Methods to Evaluate Hand Hygiene Products
Prof. Timothy Landers and Dr. David Macina
A Webber Training Teleclass

METHODS TO EVALUATE HAND HYGIENE PRODUCTS

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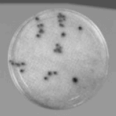
Objectives:

- Understand how the following concepts relate to hand hygiene product testing: *in vivo* testing, *in vitro* testing, log reduction, efficacy, effectiveness, and product claims.
- Apply these terms to currently approved test methods and emerging trends in the testing of hand hygiene products.
- Evaluate different test methods and their usefulness in product selection

Hands Are the Most Common Means of Microbial Spread



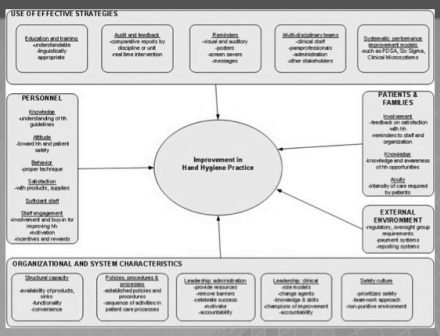
Acquisition of MRSA **on hands** after touching the bedrail of a colonized patient[1]

Acquisition of MRSA on hands after examination of a colonized patient

"Hand Hygiene is the single most important procedure for preventing the transfer of microorganisms and therefore preventing the incidence of diseases"[2]

[1]Donskey and Eckstein. *N Engl J Med* 2009; 360.
[2]WHO Guidelines on Hand Hygiene in Health Care. 2009.

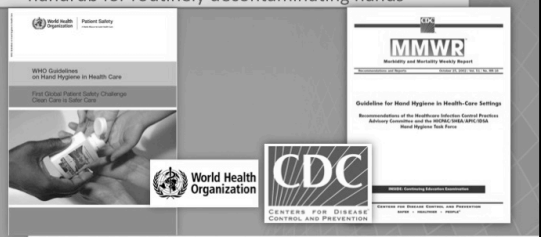
Multimodal Strategies for Hand Hygiene



Pincock T, Bernstein P, Warthman S, Holst E. Bundling hand hygiene interventions to decrease health-care associated infections. Am J Infect Control 2012; 40: S18-S27.

ABHR are Recommended in Global Hand Hygiene Guidelines

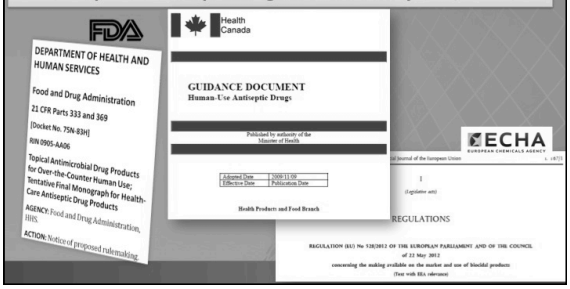
"If hands are not visibly soiled, use an alcohol-based handrub for routinely decontaminating hands"



"At present, alcohol-based handrubs are the only known means for rapidly and effectively inactivating a wide array of potentially harmful microorganisms on hands"

Regulation of Antimicrobial Hand Hygiene Products

Considered OTC drugs, biocidal products, or natural health products depending on the country and/or claims.



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Regulation of Antimicrobial Hand Hygiene Products

Regulations specify the following:

- Safe and effective active ingredients
- Usage concentrations
- Dosage forms
- Labeling
- **Efficacy testing**

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Intended Use Examples

- **Personal domestic use**
- **Personal commercial use**
- **Professional food premises**
- **Professional healthcare use**

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Labels

- "Handwash to help reduce bacteria that potentially can cause disease"
- "Hand sanitizer to help reduce bacteria on the skin"
- "Decrease transient bacteria on the skin"

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Product Claims

- **Must be "non-misleading statements"**
  - Hypoallergenic
  - Kills the most germs
  - Leaves hands feeling soft
  - Gentle on hands
  - Fragrance-free

