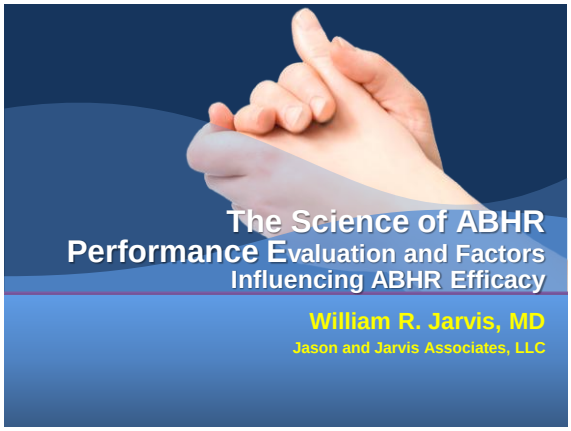
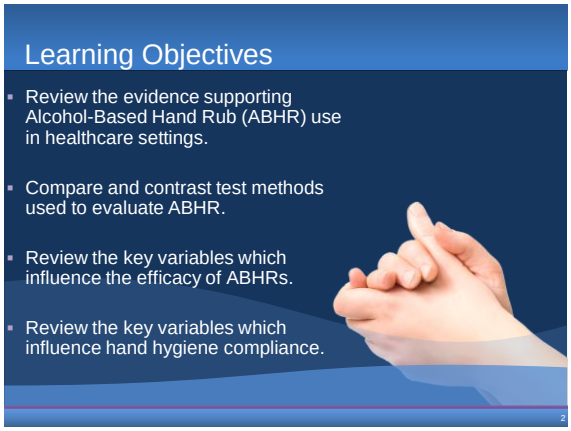

The Science of ABHR Performance Evaluation and Factors Influencing ABHR Efficacy
William R. Jarvis, MD
Jason and Jarvis Associates, LLC


Learning Objectives
Review the evidence supporting Alcohol-Based Hand Rub (ABHR) use in healthcare settings.
Compare and contrast test methods used to evaluate ABHR.
Review the key variables which influence the efficacy of ABHRs.
Review the key variables which influence hand hygiene compliance.
2


Hand Hygiene Overview: The Importance of Alcohol-Based Hand Rubs

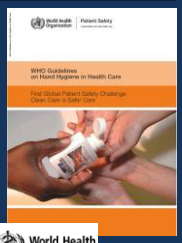
WHO Guidelines on Hand Hygiene in Health Care

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

WHO recommends alcohol-based handrubs (ABHRs) used on the following factors:

1. **Fast-acting and broad-spectrum activity** with a minimal risk of generating antimicrobial resistance
2. Can be used in **resource-limited or remote areas**
3. Process **faster and more convenient** to help promote improved hand hygiene compliance
4. **Economic benefit**
5. **Better acceptability and tolerance**

- Apply a palmful of ABHR and cover all surfaces of the hands. Rub hands until dry.



World Health Organization

PIDAC: Best Practices for Hand Hygiene

"Using alcohol-based hand rub is better than washing hands when hands are not visibly soiled."

- **Before and/or After:**
  - Contact with patient or environment
  - Performing invasive/aseptic procedure
  - Care involving contact with blood, body fluids, secretions and excretions
  - Putting on and removing gloves
  - Preparing, handling, serving food or medications
  - Moving to another activity
  - Moving from a contaminated body site to a clean body site
- **Rub hands until product is dry. This will take a minimum of 15 seconds if sufficient product is used.**

Public Health Ontario | Santé publique Ontario

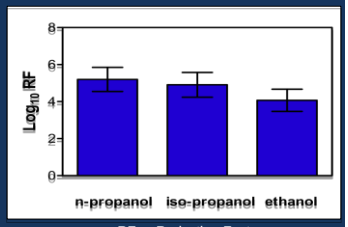
Use of Alcohol as a Skin Antiseptic

How does alcohol kill bacteria?

