

Absorption of Alcohol Hand Disinfectants

Prof. Axel Kramer, Greifswald, Germany

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propan-2-ol after excessive hygienic and surgical hand disinfection (alcohol based rubs)

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International trend to use alcohol based rubs

The CDC-guideline for hand hygiene clearly favours the use of alcohol-based hand rubs in hospitals, because antimicrobial soaps have significant disadvantages such as

- lower efficacy
- worse dermal tolerance
- higher potential for impaired efficacy due to an incorrect performance of the procedure
- the necessity of a wash basin

Boyce JM, Pittet D. Guideline for hand hygiene in health-care settings. Recommendations of the healthcare infection control practices advisory committee and the HICPAC/SHEA/APIC/IDSA hand hygiene task force. *MMWR* 2002; 51: 1-45.

Kramer A, Mersch-Sundermann V, Gerdes H, Pittet F-A, Tronnier H. Toxikologische Bewertung für die Händedesinfektion relevanter antimikrobieller Wirkstoffe. In: Kampf G, editor. *Hände-Hygiene im Gesundheitswesen*. Berlin: Springer, 2003:159-160.

Rotter ML. Hand washing and Hand disinfection. In: Mayhall CG, ed. *Hospital Epidemiology and Infection Control*, 3rd edn. Philadelphia: Lippincott Williams and Wilkins, 2004, 17:27-46

Kampf G, Kramer A. Epidemiologic Background of Hand Hygiene and Evaluation of the Most Important Agents for Scrubs and Rubs. *Clin Microbiol Rev* 2004; 17: 863-893

Aim of our study

Determination of alcohol absorption after excessive hygienic or surgical hand disinfection with hand rubs based on ethanol, propan-1-ol and/or propan-2-ol at identical test conditions and with the same volunteers

➔ to evaluate the safety/risk of alcoholic hand disinfection

We chose high exposure, because

- no exact absorption rates following hand disinfection are published
- for chemical analysis concentrations about the detection limit are necessary

Setting in our study

- Hand rubs were applied in a room of 37 m³ with two open windows and an open door
- no controlled air exchange during application
- between applications volunteers went to another room in which no one was allowed to use an alcohol-based hand rub
- blood samples were taken in a third room

Volunteers

All hand rubs were tested on the same 6 male and 6 female

Inclusion criteria

- ≥ 18 years
- ability to perform the applications

Exclusion criteria

- visible skin lesions on hands or forearms
- skin disease
- intake of ethanol in any form within 48 h before hand rub
- pregnancy or lactation
- participation at a clinical trial during 30 d before beginning of this study

Study was approved by the Ethics Committee of the Board of Physicians Mecklenburg-West Pomerania at the University of Greifswald

Trial of hygienic hand disinfection

- On 5 consecutive days for each application 4 ml were applied to both hands in the test room and rubbed in for 30 s according to the standard rub-in procedure of EN 1500
- **After a break of 1 min** outside the test room the procedure was repeated **20 times resulting in a total exposure time with each hand rub of 10 min over 30 min**
- At the end of each test day cosmetic hand cream was applied to the treated skin areas

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Relation to „worse case“ events in hospital practice

- On our intensive care unit we observed that at least 15 min will pass between hygienic hand disinfections
- Voss and Widmer¹ assumed ~20 hand disinfections per shift and HCW

¹Voss A, Widmer AF. No time for handwashing!? Handwashing versus alcoholic rub: can we afford 100% compliance? *Infect. Control Hosp. Epidemiol.* 1997; 18: 205-208

Trial of surgical hand disinfection

- Start 7 d after the trial of hygienic hand disinfection
 - on 5 consecutive days for each application 4 ml of a hand rub were applied to the hands and distributed on hands and forearms, which was repeated 5 times with the aim to keep hands and forearms wet with the hand rub for the recommended application time of 3 min
 - after a break of 5 min outside the test room, a total of 10 surgical hand disinfections were performed
- ➔ resulting in a total exposure time with each hand rub of 30 min over 80 min
- At the end of each test day a cosmetic hand cream was applied to the treated skin areas

Relation to „worse case“ events in hospital practice

- In our surgical theatre of ophthalmology we found that at least 10 min pass between cataract operations and thereby ≥ 15 min between surgical hand disinfections
- Normally surgeons carry out 3 surgical hand disinfections over 6 hours (one hand disinfection every two hours)

Blood samples

- Prior to blood sampling, skin antisepsis was performed with an alcohol-free skin antiseptic
- blood samples of 5 ml were taken through a venflon before the first daily disinfection (baseline) and 2.5, 5, 10, 20, 30, 60 and 90 min after the last application by hygienic hand disinfection resp. 5, 10, 20, 30, 60 and 90 min after the last application by surgical hand disinfection. Only for hand rub C an additional sample was taken after 120 min.
- Blood samples were stored before analysis at 4 °C for up to 12 h.

