HEALTH CANADA STANDARDS
AND FACTORS INFLUENCING
THE CLINICAL EFFECTIVENESS
OF ALCOHOL-BASED HAND RUBS
(ABHRs)

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Jason and Jarvis Associates, LLC
Learning Objectives

• Understand registration options for ABHR
• Become familiar with Health Canada standards and test requirements
• Understand key differences between ABHR product efficacy
• Learn how to make informed decisions on selecting ABHR products
Agenda

- Overview of the Health Canada Standards
- Methods to Evaluate ABHR Efficacy
- Factors Influencing ABHR Antimicrobial Efficacy
Overview of the Health Canada Standards
Health Canada Standards for ABHR Human-Use Antiseptic Drugs

Antiseptic Skin Cleanser Monograph

Guidance Document: Human-Use Antiseptic Drugs
Health Care Settings: Higher presence of pathogens that may cause HAIs than in other settings: Antimicrobial efficacy of highest priority: higher safety risk to health if the product is not effective

Professional Food Settings: (food processing plants, restaurants, retail supermarkets, fast food outlets) – product protects food handlers and prevents transmitting disease through food

Commercial:* general public, commercial or institutional settings

Personal Domestic:* self selected, domestic use

*Mongraph registration is available for Personal Domestic and Commerical Use if not securing any non-monograph claims.
# Test Differences – Monograph & Guidance Document

<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>Is <em>in vivo</em> data required?</td>
<td>• Yes</td>
<td>• Yes</td>
<td>• Yes</td>
</tr>
<tr>
<td>Is bacteria and fungi data required?</td>
<td>• Yes</td>
<td>• Yes</td>
<td>• Yes</td>
</tr>
<tr>
<td>Is mycobacteria and virus data required?</td>
<td>• No</td>
<td>• No</td>
<td>• Yes</td>
</tr>
<tr>
<td>Is data submitted to Health Canada?</td>
<td>• No</td>
<td>• Yes</td>
<td>• Yes</td>
</tr>
<tr>
<td>Is data reviewed by Health Canada?</td>
<td>• No</td>
<td>• Yes</td>
<td>• Yes</td>
</tr>
<tr>
<td>Are additional claims available?</td>
<td>• NO (not since Guidance)</td>
<td>• Yes</td>
<td>• Yes</td>
</tr>
<tr>
<td>What additional claims are available? Examples stated</td>
<td>• None</td>
<td>• Commercial Use, Log Reduction, Organism Specific, Anti-viral, Persistence...</td>
<td>• Professional Use, Log Reduction, Commercial Use, Organism Specific, Anti-viral, Persistence...</td>
</tr>
</tbody>
</table>
## Use/Purpose Differences – Monograph & Guidance Document

<table>
<thead>
<tr>
<th>Monograph uses and purposes (claims)</th>
<th>Non-monograph uses and purposes (claims)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• No data submitted or reviewed by Health Canada</td>
<td>• Data submission required and reviewed by Health Canada – varied post guidance</td>
</tr>
<tr>
<td>– Antiseptic cleanser</td>
<td>• For use on package labels</td>
</tr>
<tr>
<td>– Medicated cleanser</td>
<td>– General Indication Areas:</td>
</tr>
<tr>
<td>– Kills harmful bacteria or germs</td>
<td>• Log Reduction Claims, Persistence Claims, Time Kill Claims, Organism Specific, etc.</td>
</tr>
<tr>
<td>– Effective in destroying certain bacteria and removing impurities to provide antiseptic cleansing</td>
<td>– Label claims specific to categories:</td>
</tr>
<tr>
<td>– For personal hand hygiene to help prevent the spread of certain bacteria</td>
<td>• For Hospital and Healthcare Professional Use / For Use in Food Premises</td>
</tr>
<tr>
<td></td>
<td>• To reduce bacteria, mycobacteria, fungi, and viruses on skin</td>
</tr>
</tbody>
</table>
Frequently Asked Questions

• Are any ABHR products registered for Hospital and Healthcare Professional Use?
  – No

• Why are no ABHR products registered for Healthcare Professional Use?
  – Extensive testing requirements
  – Significant investment – time and cost
  – Human safety risks

• Are my products effective if they don’t have approved Healthcare claims?
  – Maybe. Lack of approval does not mean lack of evidence
  – Verify related efficacy data
Frequently Asked Questions

- How can I verify the efficacy of products?
  - Request third party, independent lab data using unmodified standard test methods. Manufacturers should have data on file to share.