- Damages cell membranes → loss of cell integrity
- Inactivates proteins ("denatures")
- Acts and evaporates very rapidly

Skin Antiseptic Activity of Short-Chain Alcohols

- Alcohol-in-water mixtures tested
  - 1 minute contact time
- Antiviral Efficacy:
  - Ethanol tends to have greatest activity against non-enveloped viruses



RF = Reduction Factor

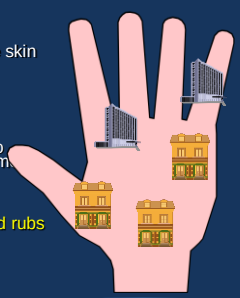
SHORT-CHAIN ALCOHOLS ARE HIGHLY EFFECTIVE AT REDUCING TRANSIENT MICROFLORA ON THE SKIN

Adapted from: Rotter M *et al.* 1977. *Mitt. D. Österr. San. Verw.* 78:170-172.

Resident and Transient Flora

Resident microflora: Normal inhabitants of the skin:
- Colonize deeper layers of the skin
- Difficult to remove
- Target for pre-surgical hand scrubs/rubs

Transient microflora: Visitors to the skin, picked up from environm
- On superficial layers of skin
- Easier to remove
- Target for alcohol-based hand rubs



Methods to Evaluate the Efficacy of Alcohol-Based Hand Rubs

Health Canada Efficacy Testing Requirements

in vitro (Time-Kill)

+

in vivo (E1174 or EN1500)

ASTM E1174: Healthcare Personnel Handwash

- Predicts the reduction of organisms by washing or sanitizing hands after handling contaminated objects
- Measures reduction of transient organisms after single or multiple product uses

Health Canada Endpoints:

Bacterial Reduction (log_{10})

1st Application: 3 log

10th Application: 3 log

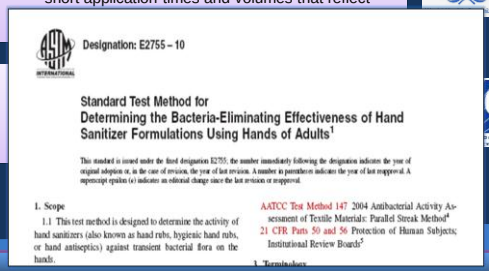
ASTM E-1174-06: Standard test method for evaluation of the effectiveness of healthcare personnel or consumer handwash formulations.

EN1500: Hygienic Hand Rub Overview

- Challenge organism: *E. coli*
- Single product cross-over design:
  - Each volunteer uses test product and an internal reference product
- Product application for defined volume & contact time
  - Typical: 3 ml for 30 sec
- Must show non-inferiority to internal reference
  - 2 x 3 ml of 60% isopropyl alcohol
  - 60 second total rub time

Expert Opinions on Hand Hygiene Test Methods

"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



Designation: E2755 – 10

Standard Test Method for
Determining the Bacteria-Eliminating Effectiveness of Hand Sanitizer Formulations Using Hands of Adults[1]

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 reapproval. A superscript epsilon (ε) indicates an editorial change since the last revision or reapproval.

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 Method[4]
21 CFR Parts 50 and 56 Protection of Human Subjects; Institutional Review Boards[5]

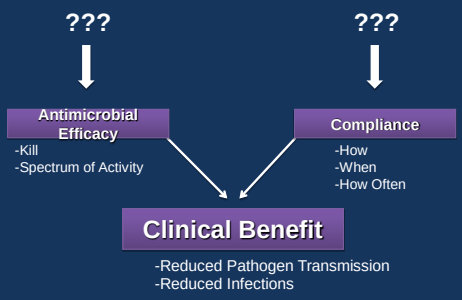
Unresolved Issues and Next Steps

- Beyond current methods:
- Predicting clinical efficacy
- Global unified method?
- In vivo antiviral methods

- Current efficacy gaps/ Future needs:
- What is the relationship between log reduction and clinical benefit?
- Improved antiviral activity (norovirus solutions)
- *C. difficile* hand hygiene solutions

Achieving Clinical Benefit With Alcohol-Based Handrubs

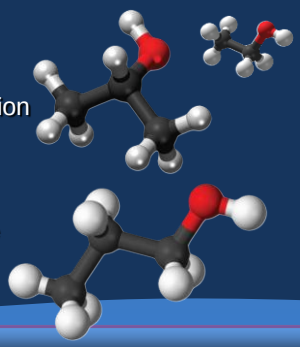
Achieving Clinical Benefit with ABHRs: Whole Systems Model



