby the development of chronically obstructive lung illness (COPD) can be caused and/or promoted**

**Unfortunately so far no investigations were conducted to investigate the possible transfer of QAC on surfaces into the indoor air.**



# Accumulation of benzalkonium chloride (BC) on surface after disinfection

The accumulation was analysed using Time-of-Flight Secondary Ion Mass Spectrometry (ToF-SIMS) and Attenuated Total Reflection (ATR)-Fourier-Transformation-Infrared (FTIR) analytic

- **Method**

after repeatedly application (32-fold) of 400 µL of a BC based disinfectant (0.1% in the use solution) on polypropylene plates (150 x 150 mm) with drying on air over 1 hour after each application + washing off with 1 ml of water

- **Results**

accumulation of BC by the factor of  $2.3-4.3 \times 10^{17}$  molecule/cm<sup>2</sup>

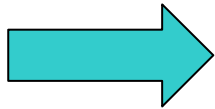
**Kramer, Below, Assadian. Health risks of surface disinfection in households with special consideration of quaternary ammonium compounds (QACs). Proc 6th Int Sci Conf Bioaerosols, Fungi, Bacteria, Mycotoxins in Indoor and Outdoor Environments and Human Health, Ney York, 2011**



# Case report No. 1

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- **A female employee in our central sterilization service department (CSSD) reacted during full protective clothing repetitive with a contact eczema induced by BC**
- **Only after conversion of the employee to a not-contaminated ward this health care worker became symptom free**



**this puts the suspicion on airborne sensitization on the dermal positively tested disinfectant on QAV basis**



## Case report No. 2

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- **December 2006:** Large area application of QAC after dampness damage in a private house, thereafter evacuation of the family in a hotel
- **April 2007:** re-entry of the family in their home
- **May 2007:** again evacuation of the family in a hotel due to strong health complaints
- **September 2007 and 2010:** cause analysis – killing of fungi, but not sufficient decontamination of destroyed fungi elements + significant increase of QAV in the house dust (exceed the 95% percentiles up to 75fold), which was the main cause of health complaints

**Kroczek C, Thumulla J. Case report QAC. Proc 15th Fungi Conf June 2011 Bad Staffelstein, Germany, 133-6.**



# Epidemiologic data

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- **Resulting of a postal questionnaire survey among 239 pig farmers and 311 rural controls among pig farmers the use of disinfectants (prevalence odds ratio 9.4, 95% confidence interval 1.6-57.2 for QAC) were associated with the prevalence of asthma symptoms**
- **But the pig farmers reported fewer allergies to common allergens ( $p < 0.001$  for pollen) and fewer symptoms of atopy in childhood ( $p < 0.05$  for one or more of four symptoms)**

**Vogelzang, van der Gulden, Tielen, et al. Health-based selection for asthma, but not for chronic bronchitis, in pig farmers: an evidence-based hypothesis. Eur Resp J 1999; 13 (1): 187-9.**



# Conclusion

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- **Addition of QAC to alcohol based hand disinfectants is dispensable.**
- **In hospitals, QACs should not be regarded as agents of first choice for surface disinfection.**
- **In households, QACs are to decline as active substance or combination partner for continuous surface disinfection.**
- **Even for single extensive sanitation of dampness damages in households QAC are to decline.**



# Alternatives for QACs

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- **Suitable substitutes are H<sub>2</sub>O<sub>2</sub> (without silver as catalysator) and other peroxides without the problem of residues for large surfaces and indoor air (and carbonic acids)**
- **Alcohols are suitable for small surfaces**
- **By indoor nebulisation of 5-6% H<sub>2</sub>O<sub>2</sub> A. brasiliensis is reduced > 4 log on vertical and horizontal surfaces. As a load of 10<sup>4</sup> to 10<sup>5</sup> fungal spores is unlikely to occur on precleaned surfaces, this efficacy seems to be sufficient .**

**Koburger, Below, Kramer. Decontamination of indoor air and adjacent wall area by nebulisation of hydrogen peroxide. GMS Krankenhaushygiene interdisz 2011, in print**

**Surface disinfection is one key element for infection prevention.**  
**But not the disinfectant with the broadest range of action is the most adequate one but the most adequate one is the disinfectant with the best risk benefit balance for the special indication.**