- Can I use products registered before the Guidance?
  - Yes. Health Canada does not require these products to be resubmitted under the Guidance.
  - If adding non-monograph claims, would use the Guidance.

- Does it make a difference if use/purpose claims were granted by Health Canada before or after the Guidance?
  - Requirements in current Guidance do not apply to pre-Guidance monograph registrations.
  - There were less standardized requirements pre-Guidance.
Frequently Asked Questions

• Are claims obtained through the Monograph before the Guidance still valid?
  – Yes. Earlier non-monograph claims (e.g., healthcare, commercial, kill claims, organism specific, etc.) are based on previous requirements, not more extensive 2009 Guidance test requirements.

• Is a Healthcare claim under the Monograph the same as Healthcare Professional use under the Guidance?
  – No. Different support documentation was needed for a pre-Guidance claim as compared to the Guidance.
Summary

- New more extensive Health Canada regulatory guidance released in 2009 for different environments
- All ABHR products with a product license can be sold in Canada
- No ABHR products are approved or Healthcare Professional Use yet
- Review of claims and third party efficacy data is important criteria for product selection to maximize patient safety
Methods to Evaluate ABHR Efficacy
### Log Reduction Tutorial

<table>
<thead>
<tr>
<th>Log Reduction</th>
<th>Percent Reduction of Bacteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>90%</td>
</tr>
<tr>
<td>2</td>
<td>99%</td>
</tr>
<tr>
<td>3</td>
<td>99.9%</td>
</tr>
<tr>
<td>4</td>
<td>99.99%</td>
</tr>
<tr>
<td>5</td>
<td>99.999%</td>
</tr>
</tbody>
</table>

**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
Health Canada Efficacy Testing Requirements

**in vitro**
(Time-Kill) broad range of pathogens

**in vivo**
representative organisms only

**In vitro** data (test tube) is not always predictive of
**in vivo** (on hands) results and should be interpreted cautiously.
Health Canada Standard for \textit{in vitro} Efficacy Tests

Data request on key subset of Bacteria (20), Fungi (2) and Viruses (14)

\textbf{Minimum Acceptable Level of Efficacy (Canada)}:

- Bacterial ($\log_{10}$) = 5 (99.999%)
- Fungi & Viruses ($\log_{10}$) = 4 (99.99%)

\textit{In vitro} results do not predict antimicrobial performance on hands
Comparison of *in vivo* Bactericidal Test Methods

**ASTM E1174/ Healthcare Personnel Handwash (HCPHW)**
- Product evaluated at single and multiple uses
- No specified application volume

**EN1500: Hygienic Hand Rub**
- Single product cross-over design
- Typically 3 mL for 30 seconds
- Must show non-inferiority to internal reference.
• Predicts the reduction of organisms by washing or sanitizing hands after handling contaminated objects

• Measures reduction of transient organisms after single and/or multiple product uses

Health Canada Endpoints:

Bacterial Reduction ($\log_{10}$)

1st Application: 3 log
10th Application: 3 log

**In vivo Fingerpad Method (Fungal)**

1. Wash hands, dry, mark fingerpads
2. Add test organism suspension to fingerpad
3. Allow test organism to dry on fingerpads
4. Expose fingerpad to hand sanitizer
5. Hand sanitizer removes and/or inactivates test organism
6. Expose finger to buffer to remove any remaining test organism
7. Calculate test organism reduction

Test Organism suspension
Summary and Conclusions

- It is important to understand ABHR test methods when evaluating and interpreting product claims
  - Data from *in vivo* methods is essential to differentiate ABHR efficacy
  - Be cautious of “99.99999% game”

- Health Canada requires testing using various test methods

- It is important to ask manufacturers for the test data to ensure products were evaluated *in vivo* using methods that are accepted by Health Canada
Factors Influencing ABHR Antimicrobial Efficacy
Multiple Factors of Antimicrobial Efficacy:

Application Technique

Alcohol Type

Application Volume

Alcohol Concentration

Product Format

Product Formulation

Concentration 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

Influence of ABHR Formulation

- ABHR formulations often contain:
  - Alcohol
  - Water
  - Thickeners
  - Moisturizers
  - Buffering Systems
  - Secondary Actives
  - Surfactants

- 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 = 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

Does Product Form Influence Efficacy?