Factors Influencing ABHR Antimicrobial Efficacy

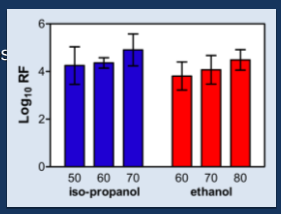
Factors Influencing ABHR Antimicrobial Efficacy:

- Alcohol Type
- Alcohol Concentration
- Formulation
- Product Form
- Application Volume



Concentration Dependence of the Activity of Short-Chain Alcohols

- Test substances:
  - Alcohol-in-water mixtures
- Test Method = EN1500
  - 1 minute contact time



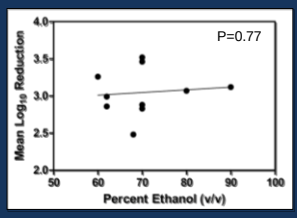
EFFICACY OF ALCOHOL-IN WATER SOLUTIONS INFLUENCED BY ALCOHOL CONCENTRATIONS.

Adapted from: Rotter et al. 1977. *Mitt. D. Österr. San. Verw.* 78:170-172.

Influence of ABHR Formulation

- ABHR formulations often contain:
  - Alcohol
  - Water
  - Thickeners
  - Buffering Systems
  - Secondary Actives
  - Surfactants
  - Secondary Actives
- Ingredients create specific attributes:
  - Skin tolerance, skin moisturization, aesthetic properties (e.g., skin feel, fragrance)
  - Enable specific delivery formats (rinse, gel, foam)
- Specific ingredients may improve or inhibit antimicrobial efficacy of ABHR formulations

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



- Method = ASTM E1174
- 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*. IN PRESS.

Does Product Form Influence Efficacy?

Efficacy of ethanol-based hand foams using clinically relevant amounts: a cross-over controlled study among healthy volunteers

Günter Kampf[*1,2], Sigunde Marschall[3], Sven Eggerstedt[3] and Christiane Ostermeyer[4]

BMC Infect Dis. 2010;10:78

FEATURE

A scientific study that proves alcohol hand sanitiser is more efficacious when dispensed onto the hands as foam rather than as gel

Authors:
(*) Christine Lens, PhD

ABSTRACT

The purpose of this study was to test

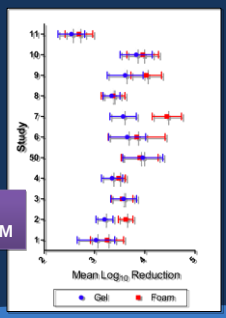
FIGURE 1

CJIC. 2011;26:21

Influence of Product Form on in vivo ABHR Efficacy: Meta-Analysis

- Methods:
- 11 independent ATM E1174 experiments (2 labs)
- 2 ml application volume of 70% ethanol gel and foam ABHR formulations

META-ANALYSIS: NO SIGNIFICANT DIFFERENCES BASED ON ABHR FORM



Edmonds et al. Abstract. The Influence of ABHR Product Format on *In Vivo* Efficacy: A Meta-Analysis. APIC's 39th Annual Educational Conference & International Meeting, San Antonio, TX. June 2012

Recommendations Regarding ABHR Application Volume

- "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)

"Apply sufficient product such that it will remain in contact with the hands for a minimum of 15 seconds before the product becomes dry (usually one to two pumps).

PIDAC Best Practices in Hand Hygiene in Health-Care Settings (2010)

"Ideal volume of product to apply to the hands is not known and may vary for different formulations. However, if hands feel dry after rubbing hands together for 10–15 seconds, an insufficient volume of product likely was applied"

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

Audience Poll:

- Is ABHR efficacy dependent upon how much I apply to my hands?

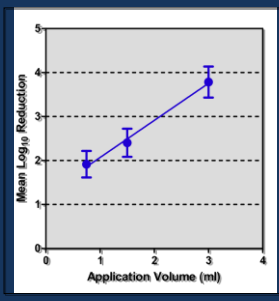
Healthcare Workers' Perceptions of ABHR Application Volume

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

Influence of Application Volume on in vivo ABHR Efficacy

- Test method: E2755
- Test product: 62% ethanol ABHR gel

ABHR EFFICACY INCREASES LINEARLY WITH APPLICATION VOLUME



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

…But how long are healthcare workers willing to spend sanitizing their hands?