Analysis of alcohols, acetaldehyde, acetone and propionaldehyde

- Gas chromatography (modification of Römheld¹) by head-space injection (CombiPal-Autosampler, CTC Analytics) with flame-ionisation detection (GC 5890 Hewlett Packard) and DB 624 column for separation (60 m x 0.32 mm x 1.8 µm; J&W). Conditions: 150 °C injector temperature, 250 °C detector temperature, column temperature programme 40 °C (8min), 3 °C/min to 120 °C (0 min), 30 °C/min to 230 °C (5 min). Nitrogen (5.0) served as carrier gas with 1.45 ml/min (21.9 cm/s).
- 1 ml sample or standard and 0.5 g glowed Na₂SO₄ were filled in 1.5 ml head space vials, incubated 45 min at 75 °C, and 2.5 ml were injected splitless
- Calibration with external or self made standard, if the sample concentration did not lie in the calibration level (ethanol) or is commercially not available (acetaldehyde).

¹Römheld W, Krause D, Bartels H, Wittig H. Begleitstoffanalyse mittels "Headspace"-GC/MS. *Blutalkohol* 1998; 35: 10-18

Detection thresholds

Compound	limit (mg/ml) of		
	detection	determination	recording
Ethanol	0.14	0.28	0.34
Propan-1-ol	0.13	0.26	0.34
Propan-2-ol	0.03	0.06	0.09
Acetaldehyd	0.07	0.15	0.29
Aceton	0.01	0.02	0.03
Propionaldehyd	0.02	0.05	0.07

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Calculation of absorbed alcohols

- Median ethanol concentration was calculated at each time point.
- The proportion of absorbed ethanol and acetaldehyde was determined for each hand rub and type of application by the method of Wittmann:
$$\text{Absorbed amount (mg)} = \text{body mass (kg)} \times r \times \text{max. serum level (mg/l)}$$
$$r = 0.7 \text{ for male resp. } 0.6 \text{ for female}$$

Wittmann et al. *Isopropanol- und Acetonspiegel im Serum nach präoperativer Flächendesinfektion mit isopropanolhaltigen Antiseptika. Blutalkohol* 1992; 29: 326-335.

Part I: Absorption of ethanol

Use of three hand rubs with different ethanol content

→ to prove the statement, that ethanol at a concentration between 55% and 95% is considered to be safe¹ for topical use on hands

¹Anonymous. Tentative final monograph for health care antiseptic products; proposed rule. Fed. Reg. 1994; 59: 31401-31452

No data in literature on ethanol absorption by hand disinfection

Despite the worldwide use of ethanol-based hand rubs only few studies have addressed the issue of absorption of ethanol when used on skin with the result

→ no rise of ethanol in serum was found

even after excessive exposure by using dressings for 3 h soaked with 200 ml ethanol

Bowers RV et al. Alcohol absorption from skin in man. *Quart. J. Stud. Alcohol* 1942; 3: 31
Meyer F, Ziegenmeyer J. Resorptionsmöglichkeiten der Haut. *J Soc Cosmet Chem* 1975; 26: 93-104

Tested hand rubs

Three blinded ethanol-based hand rubs:

A = 95% w/w ethanol (solution)

B = 85% w/w ethanol (gel)

C = 55% w/w ethanol (solution)

Baseline values in volunteers

- Baseline data for ethanol 0.01-10 mg/l^{1,2}; for acetaldehyde 0.31^{1,2}
- in 83.8% of samples (57 of 68) the baseline of ethanol concentration was below the limit of detection with median of 0.7 mg/l and highest baseline concentration of 1.7 mg/l
- for acetaldehyde 5.9 % of the baseline values (4 of 86) were below the limit of detection. The median was 0.2 mg/l, the highest baseline concentration was 1.95 mg/l