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Efficacy Testing Requirements (Overview)

in vitro
(in a test tube)

+

in vivo
(using human test subjects)

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Methodologies for evaluating the efficacy of alcohol-based hand rubs

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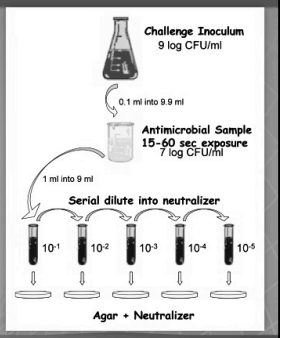
In vitro Microbicidal Activity "Time-Kill"

- Measures rapid microbicidal (killing) action of products
- Can test almost any microorganism by this method

***In vitro* results do not predict antimicrobial performance on hands.**



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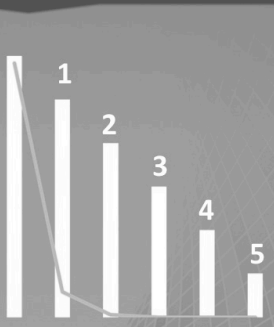
Logarithmic vs linear measures



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Log Reduction Tutorial

Log Reduction	Percent Reduction of Bacteria
1	90%
2	99%
3	99.9%
4	99.99%
5	99.999%

Example: Start with 1 million bacteria

- 1 log reduction: 900,000 are killed and 100,000 remain
- 2 log reduction: 990,000 are killed and 10,000 remain
- 3 log reduction: 999,000 are killed and 1,000 remain

Examples of *in vitro* Microbicidal Methods

- **Bactericidal:**
  - ASTM E2783, EN 1040, EN 13727,
- **Yeasticidal/Fungicidal**
  - EN 1275, EN 13624
- **Mycobactericidal**
  - EN 14348
- **Virucidal**
  - ASTM E1052, EN14476
- **Sporicidal**
  - EN 14347

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Healthcare Personnel Handwash: ASTM E1174

- Predicts the reduction of transient microorganisms by washing sanitizing hands.
- Measures reduction of a marker organism.
- Test products evaluated after single or multiple product uses.
- Originally designed to evaluate handwash products and later adapted to evaluate ABHR.

US FDA Endpoints:

Bacterial Reduction (log_{10})

1st Application: 2 log

10th Application: 3 log

- ASTM International. E-1174-13: *Standard test method for evaluation of the effectiveness of healthcare personnel or consumer handwash formulations.* 2013. ASTM International.
- Food and Drug Administration. Federal Register 1994;59:31441-31452.

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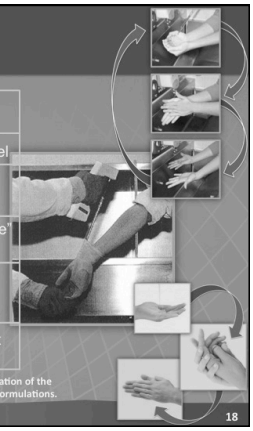
ASTM E1174 Overview

- Contaminate hands with 10^9 cfu *Serratia marcescens*
- Sample hands to obtain "baseline" level
- Contaminate hands again and apply test product
- Sample hands to obtain "post exposure" level
- Perform a total of 9 additional contamination and product application cycles
- Sample hands after final (10^{th}) product application



ASTM International. E-1174-13: Standard test method for evaluation of the effectiveness of health care personnel or consumer handwash formulations.

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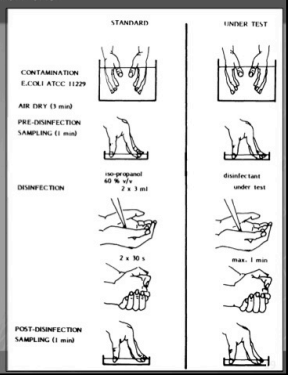
EN1500: Hygienic Handrub

- Challenge organism: *E. coli*
- Single product use
- Defined volume & contact time
- Cross-over design:
  - Subjects evaluate both the test product and an internal reference
  - Test product must show non-inferiority to internal reference



European Committee for Standardization. Chemical disinfectants and antiseptics—hygienic handrub test method and requirements (phase2/step2) [European standard EN 1500]. 1997.

