

Methods to Evaluate Hand Hygiene Products

Prof. Timothy Landers and Dr. David Macina

A Webber Training Teleclass

METHODS TO EVALUATE HAND HYGIENE PRODUCTS

Timothy Landers, RN, CNP, PhD & David R Macina, PhD
 Professor, College of Nursing, The Ohio State University & Research Fellow, Microbiology, Clinical and Applied Science
 GOJO Industries, Inc.

Hosted by Paul Webber
 paul@webbertraining.com

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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 patient¹
 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

¹Donsky and Eckstein, *N Engl J Med* 2009; 360.
²WHO 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.

ACTION: Notice of proposed rulemaking

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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

7

Intended Use Examples

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

8

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”

9


Product Claims

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

10


Efficacy Testing Requirements (Overview)

in vitro
(in a test tube)



+

in vivo
(using human test subjects)



11

Methodologies for evaluating the efficacy of alcohol-based hand rubs



12

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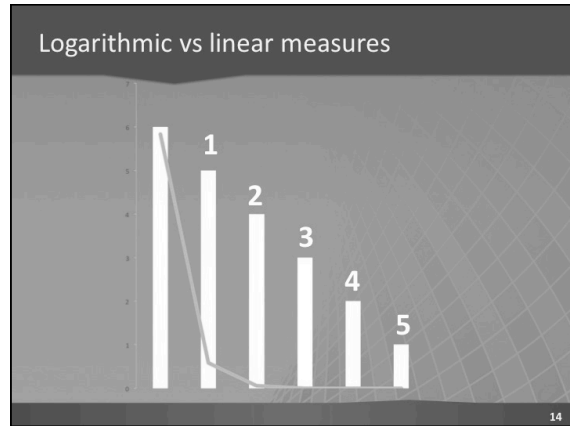
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In vitro Microbicidal Activity "Time-Kill"

- 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.**

13



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

15

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

16

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 (log₁₀)

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;99:31441-31452.

17

ASTM E1174 Overview

- Contaminate hands with 10⁹ 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 (10th) product application

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

18

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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

The diagram compares two methods: STANDARD and FINDEX TEST. The STANDARD method involves: CONTAMINATION (E. coli ATCC 12229), AIR DRY (3 min), PRE-DISINFECTION SAMPLING (1 ml), DISINFECTION (2 x 30 s), and POST-DISINFECTION SAMPLING (1 ml). The FINDEX TEST method involves: CONTAMINATION (E. coli ATCC 12229), AIR DRY (3 min), PRE-DISINFECTION SAMPLING (1 ml), DISINFECTION (2 x 30 s), and POST-DISINFECTION SAMPLING (1 ml). The FINDEX TEST method also includes a 'disinfectant under test' and a 'max. 1 min' duration for the disinfection step.

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
 Centers for Disease Control and Prevention

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”

World Health Organization

WHO Guidelines on Hand Hygiene in Health Care (2009)

20

Challenges When Using ASTM E1174 to Measure ABHR Efficacy

The diagram illustrates four challenges: 1. Hands are contaminated with a large volume of challenge bacteria. 2. Challenge bacteria remains wet on the hands. 3. Test product applied to wet hands, diluting the alcohol below the level required to achieve maximum kill. 4. Product dry time increases and activity of the product declines as hands become wetter.

A bar chart shows Average Log₁₀ Reduction vs. Wash (1, 3, 7, 10). The reduction is highest at Wash 1 and decreases as the number of washes increases.

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

21

“Low Volume” Contamination

The diagram shows four steps: 1. Grow *S. marcescens* at 35°C with vigorous shaking (~10¹⁰ cfu/ml). 2. Concentrate culture 10-fold by centrifugation and re-suspension in 1:10 volume of fresh broth. 3. Rub contamination into all surfaces of hands for 30 sec. 4. Dispense 0.2 ml of *S. marcescens* into the subjects' cupped hands.

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

22

“Low Volume” Contamination Test Results

ABHR Dry Time on Hands

The line graph shows Product Dry Time (min) vs. Product Application (1 to 10). The dry time increases from approximately 2.5 minutes at application 1 to 4.5 minutes at application 10.

Log Reductions

The bar chart shows Mean Log₁₀ Reduction vs. Wash (1, 10) for 1.5 ml Application Volume. The reduction is highest at Wash 1 (approx. 3.5) and decreases at Wash 10 (approx. 1.8).

Legend: Broth Contamination (HCPHW), Low-volume Contamination.