¹Wittmann S, Gilg T, Dietz HG, Grantzow R, Peschel O, Meyer L. Isopropanol- und Acetonspiegel im Serum nach präoperativer Flächendesinfektion mit isopropanolhaltigen Antiseptika. *Blutalkohol* 1992; 29: 326-335

²Iffland R, Balling P, Oehmichen M, Lieder F, Norpoth T. Methanol, Isopropanol, n-Propanol - endogene Bildung unter Äthanoleinfluß? *Blutalkohol* 1989; 26: 87-97

Interpretation of baseline values

Results indicate the abstinence of volunteers from ethanol before beginning the experiments

Origin of endogenous ethanol is mainly the metabolism of normal intestinal flora which is then absorbed by the host^{1,2}

¹Petrides PE. Ernährung. In: Löffler G, Petrides PE, editors. *Biochemie und Pathobiochemie*. 5th ed. Berlin: Springer; 1997:707-728

²Iffland R, Balling P, Oehmichen M, Lieder F, Norpoth T. Methanol, Isopropanol, n-Propanol - endogene Bildung unter Äthanoleinfluß? *Blutalkohol* 26: 87-97.

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Exposure by hygienic hand disinfection

During 20 hygienic hand disinfections, volunteers were exposed for a contact time of 10 min within a period of 30 min to **80 ml** (20 x 4 ml) of hand rub, corresponding to

- 60 g ethanol with hand rub A
- 56.2 g ethanol with hand rub B
- 39.6 g ethanol with hand rub C

Ethanol absorption by hygienic hand disinfection

Highest serum levels (median) of ethanol was found 30 min after the last application

- 20.9 mg/l with hand rub A (equivalent to 0.02‰ ethanol)
- 11.45 mg/l with hand rub B (equivalent to 0.011‰ ethanol)
- 6.9 mg/l with hand rub C (equivalent to 0.007‰ ethanol)

Total amount of absorbed ethanol

- 1356 mg with hand rub A (95 % ethanol content)
- 630 mg with hand rub B (85 % ethanol content)
- 358 mg with hand rub C (55% ethanol content)

Based on the total amount of applied ethanol, the **proportion of absorbed ethanol** was

- **2.3 %** for hand rub A
- **1.1 %** for hand rub B
- **0.9 %** for hand rub C

Blood concentration of acetaldehyde (mg/l) after hygienic hand disinfection

Hand rub	Before first application	30 min after last application	90 min after last application
A	0.06	0.4	0.2
B	0.08	0.4	0.3
C	0.1	0.6	0.3

Interpretation of acetaldehyde levels



all values are within physiological range

Exposure by surgical hand disinfection

During 10 surgical hand disinfections, volunteers were exposed for a contact time of 30 min within a period of 80 min to a total of **200 ml** of hand rub, corresponding to

- 150 g ethanol with hand rub A
- 140 g ethanol with hand rub B
- 99 g ethanol with hand rub C

Absorption by surgical hand disinfection

Highest serum levels (median) of ethanol was found 30 min after the last application

- 17.5 mg/l with hand rub A (equivalent to 0.017‰ ethanol)
- 30.1 mg/l with hand rub B (equivalent to 0.029‰ ethanol)
- 8.8 mg/l with hand rub C (equivalent to 0.008‰ ethanol)

Total amount of absorbed ethanol

- 1067 mg with hand rub A (95 % ethanol content)
- 1542 mg with hand rub B (85 % ethanol content)
- 477 mg with hand rub C (55% ethanol content)

Based on the total amount of applied ethanol, the **proportion of absorbed ethanol** was:

- **0.7 %** for hand rub A
- **1.1 %** for hand rub B
- **0.5 %** for hand rub C

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Blood concentration of acetaldehyde (mg/l) after surgical hand disinfection

Hand rub	Before first appl.	30 min 90 min 120 min after last application		
A	0.8	3.6	2.6	not done
B	0.6	3.3	1.3	not done
C	0.4	0.9	1.0	1.0

Interpretation of acetaldehyde levels

All values are within physiological range

- with all hand rubs concentration of acetaldehyde was significantly above baseline of 0.2 mg/l throughout the observation period ($p < 0.05$)
- after 30 to 60 min, levels of acetaldehyde began to go down slowly

Assessment of exposure

- In our test model as well as in practise its not possible to distinguish between dermal and pulmonary absorption, so we described the overall absorption by practical hand disinfection.
- Some of the observed absorption is certainly explained by pulmonary uptake. If for example 200 ml of hand rub A is applied within 80 min, a total of 190 g ethanol is going to evaporate into the air from the skin. If no air exchange takes place it would have resulted in an ethanol concentration in air of 4.1 g/m³ which is almost three times above the maximum occupational exposure concentration of ethanol (1.9 g/m³).
- But the increase of blood levels after the last application up to 30 min could be explained only by dermal absorption.