Expert Opinions on Hand Hygiene Test Methods

"New Methods For The Future"…
"To be plausible, results of *in vivo* models should show that they are realistic under practical conditions such as the duration of application…"

CDC Guideline for Hand Hygiene in Health-Care Settings (2002)

"Hand Hygiene Research Agenda"…
"Develop new protocols for evaluating the *in vivo* efficacy of agents, considering in particular short application times and volumes that reflect actual use in HC Facilities"

WHO Guidelines on Hand Hygiene in Health Care (2009)

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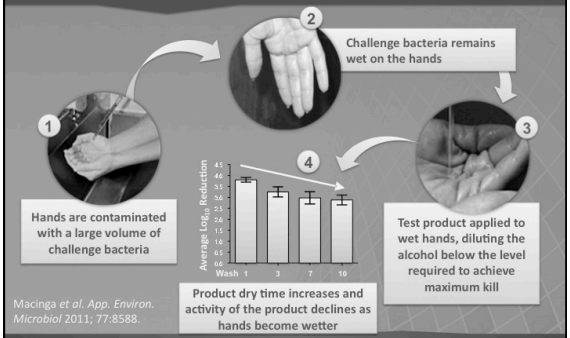
Challenges When Using ASTM E1174 to Measure ABHR Efficacy



Macinga *et al. App. Environ. Microbiol* 2011; 77:8588.

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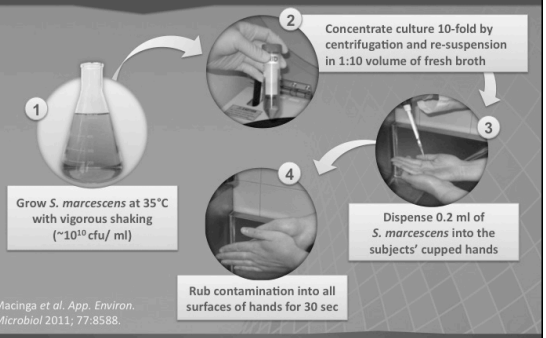
"Low Volume" Contamination



Macinga *et al. App. Environ. Microbiol* 2011; 77:8588.

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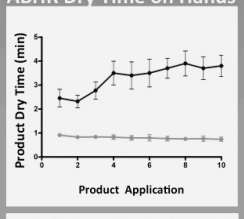
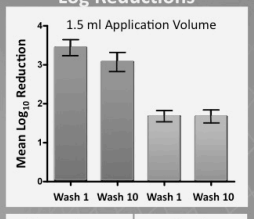
"Low Volume" Contamination Test Results

ABHR Dry Time on Hands



Log Reductions



Broth Contamination (HCPHW)
Low-Volume Contamination

Low-volume Contamination | Broth Contamination

Macinga et al. *App. Environ. Microbiol.* 2011; 77:8588.

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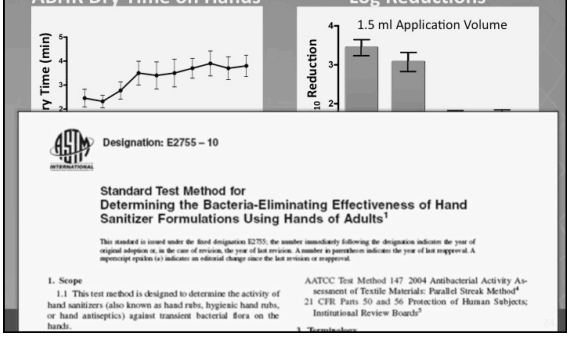
"Low Volume" Contamination Test Results

