Comparison of the *In Vivo* Efficacy of Alcohol-based Pre-surgical Hand Rubs: Chlorhexidine Gluconate is Not Necessary to Meet FDA Efficacy Requirements

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ABSTRACT

Background/Objectives

Pre-surgical hand disinfection by OR staff is critical to reducing bacterial load on hands and, thereby, the risk of microbial entry into the surgical wound during surgery. The FDA requires that products produce an immediate reduction of the skin microflora and to maintain microbial counts below baseline for six hours after use (persistence). A significant proportion of the products used in US hospitals are waterless alcohol-based pre-surgical handrubs. Products may be based on alcohol alone or contain chlorhexidine gluconate (CHG), which is believed to enhance persistent activity because it remains on skin after the alcohol has evaporated. The study objectives were to compare efficacy of commercial alcohol-based pre-surgical handrubs and determine whether CHG is necessary for meeting FDA efficacy criteria.

Methods

Test products included 3 commercial alcohol-based pre-surgical hand rubs and a 70% ethanol in water control. Product A was a 70% ethanol gel, Product B was an 80% ethanol rinse and Product C was a 61% ethanol and 1% CHG gel. Test products were evaluated according to the ASTM E1115 Surgical Scrub method, as required by the FDA. All products were applied using 3 applications of 2 ml (6 ml total). However for Product B, an average of 2 ml additional product was applied to keep hands wet for 90s according to manufacturer's instructions. Test products were used 11 times over a period of 5 days.

Results

All 3 test products and the control met FDA efficacy requirements for a 1 log immediate reduction on day one, 2 log immediate reduction on day two, and met persistence requirements (maintained counts below baseline for 6 hours on day one). However, only Product A, the 70% ethanol gel, met FDA requirements for a 3 log immediate reduction on day five.

Conclusions

Addition of CHG to alcohol-based pre-surgical handrubs is not necessary to meeting FDA persistence requirements and does not guarantee a product will meet FDA efficacy requirements. Product A, containing only alcohol as the active, was the only product to meet FDA requirements, which calls into question recommendations for including CHG in alcohol-based pre-surgical handrubs. Additionally, Product A outperformed Product B, which contained higher alcohol concentration and had a higher application volume, indicating overall product formulation is more important for efficacy of a waterless surgical handrub than active level. Infection preventionists should evaluate manufacturer's efficacy data for products, as the active alone does not predict efficacy.

METHODS

Products were evaluated in a head to head test according to ASTM E1115 as described in the 1994 FDA Tentative Final Monograph for Healthcare Antiseptic Drug Products (21 CFR Parts 333 & 369). Products were used eleven times over a period of five days, and the reduction of resident skin flora was measured after the first wash on days 1, 2, and 5. Measurements were also done 6 hours after these washes, to measure persistence. The FDA requires that surgical scrub formulations achieve immediate $\log_{10}$ reductions of 1, 2, and 3 on the first wash of Day 1, Day 2 and Day 5, respectively. The FDA also requires that the bacterial cell count does not subsequently exceed baseline within 6 hours of the first application on Day 1 under glove occlusion. Efficacy of products was compared using a 1-way ANOVA with Bonferroni post-hoc analysis ($\alpha = 0.05$).

Table 1. Test Products

Code	Active (s)	Product Name
Alcohol Control	70% Ethanol	Alcohol in water control
Product A	70% Ethanol	PURELL® Waterless Surgical Scrub
Product B	80% Ethanol	Sterillium® Rub Surgical Hand Antiseptic
Product C	61% Ethanol 1% CHG	Avagard™ Surgical and Healthcare Personnel Hand Antiseptic with Moisturizers

RESULTS

Table 2. Summary of Log_{10} Reductions for Test Products

		Day 1		Day 2		Day 5		
Sample	N	Immediate LR (95% CI)	6 Hour LR (95% CI)	Immediate LR (95% CI)	6 Hour LR (95% CI)	Immediate LR (95% CI)	6 Hour LR (95% CI)	Meets FDA Efficacy Criteria
70% Alcohol Control	14	1.76 (1.41-2.12)	0.50 (0-1.06)	1.91 (1.66-2.16)	0.26 (0-0.58)	2.07 (1.75-2.39)	0.68 (0.25-1.10)	No
Product A	18	2.71 (2.41-3.01)	2.55 (2.26-2.83)	2.87 (2.59-3.15)	2.57 (2.37-2.77)	3.06 (2.84-3.28)	2.53 (2.15-2.91)	Yes
Product B	19	2.13 (1.93-2.31)	0.88 (0.61-1.16)	2.43 (2.17-2.69)	1.07 (0.76-1.38)	2.43 (2.14-2.73)	1.48 (1.07-1.89)	No
Product C	19	2.21 (1.86-2.56)	2.65 (2.27-3.03)	2.34 (2.02-2.67)	2.76 (2.36-3.17)	2.70 (2.38-3.03)	3.06 (2.78-3.33)	No
FDA Criteria	-	>1	>0	>2	n/a	>3	n/a	

LR=Log reduction, 95% CI=95% confidence interval, Numbers highlight in red failed to meet FDA criteria

Only Product A, the 70% ethanol surgical hand rub, met FDA efficacy requirements on Days 1, 2 and 5. All other products failed to meet the Day 5 immediate log_{10} reduction requirements.

Statistical Analysis:
Day 1: Immediate log_{10} reductions for Product A were significantly higher than the Alcohol Control and Product C ($P<0.05$), and after 6 hours the log_{10} reductions for Product A and Product C were both superior to the Alcohol Control and Product B ($P<0.0001$).

Day 2: Product A was statistically superior to Product C ($P<0.05$) and the Alcohol Control ($P<0.0001$) for the immediate reduction; and Product A and Product C were statistically superior to the Alcohol Control and Product B ($P<0.0001$) at 6 hours after application.

Day 5: Product A ($P<0.0001$) and Product C ($P<0.05$) were statistically superior to the Alcohol Control immediately after application, and Product A was also statistically superior to Product B ($P<0.05$) immediately after application. At 6 hours post-application Product A and Product C were statistically superior to the Alcohol Control and Product B ($P<0.001$).

CONCLUSIONS

- **The most important criteria for choosing a pre-surgical hand antiseptic is the demonstrated ability to meet efficacy criteria established by the FDA, skin tolerability, and end user acceptance.**
- **Overall product formulation has the greatest impact in determining efficacy of alcohol-based surgical scrubs; and is more important than either alcohol concentration alone or the inclusion of CHG.**
- **Although CHG may help suppress bacterial regrowth at 6 hours following surgical hand antisepsis, it's inclusion is not required to meet FDA persistence requirements and will not guarantee a product will meet immediate kill requirements. Therefore the use of CHG in pre-surgical hand antiseptics is not justified.**

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