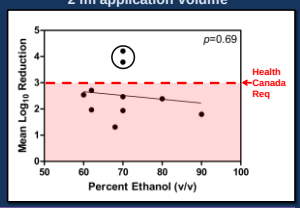
Most common answer = 5 seconds!

HEALTHCARE WORKERS DO NOT WANT TO SPEND A LOT OF TIME PERFORMING HAND HYGIENE

In vivo ABHR Efficacy at More Realistic Volumes

- ASTM E1174: Application 10 log reductions for various marketed ABHRs
- Only 2 products met Health Canada efficacy requirements at 2 ml application volume
- Alcohol concentration does not drive efficacy

Application 10 log reductions 2 ml application volume



MAJORITY OF PRODUCTS DO NOT MEET HEALTH CANADA EFFICACY REQUIREMENTS AT REALISTIC DOSES.

Edmonds, S.E., Macinga, D.R., Mays-Suko, P., Daley, C., Rutter, J., **Jarvis, W.R.** James W. Arbogast, J.W. 2012. *Amer. J. Infect. Control.* IN PRESS.

Factors Influencing Hand Hygiene Compliance

Factors Influencing Hand Hygiene Compliance

- Multimodal Hand Hygiene Program
- ABHR Product Attributes
- ABHR Dispensing and Delivery

Reasons Reported by Healthcare Workers for Lack of Adherence with Hand Hygiene Recommendations

- Skin irritation
- Inaccessible supplies
- Interference with worker/patient relation
- Patient needs perceived as priority
- Wearing gloves
- Forgetfulness
- Ignorance of guidelines
- Insufficient time
- High workload and understaffing
- Lack of scientific information demonstrating impact of improved hand hygiene on hospital infection rates

Pittet D. et al. *Emerging Infectious Diseases.* 2001;7:234

Multimodal Strategies for Successful Promotion of Hand Hygiene

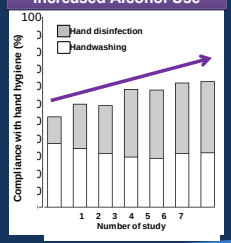
Multimodal strategy		Minimum criteria for implementation
1A.	System change: alcohol-based handrub	Bottles of alcohol-based handrub positioned at the point of care in each ward, or given to staff
1B.	System change: access to safe continuous water supply and towels	One sink to at least every 10 beds Soap and fresh towels available at every sink
2.	Training and education	All staff involved in the test phase receive training during Step 3 A programme to update training over the short-, medium- and long-term is established
3.	Observation and feedback	Two periods of observational monitoring are undertaken during Steps 2 and 4
4.	Reminders in the workplace	"How to" and "5 Moments" posters are displayed in all test wards (e.g., patients' rooms; staff areas; out-patient/ambulatory departments)
5.	Institutional safety climate	The chief executive, chief medical officer/medical superintendent and chief nurse all make a visible commitment to support hand hygiene improvement during Step 3 (e.g., announcements and/or formal letters to staff)

WHO Hand Hygiene Guidelines on Hand Hygiene in Health Care. 2009.

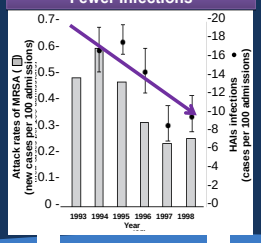
Impact of a Multimodal Hand Hygiene Program

- ABHR use associated with increasing compliance and reduction of transmission of healthcare-associated infections (HAIs)

Increased Alcohol Use



Fewer Infections



Pittet D et al. *Lancet.* 2000;356:1307-12.