Risk assessment for determined ethanol absorption

- Under the extreme test conditions, which will not be found in hospitals, only 0.5 % to 2.3% of applied ethanol is absorbed, and nearly independent of ethanol concentration in the disinfectant
 - Calculation under real conditions: At 3 surgical hand disinfection with hand rub A with the highest ethanol concentration (95%) over 6 h, exposition is 15.1 g ethanol every 2 h. Approx. 0.7% of the applied ethanol will be absorbed (= 106 mg ethanol). The average man/woman has a body weight of 70/60 kg with 40.6/28.8 l total body water. Systemic availability of ethanol after surgical hand disinfection is therefore in man approx. 0.0025‰ (= 2.61 mg/l), in woman 0.0035‰ (= 3.68 mg/l).
- ➔ both ethanol levels are systemically safe, there are only 2 fold higher than the baseline in our study and are distinctly lower than the maximum of physiological value of 0.01

Risk assessment for determined ethanol absorption

The average metabolisation rate of ethanol is 150 mg/l/h or 0.15‰/h¹

As consequence, in real time intervals between hand disinfections, the effective resulting level of Ethanol in blood would be remarkably lower than in our model

¹Anonymous. Alkohole. In: Marquardt H, Schäfer SG (ed.) *Lehrbuch der Toxikologie*. Mannheim: BI Wissenschafts-Verlag, 1994:392-396.

Risk assessment for determined ethanol absorption

- Apple juice may contain 2 g ethanol/l¹
 - drinking of 0.5 l apple juice will result in man of 75 kg ➔ 0.17‰
woman of 60 kg 0.25‰
- ~ 10 times higher compared with the ethanol absorption in our test model with extremely high exposure

¹Windirsch B, Brinkmann B, Taschan H. Alkoholgehalte ausgewählter Lebensmittel. *Lebensmittelchemie* 2005; 59: 149-150

Part II: Absorption of propan-1-ol and propan-2-ol

Origin of baseline levels

- **Ethanol:** intestinal flora, fruit juices, antiseptic mouth washes
- **Propan 1 ol** & no baseline levels known
- **Propan 2 ol** & reduction of acetone

Knowledge on absorption of propan-1-ol

no data in literature on absorption of propan-1-ol

- ➔ on isolated human epidermis the constant of permeability is
- ethanol $0.8 \times 10^{-3} \text{ cm/h}^1$
 - propan-1-ol $1.2 \times 10^{-3} \text{ cm/h}^2$
 - propan-2-ol $1.35 \times 10^{-3} \text{ cm/h}^1$

¹Scheuplin RJ, Blank ICH (1973) Mechanism of percutaneous absorption. IV. Penetration of nonelectrolytes (alcohols) from aqueous solutions and from pure liquids. *J Invest Dermatol* 60: 286-296
²Boatman RJ, Perry LG, Florica LA, English JC, Kapp RW Jr, Bevan C, Tyler TR, Banton MI, Wright GA (1998) Dermal absorption and pharmacokinetics of isopropanol in the male and female F-344 rat. *Drug Metab Disp* 26: 197-202

Knowledge on absorption of propan-2-ol

- Study¹ on 10 volunteers: hand disinfection every 10 min over 4 hours (52.6 % w/w propan-2-ol)
- ➔ 0.5-1.8 mg/l (1 = no detectable level)

Conclusion: 500 mg/l are associated with mild absorption², further studies are necessary¹

¹Turner P, Saeed B, Kelsey MC. Dermal absorption of isopropyl alcohol from a commercial hand rub: implications for its use in hand decontamination. *J Hosp Infect* 2004;56(4):287-290
²Kapp RW, Bevan C, Gardiner TH, Banton MI, Tyler TR, Wright GA. Isopropanol: summary of TSCA test ruke studies and relevance to hazard identification. *Regul Toxicol Pharmacol* 1996;23: 183-192