ABHR Dry Time on Hands

Log Reductions



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Achieving Clinical Benefit With Alcohol-Based Handrubs

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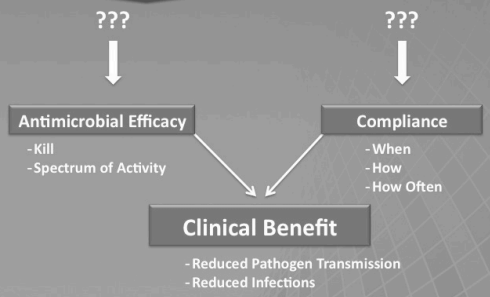
Efficacy vs. Effectiveness

- Efficacy – A measure of the reduction of pathogenic transient microorganisms on the hands.
  - Relates to controlled laboratory or clinical trials
- Effectiveness – A measure of the interruption the spread of pathogens and the acquisition of healthcare associated infections.
  - Relates to use in clinical practice

Achieving Clinical Benefit (Effectiveness) with ABHRs: Whole Systems Model



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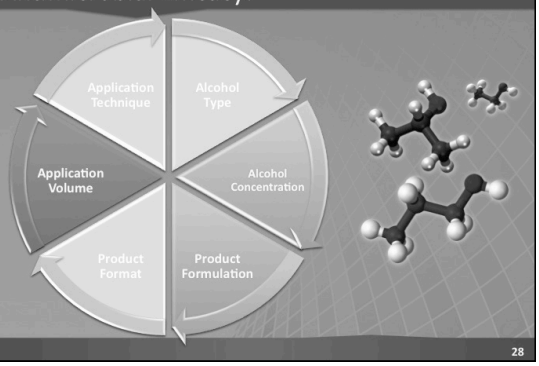
Factors Influencing ABHR Antimicrobial Efficacy:



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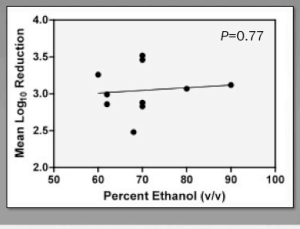
In vivo ABHR Efficacy: Formulation has a Greater Influence than Alcohol Concentration



- Method = HCPHW
  - 2 ml application volume
- Test products = Commercial healthcare ABHRs
- No relationship between efficacy and ethanol concentration

IN FORMULATED ABHR PRODUCTS ALCOHOL CONCENTRATION IS NOT THE CRITICAL DETERMINANT OF EFFICACY: FORMULATION MATTERS

Edmonds, S.E., Macinga, D.R., Mays-Suko, P., Duley, C., Rutter, J., Jarvis, W.R., Arbogast, J.W. 2012. *Amer. J. Infect. Control.* 40:521-5.

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Influence of ABHR Application Volume on Efficacy

- Does Volume Matter
- How Much is Enough?

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Sources of (Conflicting?) Information

Guidance / Expert Opinions on ABHR Application Volume

Guidance/ Expert Opinion

"Apply a palmful of alcohol-based handrub and cover all surfaces of the hands [and] rub hands until dry" (Entire process should take 20–30 seconds.)

WHO Guidelines on Hand Hygiene in Health Care (2009)

"Ideal volume of product to apply to the hands is not known and may vary for different formulations."

CDC Guideline for Hand Hygiene in Health-Care Settings (2002)

"No Time For Handwashing"
- Time to complete ABHR episode assumed to be 20s
- Time to complete HW assumed to be 40s to 80s

Voss A, Widmer AF. Infect Control Hosp Epidemiol 1997;18:205-208.

"The technique of hygienic hand rubs includes rubbing small portions of 3 to 5 mL of a fast-acting antiseptic preparation onto both hands. "

Rotter M. 2012. in "Hospital Epidemiology and Infection Control", Fourth Edition . Editor. C. Glen Mayhall .