ABHR Product Attributes Which Can Influence Compliance

Skin tolerability

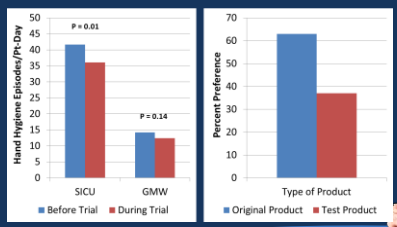
- Alcohol concentration and type
- Presence (or absence) of emollients and moisturizers
- Excipient ingredients

Feel and aesthetics

- Product form
- Emollients and moisturizers
- Excipient Ingredients

Impact of ABHR Acceptance on Hand Hygiene Frequency

- **Prospective evaluation of a new ABHR formulation conducted in a SICU and on a general medical ward**
- Hand hygiene frequency monitored using electronic counters



Boyce JM et al. 5th Decennial Conference on HAIs, March 2010 Abstr # 27

Product Acceptance & Clinical Effectiveness

- **The "best" ABHR are those that achieve at least a threshold of antimicrobial efficacy while optimizing product acceptance elements to ensure maximum product usage**
- **Product efficacy can be outweighed if products are not accepted by healthcare workers**
  - **Lower compliance may result in increased infection rates**
- **The most efficacious product is not necessarily the most effective (Semmelweis)**
- **The importance of product acceptability is noted in both the CDC and WHO Hand Hygiene Guidelines**

Boyce, J. M. and Pittet, D.. 2002. MMWR Recomm. Rep. 51:1-45.
World Health Organization. WHO Guidelines for Hand Hygiene in Health Care. 2009;7:202.
Larson, E. et al.. American Journal of Infection Control. 2006;34: 627-35.
The Joint Commission Center for Transforming Healthcare(2010). Hand Hygiene Project: Best Practices from Hospitals Participating in the Joint Commission Center for Transforming Healthcare Project.

Impact of Product Dispensing on Compliance

- **Dispenser Placement…**
  - Point of Care vs. hallway dispensers
- **Reliability…**
  - Are the dispensers functional?
  - Batteries?
- **Dispensed Volumes…**
  - Influence product dry time
  - Influence product feel
- **Manual or Touch Free…**
  - Touch-free dispensers may promote compliance*

*Larson et al. 2005. Am J Crit Care. 14:304-11.
*Scheithauer et al. 2011. Hyg. Med. 36:496.

Influence of Dispenser Type on Hand Hygiene Frequency

- Frequency of use of manually operated and touch-free ABHR dispensers compared over 4 month period.

Table 2 Daily uses of alcohol dispenser by type of dispenser

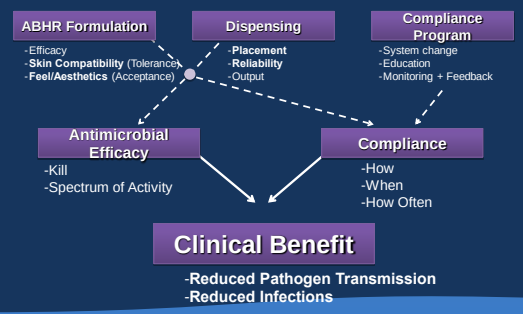
Count	Type of dispenser: Manual	Touch-free	*P*
No. of uses per dispenser per day, mean (SD)*	25.6 (19.6)	41.2 (26.9)	.02
No. of episodes of hand hygiene per patient per hour, mean (SD)†	3.33 (2.7)	4.42 (2.8)	.04
No. of episodes of hand hygiene before contact with a patient per hour, mean (SD)†	1.26 (1.74)	1.58 (1.59)	.003

*Measured by using installed counters.
†Measured by using direct observation.

Touch-free dispensers were used significantly more often than manual dispensers

Larson EL et al. Am J Crit Care 2005;14:304

Achieving Clinical Benefit with ABHR: Whole Systems Model



Open Questions and Future Research

- **Relative influence of the variables on clinical effectiveness is unknown**
  - Do differences in product efficacy translate to measurable differences in clinical effectiveness?
  - How much of an increase in compliance is needed to significantly improve effectiveness?
  - What is the optimal ABHR use volume and are current ABHR use volumes too low?

Conclusions

- **ABHRs should be considered from a whole system approach to maximize clinical effectiveness**
- **Formulation matters**
  - **Efficacy should be judged on in vivo Health Canada performance criteria and not on only alcohol content or dry time**
- **Dispenser output matters**
  - **When evaluating in vivo data, the test volume relative to dispenser output is critical**
- **Product acceptance and tolerability is critical to driving compliance**
  - **End user trials of both formulations and dispensers should be conducted to aid in purchasing decisions**

- Thank you!