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

23

“Low Volume” Contamination Test Results

ABHR Dry Time on Hands

The line graph shows Product Dry Time (min) vs. Product Application (1 to 10). The dry time increases from approximately 2.5 minutes at application 1 to 4.5 minutes at application 10.

Log Reductions

The bar chart shows Mean Log₁₀ Reduction vs. Wash (1, 10) for 1.5 ml Application Volume. The reduction is highest at Wash 1 (approx. 3.5) and decreases at Wash 10 (approx. 1.8).

Designation: E2755 – 10

Standard Test Method for Determining the Bacteria-Eliminating Effectiveness of Hand Sanitizer Formulations Using Hands of Adults¹

This standard is issued under the fixed designation E2755; the number immediately following the designation indicates the year of original adoption or, in the case of revision, the year of last revision. A number in parentheses indicates the year of last approval. A superscript letter (s) indicates an editorial change since the last revision or approval.

1. Scope

1.1 This test method is designed to determine the activity of hand sanitizers (also known as hand rubs, hygienic hand rubs, or hand antiseptics) against transient bacterial flora on the hands.

AATCC Test Method 147: 2004 Antibacterial Activity Assessment of Textile Materials: Parallel Streak Method²
 21 CFR Parts 50 and 56: Protection of Human Subjects; Institutional Review Board³

1. Terminology

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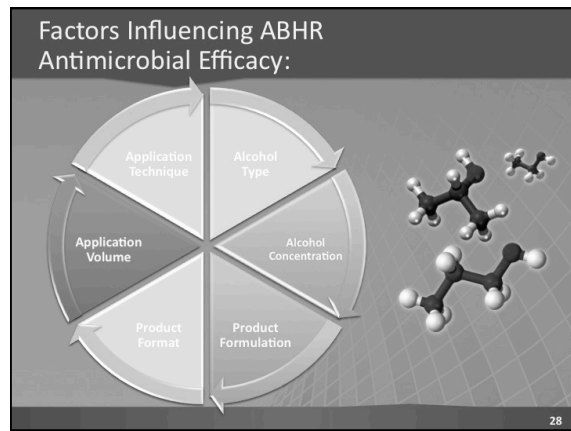
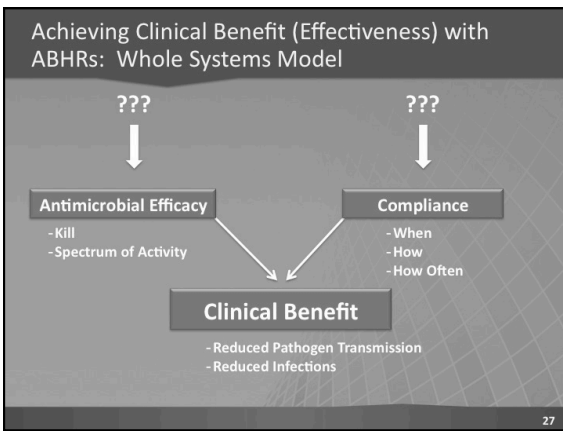
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Efficacy vs. Effectiveness

- **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



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

Percent Ethanol (v/v)	Mean Log ₁₀ Reduction
60	3.2
65	2.8
70	3.5
70	2.8
70	2.5
80	3.1
90	3.1

- 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. 29

Influence of ABHR Application Volume on Efficacy

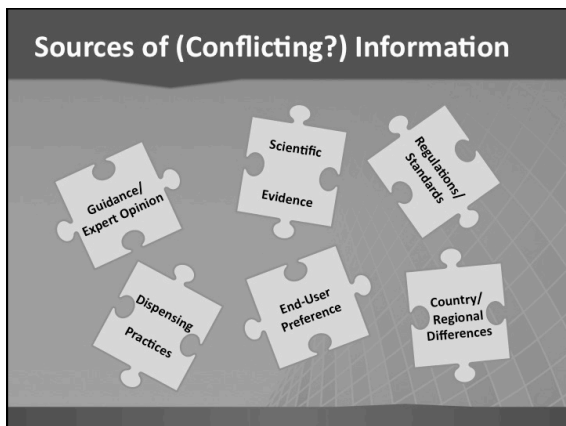
- Does Volume Matter
- How Much is Enough?

30

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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)

CDC
 “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 Mavriani.

32

Typical ABHR Dispenser Outputs and ABHR Dry Times

Dispensing Practices

^a10-stroke average output

^bA 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.