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Typical ABHR Dispenser Outputs and ABHR Dry Times

Dispensing Practices

[a]10-stroke average output

[b]A single actuation of product was applied to subjects hands and the time to rub in dry was measured. *N*= 10-12

Current dispenser outputs for gels consistent with CDC guidelines.

Output for some foam dispensers may be too low.

Touch-Free Gel Dispensers

Code	ABHR Active:	Output (ml)[a]	Dry Time(s)[b]
A	70% ethanol	1.2 ml	22
B	70% ethanol	1.1 ml	21
C	62% ethanol	1.3 ml	25
D	61% ethanol (w/w)	1.3 ml	26
E	63% isopropanol	0.9 ml	21
F	85% EtOH (w/w)	1.0 ml	17

Touch-Free Foam Dispensers

Code	Active:	Output (ml)[a]	Dry Time(s)[b]
H	70% ethanol v/v	0.9 ml	16
I	70% ethanol v/v	1.1 ml	21
J	70% ethanol (v/v)	0.6 ml	12
K	70% ethanol (v/v)	0.6 ml	15

Macinga *et al. Infect Control Hosp Epidemiol.* 2013, 34:299.

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…But how long do healthcare workers spend disinfecting their hands?

End-User Preference

The average duration of hand hygiene by HCWs has been observed to be less than 15s in most studies.[1-3]

HEALTHCARE WORKERS EXPECT HAND HYGIENE TO BE QUICK

Most common answer = 5 seconds!

Macinga et al. Abstract. APIC's 39th Annual Educational Conference & International Meeting, San Antonio, TX. June 2012

1. WHO Guidelines on Hand Hygiene in Health Care (2009)
2. Larson et al. 2001. Crit. Care Med. 29:944.
3. Rotter et al. 2009. J Hosp Infect. 73:91.

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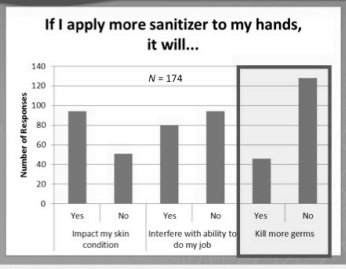
Healthcare Workers' Perceptions of ABHR Application Volume

End-User Preference



3/4 of HEALTHCARE WORKERS DO NOT BELIEVE APPLICATION VOLUME INFLUENCES EFFICACY

Macinga et al. Abstract. APIC's 39th Annual Educational Conference & International Meeting, San Antonio, TX. June 2012

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Influence of Application Volume on *in vivo* ABHR Efficacy

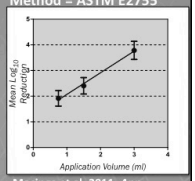
Scientific Evidence

Method = EN 1500

Product Applied volume (mL)	Mean $\log_{10}$ reduction
Product A	
4	4.19
3	3.94
2	3.34
Product B	
4	4.52
3	4.47
2.5	3.99
2	3.37

Goroncy-Bermes et al. 2010. J. Hosp. Infect. 74:212

Method = ASTM E2755



Macinga et al. 2011. *App. Environ. Microbiol.* 77:8588.

ABHR EFFICACY INCREASES LINEARLY WITH APPLICATION VOLUME

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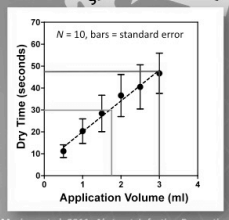
Relationship Between ABHR Application Volume and Product Rub-in Time.

Regulations/ Standards

Scientific Evidence

- Linear relationship between volume of product applied and Rub-In time.
  - Greatly influenced by test subject.
  - Influenced by alcohol type and concentration.
  - Not influenced by product form.



Macinga et al. 2011. *Abstract*. Infection Prevention

- **If 3 ml of ABHR is used in clinical practice, the "time saving" benefit is diminished.**
- **With EN 1500 there is a disconnect between ABHR application volume and rub-in time (i.e. hands are rinsed and sampled before product is dry).**
  - **This has lead to confusion regarding how much product is needed to be efficacious under clinical use conditions.**

What is the optimal ABHR use volume?