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

Günter Kampf1,2, Sigunde Marschall3, Sven Eggerstedt3 and Christiane Ostermeyer4

BMC Infect Dis. 2010;10:78

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

CJIC. 2011;26:21
Product Form Does Not Influence Efficacy

- Both gel and foam formulations met *in vivo* HCPHW requirements
- Formulation more important than product form

Guidance 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)
Is ABHR efficacy dependent upon how much I apply to my hands?
Healthcare Workers’ Perceptions of ABHR Application Volume

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

- Impact my skin condition
- Interfere with ability to do my job
- Kill more germs

$N = 174$

3/4 of Healthcare Workers do not believe application volume influences efficacy

Influence of Application Volume on \textit{in vivo} ABHR Efficacy (ASTM E2755)

- Test product: 62\% ethanol ABHR gel

ABHR efficacy increases linearly with application volume.

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

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

Most common answer = 5 seconds!

Healthcare workers expect Hand Hygiene to be relatively quick

Typical ABHR Dispenser Outputs and ABHR Dry Times

### Touch-Free Gel Dispensers

<table>
<thead>
<tr>
<th>Code</th>
<th>ABHR Active:</th>
<th>Output (mL)(^a)</th>
<th>Dry Time(s)(^b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>70% ethanol</td>
<td>1.2 mL</td>
<td>22</td>
</tr>
<tr>
<td>B</td>
<td>70% ethanol</td>
<td>1.1 mL</td>
<td>21</td>
</tr>
<tr>
<td>C</td>
<td>62% ethanol</td>
<td>1.3 mL</td>
<td>25</td>
</tr>
<tr>
<td>D</td>
<td>61% ethanol (w/w)</td>
<td>1.3 mL</td>
<td>26</td>
</tr>
<tr>
<td>E</td>
<td>63% isopropanol</td>
<td>0.9 mL</td>
<td>21</td>
</tr>
<tr>
<td>F</td>
<td>85% EtOH (w/w)</td>
<td>1.0 mL</td>
<td>17</td>
</tr>
</tbody>
</table>

\(^a\)10-stroke average output

\(^b\)A single actuation of product was applied to subjects hands and the time to rub in dry was measured. \(N=10-12\)

### Touch-Free Foam Dispensers

<table>
<thead>
<tr>
<th>Code</th>
<th>Active:</th>
<th>Output (mL)(^a)</th>
<th>Dry Time(s)(^b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>H</td>
<td>70% ethanol v/v</td>
<td>0.9 mL</td>
<td>16</td>
</tr>
<tr>
<td>I</td>
<td>70% ethanol v/v</td>
<td>1.1 mL</td>
<td>21</td>
</tr>
<tr>
<td>J</td>
<td>70% ethanol (v/v)</td>
<td>0.6 mL</td>
<td>12</td>
</tr>
<tr>
<td>K</td>
<td>70% ethanol (v/v)</td>
<td>0.6 mL</td>
<td>15</td>
</tr>
</tbody>
</table>

Current dispenser outputs for gels consistent with Canada, WHO and CDC guidelines.

Output for some foam dispensers may be too low.

**Macinga et al. Infect Control Hosp Epidemiol. 2013, 34:299.**
**In vivo ABHR Efficacy at More Realistic Volumes**

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

Application 10 log reductions for various marketed ABHRs at 2 mL application volume.

**Majority of products do not meet Health Canada efficacy requirements at realistic doses**

What’s next?

- Science advances the guidelines
- Guidance set standards
- Need to demand more efficacious products through substantiated efficacy
- User acceptance still critical to compliance – extreme efficacy standards could have adverse impact on user acceptance if not formulated properly
Summary and Conclusions

• **Formulation matters**
  – Efficacy should be judged on *in vivo* Health Canada performance criteria and not on just alcohol content or wet/dry time
  – Know the *in vivo* efficacy of the products, scrutinize the methods, data, dispensed vs. tested volumes

• **Complexity in ABHR registration in Canada**
  – Multiple paths for different environments
  – Significant updates to submission process in the last 6 years

• **Data is needed to make informed product choices**
  – Get manufacturer data
  – Ensure studies conducted by independent, third party
  – Ensure tests use standard, un-modified test methods as recommended by Health Canada
THANK YOU

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