Code	ABHR Active:	Output (ml)	Dry Time(s)
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

Code	Active:	Output (ml)	Dry Time(s)
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

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

33

...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

When I use a hand sanitizer, how long should it take to dry?

N = 174 US healthcare workers

Most common answer = 5 seconds!

Macina 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. Larsson et al. 2001. Crit. Care Med. 29:944.
3. Rotter et al. 2009. J Hosp Infect. 73:91.

34

Healthcare Workers' Perceptions of ABHR Application Volume

End-User Preference

If I apply more sanitizer to my hands, it will...

N = 174

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

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

35

Influence of Application Volume on *in vivo* ABHR Efficacy

Scientific Evidence

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	

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

ABHR EFFICACY INCREASES LINEARLY WITH APPLICATION VOLUME

Macina et al. 2011. Appl. Environ. Microbiol. 77:8588.

36

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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

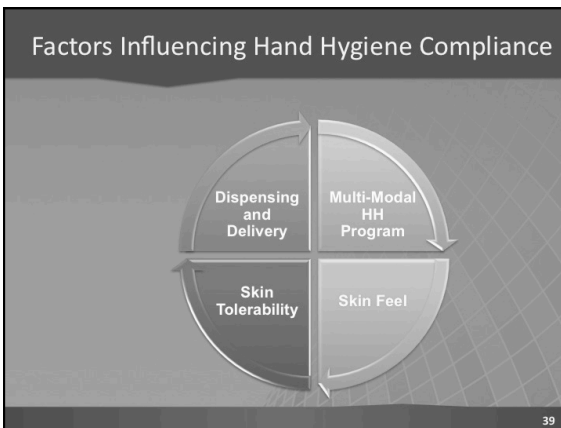
- If 3 ml of ABHR is used in clinical practice, the "time saving" benefit is diminished.
- With EN 1500 there is a disconnect between ABHR application volume and rub-in time (i.e. hands are rinsed and sampled before product is dry).
 - This has led to confusion regarding how much product is needed to 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 efficacy¹

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

38

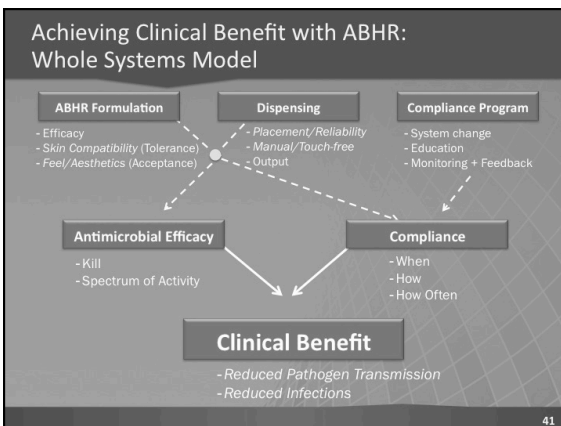


ABHR Product Attributes Which Can Influence Compliance

Skin tolerability	Feel and aesthetics
<ul style="list-style-type: none"> Alcohol concentration and type Emollients and moisturizers Excipient ingredients 	<ul style="list-style-type: none"> Product form Emollients and moisturizers Excipient Ingredients Application Volume

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

40



Tips for evaluating effectiveness

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

42

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Evaluating efficacy

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

43

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/

44

WHO Protocol for Evaluation of ABHR

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

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

45

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.

46

Coming Soon

May 26 (Free ... Broadcast Live from 2014 IPAC-Canada Conference)
TOO POSH TO WASH followed by **ICP EDUCATION PANEL**
 Martin Kiernan, Southport and Ormskirk NHS Trust, UK
 Teleclass broadcast sponsored by GOJO (www.gojo.com)

May 27 (Free ... Broadcast Live from 2014 IPAC-Canada Conference)
INFECTION CONTROL IN LONG TERM CARE
 Tina MacNamara, Queen Elizabeth II Health Centre, Halifax, Nova Scotia
 Jim Gauthier, Providence Care, Kingston, Ontario

June 5 **COME HELL OR HIGH WATER – INFECTION CONTROL DURING AND AFTER FLOODS**
 Gwyneth Meyers & Barbara Long, Alberta Health Services, Calgary, Alberta

June 9 (Free ... Broadcast Live from 2014 APIC Conference)
THE INFECTION PREVENTIONIST AS A LEADER: REFINING COMMUNICATION SKILLS, BUILDING RELATIONSHIPS, AND BREAKING DOWN SILOS

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