Knowledge on absorption of propan-2-ol

Different case reports published on dermal + inhalative intoxication

- 6 month old child, 2 compresses within 2 h over 30 min to decrease fever: after 8 h comatose (blood level > 2 ‰), after 34 h complete recovery¹
- results has been published on children with blood levels up to 1.25‰^{2,3}

¹McFadden SW, Haddow JE (1969) Coma produced by topical application of isopropanol. *Pediatrics* 43: 622-623
²Garrison RF (1953) Acute poisoning from use of isopropyl alcohol in tepid sponging. *J Amer Med Assoc* 152: 317-318
³Senz EH, Goldfarb DL (1958) Coma in a child following use of isopropyl alcohol in sponging. *J Pediatr* 53: 323-324

Metabolism of alcohols

- Ethanol linear elimination rate (to acetaldehyde) ~0.1-0.2‰/h
- Propan-1-ol (to propionaldehyd) and propan-2-ol (acetone) exponential elimination rate
 - half life time/human for ethanol 2-6 h¹
 - half life time/rat for propan-1-ol ~ 45 min²
 - half life time/rat for propan-2-ol 1-4 h^{2,3}
 - half life time/man for propan-2-ol 170 min⁴

¹www.ma.uni-heidelberg.de/inst/ikc/ikc-normbereiche_kc.html - 387k
²Bonte W (1987) Begleitstoffe alkoholischer Getränke: Biogenese, Vorkommen, Pharmakologie, Physiologie und Begutachtung. Schmidt-Römhild, Lübeck
³Slauter RW, Coleman DP, Gaudette NF, McKee RH, Masten LW, Gardiner TH, Strother DE, Tyler TR, Jeffcoat AR (1994) Disposition and pharmacokinetics of isopropanol in F-344 rats and B6C3F1 mice. *Fundam Appl Toxicol* 23: 407-420
⁴Daniel DR, McAnalley BH, Garriott JC (1981) Isopropyl alcohol metabolism after acute intoxication in humans. *J Anal Toxicol* 5: 110-112

Consequences

no risk of accumulation to blood levels about 0.1‰ by usual hand disinfection

Tested hand rubs

Blinded rubs:

- D = propan-1-ol 30 % w/w +
propan-2-ol 45 % w/w (solution)
- E = propan-2-ol 70 % w/w (solution)

Baseline values for trial with propan-1-ol based rub

Baseline data for propan-1-ol ≤ 0.05 mg/l¹, for acetone 0.2-14.4 mg/l^{1,2}, for propionaldehyde no data in literature – see our results:

- **Propan-1-ol**: in the first trial (hygienic hand rub) all volunteers < 0.1 mg/l were detectable, in the second trial only one volunteer (0.07 mg/l), for the other the concentrations were below the limit of detection
- Acetone: 5.9 % of the baseline values (4 of 86) were below the limit of detection. The median was 0.2 mg/l, the highest baseline concentration was 1.95 mg/l
- Propionaldehyd: 0.1mg/l
- **Propan-2-ol**: only one volunteer was detectable with 0.07 mg/l, for the other the concentrations were below the limit of detection

¹Wittmann S, Gilg T, Dietz HG, Grantzow R, Peschel O, Meyer Lyon (1992): Isopropanol- und Acetonspiegel im Serum nach präoperativer Flächendesinfektion mit Isopropanolhaltigen Antiseptika. Blutalkohol 29: 326-335
²Felby S, Nielsen E (1995): Congener production in blood samples during preparation and storage. Blutalkohol 32: 50-58

Interpretation of baseline values

Our median baseline values indicate abstinence of volunteers from alcohol (congeners) before beginning the experiments.

Exposure by hygienic hand disinfection

During 20 hygienic hand disinfections, volunteers were exposed for a contact time of 10 min within a period of 30 min, using 80 ml (20 x 4 ml) of hand rub, corresponding to

- 18.9 g propan-1-ol with hand rub D
- 28.4 g propan-2-ol with hand rub D
- 43.7 g propan-2-ol with hand rub E

propan-1-ol absorption by hygienic hand disinfection

Highest serum levels (median) of propan-1-ol was found 30 min after the last application for hand rub D:

- 12.6 mg/l (equivalent to 0.012‰)

The total amount of absorbed propan-1-ol :

- 599.8 mg

Based on the total amount of applied **propan-1-ol**, the proportion of **absorbed propan-1-ol** was:

- 3.2 %

propan-2-ol absorption by hygienic hand disinfection

Highest serum levels (median) of propan-2-ol was found 60 min after the last application :

- 6.6 mg/l with hand rub D (equivalent to 0.006‰)
- 7.8 mg/ml for hand rub E (equivalent to 0.0075‰)

Total amount of absorbed propan-2-ol :

- 309.5 mg with hand rub D (45 % propan-2-ol content)
- 309.5 mg with hand rub E (70 % propan-2-ol content)

Based on the total amount of applied propan-2-ol, the proportion of **absorbed propan-2-ol** was:

- 1.1 % for hand rub D
- 0.7 % for hand rub E

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Blood concentration of acetone (mg/l) after hygienic and surgical hand disinfection

Hand rub	before first appl.	30 min 90 min 120 min after last application		
D hygienic surgical	1.6	3.4	4.4	not determined
	2.6	4.7	4.6	
E hygienic surgical	1.7	4.2	5.0	5.0
	1.7	4.4	5.0	4.4

Exposure by surgical hand disinfection

During 10 surgical hand disinfections, volunteers were exposed for a contact time of 30 min within a period of 80 min to a total of 200 ml of hand rub, corresponding to

- 47.3 g propan-1-ol with hand rub D
- 71.0 g propan-2-ol with hand rub D
- 109.2 g propan-2-ol with hand rub E

propan-1-ol absorption by surgical hand disinfection

Highest serum levels (median) of propan-1-ol was found min after the last application for hand rub D

- 23.2 mg/l (equivalent to 0.022‰)

The total amount of absorbed propan-1-ol

- 918.2 mg

Based on the total amount of applied **propan-1-ol**, the proportion of absorbed **propan-1-ol** was

- 1.9 %

propan-2-ol absorption by surgical hand disinfection

Highest serum levels (median) of propan-2-ol was found min after the last application

- 12.7 mg/l for hand rub D (equivalent to 0.012‰)
- 10.1 mg/l for hand rub E (equivalent to 0.0097‰)

Total amount of absorbed propan-2-ol

- 598.6 mg for hand rub D
- 471.6 for hand rub E

Based on the total applied amount of propan-2-ol, the proportion of **absorbed propan-2-ol** was

- 0.8 %
- 0.4 %

Conclusion

The absorption and the metabolism rate of the three alcohols is nearly the same, but ethanol is less toxic than the propanols

agent	oral LD ₅₀ (mg/kg) for rat	total absorbed amount (mg/kg)
ethanol	14000	22.0
propan-1-ol	5400	13.1
propan-2-ol	5840	8.1

Risk assessment by LD₅₀ and absorption

Quotient of LD₅₀ and total absorbed amount at unrealistically high test exposure!

- ethanol 636.4
- propan-1-ol 412.2
- propan-2-ol 720.0



obviously no toxic risks

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Risk assessment by acceptable daily intake (ADI)

- WHO: Recommendation for **ethanol = 7 g/d**
 highest absorbed amount in our extreme exposure test 1,5 g
- EFSA¹: ADI for **propan-2-ol 2.4 mg/kg** = 144 mg/60 kg
 highest absorbed amount in our extreme exposure test 598.6 mg
- no ADI allocated for propan-1-ol

¹European Food Safety Association

Conclusion

- **Absorption of the three alcohols is low < 0.03.**
- **The possibility of systemic toxic effects can be effectively ruled out.**
- **Our recommendation: For skin antiseptics on newborns, ethanol-based preparations are preferred because dermal absorption and inhalative properties are more tolerable than propanols. For premature newborns non-absorbable antiseptics should be used (i.e. octenidine).**

Conclusion

- **A hand rub must be safe and effective**
- The exposure to a hand rub should be only as long as necessary to ensure the required efficacy, tolerance and compliance
 recent data suggest that 1.5 min application time for surgical hand antiseptics is as effective as 3 min application of the reference 60 % propan-1-ol^{1,2}

¹Kampf G et al. Surgical hand disinfection with a propanol-based hand rub: equivalence of shorter application times. *J Hosp Inf* 2005; 58: 304-310

²Hübner NO, Kampf G, Kamp P, Kohlmann T, Kramer A. Does a preceding hand wash and drying time after surgical hand disinfection influence the efficacy of a propanol-based hand rub? *BMC Microbiology* 2006; 6 (1):57-62

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