- Current *in vivo* test methods are not designed to answer this question
- Data linking product efficacy to effectiveness in clinical settings is lacking
- Current "typical" ABHR use volumes may be insufficient
  - A recent study suggest that HC workers are not willing to use enough product to achieve adequate efficacy[1]

1. Hines, JD, et al. 2013. Abstract. International Conference on Prevention and Infection Control. Geneva, Switzerland.

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Factors Influencing Hand Hygiene Compliance

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ABHR Product Attributes Which Can Influence Compliance

Skin tolerability	Feel and aesthetics
• Alcohol concentration and type	• Product form
• Emollients and moisturizers	• Emollients and moisturizers
• Excipient ingredients	• Excipient Ingredients
	• Application Volume

Product efficacy can be outweighed if products are not accepted by healthcare workers

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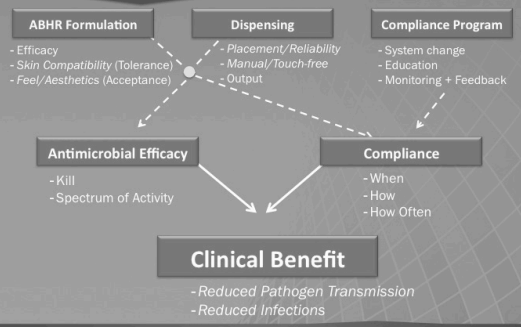
Achieving Clinical Benefit with ABHR: Whole Systems Model



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Tips for evaluating effectiveness

- Know approved labelled indications
- What is the desired use?
- Which test method was used?
- Were outside/third party labs used?

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Evaluating efficacy

- Local product testing essential
- Regulatory or local requirements
- Consider all components of a program

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WHO Protocol for Evaluation of ABHR

- **40 participants**
- **3-5 days of use**
- **Compare test product to current product (Method 1) or two test products (Method 2)**
- **Demographics**
- **Skin conditions**
- **Current self-reported practices**
- **Measure use of each product**

http://who.int/gpsc/5may/tools/system_change/en/

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WHO Protocol for Evaluation of ABHR

What is your opinion of the test product for hand hygiene?

Colour	Unpleasant	Pleasant
Smell	Unpleasant	Pleasant
Texture	Very sticky	Not sticky at all
Irritation *(stinging)*	Very irritating	Not irritating
Drying effect	Very much	Not at all
Ease of use	Very difficult	Very easy
Speed of drying	Very slow	Very fast
Application	Very unpleasant	Very pleasant
Overall evaluation	Dissatisfied	Very satisfied

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Summary

- *In vitro* and *in* vivo test methods are used to evaluate the efficacy of alcohol-based handrubs
- Global experts have called for the development of new methods that accurately simulate clinical use conditions and performance.
- Future studies are needed to establish evidence-based efficacy requirements and in use volume recommendations.
- Clinical effectiveness is influenced by both product efficacy and healthcare worker compliance (…which can be influenced by product attributes)
- Product selection should include evaluation of efficacy claims and local product testing.

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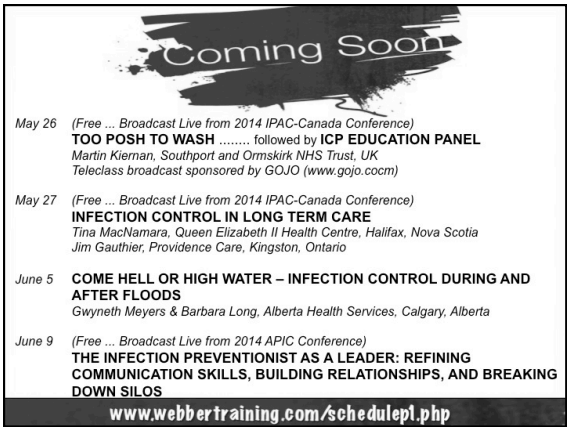

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