Health Canada Santé Canada

December 3, 2009

NOTICE

Our file number: 09-131213-24

Release of the Final Guidance Document*: Human-Use Antiseptic Drugs*

The final version of this Health Canada *g*uidance document ***Human-Use Antiseptic Drugs*** is now available. Comments and suggestions received from the consultation on the draft version of the guidance were reviewed and considered in the finalization of this document, and are available upon request.

This guidance applies to antiseptic skin products for human use and is applicable to both pharmaceuticals (both Division 1 and Division 8) and natural health products, falling outside the scope of the Category IV Antiseptic Skin Cleanser Monograph for personal domestic use products. Specifically, it covers professional and commercial use antiseptic skin products, as well as non-Monograph personal use products such as those making viral, specific organisms, persistence and/or log reduction claims.

The guidance outlines the categories of antiseptic products, the submission filing process, and the basic documentation required to support product efficacy. It also provides information on test organisms and detailed data requirements necessary to support specific claims and enhanced labelling.

Of particular note, the *in vivo* test methods (e.g. "Meets EN 1500") may now be reflected on the label in cases where the data requirements outlined in the guidance have been met. It is Health Canada's expectation that professional use products would seek this new enhanced labelling. Health Canada will be communicating the updated expectations and labelling to healthcare practitioners and food handlers. In addition, the Drug Product Database and the Licensed Natural Health Products Database will now reflect which products have been authorized for professional, commercial and/or personal use. Products authorized for use in professional food premises are listed on the Canadian Food Inspection Agency (CFIA) Web site.

Manufacturers of authorized products intending to upgrade to the enhanced labelling outlined in this guidance should file according to the relevant sections of the *Post-DIN Changes* guidance document or the *Post Licensing Guidance Document* guidance document as appropriate.

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The guidance will become effective upon posting on Health Canada's website. In the interim, Health Canada will accept submissions compliant with this guidance from any manufacturers wishing to pursue the indications and/or enhanced labelling.

Should you have any questions or comments regarding the content of the guidance, please contact:

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Health Canada Santé Canada

GUIDANCE DOCUMENT
Human-Use Antiseptic Drugs

Published by authority of the
Minister of Health

Adopted Date	2009/10/21
Effective Date	2009/11/27

Health Products and Food Branch

Canada

Our mission is to help the people of Canada maintain and improve their health. *Health Canada*	The Health Products and Food Branch's mandate is to take an integrated approach to the management of the risks and benefits to health related products and food by: • Minimizing health risk factors to Canadians while maximizing the safety provided by the regulatory system for health products and food; and, • Promoting conditions that enable Canadians to make healthy choices and providing information so that they can make informed decisions about their health. *Health Products and Food Branch*

Également disponible en français sous le titre : Ligne directrice : Médicaments antiseptiques à usage humain

FOREWORD

Guidance documents are meant to provide assistance to industry and health care professionals on **how** to comply with governing statutes and regulations. Guidance documents also provide assistance to staff on how Health Canada mandates and objectives should be implemented in a manner that is fair, consistent and effective.

Guidance documents are administrative instruments not having force of law and, as such, allow for flexibility in approach. Alternate approaches to the principles and practices described in this document ***may be*** acceptable provided they are supported by adequate justification. Alternate approaches should be discussed in advance with the relevant program area to avoid the possible finding that applicable statutory or regulatory requirements have not been met.

As a corollary to the above, it is equally important to note that Health Canada reserves the right to request information or material, or define conditions not specifically described in this document, in order to allow the Department to adequately assess the safety, efficacy or quality of a therapeutic product. Health Canada is committed to ensuring that such requests are justifiable and that decisions are clearly documented.

This document should be read in conjunction with the accompanying notice and the relevant sections of other applicable guidance documents.

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1 INTRODUCTION

As per the *Food and Drugs Act*, any substance that is manufactured, sold or represented for use in the "mitigation or prevention of disease" is a drug. Section 9(1) of the *Act* also specifies that a drug must not be labelled "…in a manner that is false, misleading or deceptive or is likely to create an erroneous impression…"

An antiseptic product is considered to be one that inactivates, reduces, prevents or arrests growth of microorganisms with the inherent intent to mitigate or prevent disease. This includes antiseptic products whether they are regulated under the *Food and Drug Regulations (FDR)* or the *Natural Health Products Regulations (NHPR)*. This guidance document provides recommendations regarding the information considered necessary by Health Canada in order to support these types of claims.

1.1 Policy Objectives

Pursuant to Section 9(1) of the *Act*, it is Health Canada's policy that an application for an antiseptic product explicitly or implicitly claiming that the product mitigates or prevents disease be adequately supported by appropriate data. The supporting data may vary relative to the risk associated with the antiseptic product's environment for use and its specific claims.

1.2 Policy Statement

Sufficient information to support the labelled claim of an antiseptic product for human use should be made available to Health Canada.

> This information should include evidence of positive supportive results of *in vivo* and *in vitro* testing conducted in accordance with acceptable test methods, and for *in vivo* studies, under the conditions of use prescribed on the label.

1.3 Scope and Application

This guidance applies to antiseptic skin products for human use that are intended for use in professional and commercial settings. The guidance is applicable to pharmaceutical antiseptic products (both Division 1 and Division 8) as well as to natural health antiseptic products. The guidance does not provide data recommendations to support personal domestic use products, except when such products make claims of efficacy against specific organisms, persistence, log reduction or % reduction and/or antiviral claims.

The guidance does not apply to human-use antiseptic products for burn victims, first aid, or application to sites other than the skin (for example (e.g.) mucous membranes, catheter insertion, etc.). Applicants seeking authorization for such products should request a presubmission meeting to discuss appropriate supporting data. Further, the guidance does not apply to hard surface disinfectants (see Health Canada's *Guidance Document: Disinfectant Drugs* for more information).

The guidance will outline the categories of antiseptic products, the filing process for antiseptic submissions, the basic documentation required to support the efficacy for all categories of antiseptic products covered in the guidance, and the additional detailed data recommendations for specific claims.

For the purpose of this guidance, microorganisms are defined as bacteria, yeast, fungi, and viruses. Helminths and protozoan parasites are recognized to be organisms of concern for professional use products. Representation that a product reduces parasites will be reviewed on a case by case basis outside of this guidance document and sponsors are encouraged to seek a presubmission meeting to discuss the data recommended to support the application.

1.4 Background

Sponsors of antiseptic products for human use containing ingredients that meet the definition of Schedule 1 of the *NHPR* are required to submit an application for a Natural Product Number (NPN) with the Natural Health Products Directorate (NHPD) as per Section 5 of the *NHPR*. Sponsors of antiseptic products for human use containing ingredients other than those that meet the definition of Schedule 1 of the *NHPR* are required to file an application for a Drug Identification Number (DIN) with the Therapeutic Products Directorate (TPD) as per Part C, Section C.01.014 of the *FDR*.

A drug is defined in part by the *Act* as *"…any substance or mixture of substances manufactured, sold or represented for use in… mitigation or prevention of a disease."* Furthermore, Section 9(1) of the *Act* states:

No person shall label, package, treat, process, sell or advertise any drug in a manner that is false, misleading or deceptive or is likely to create an erroneous impression regarding its character, value, quantity, composition, merit or safety.

A labelled claim may be implicit or explicit with respect to mitigating or preventing disease. For example, a claim stated as "prevents the spread of disease X" would be considered explicit. If the claim were stated as "kills organism Y" and organism Y is known to cause disease X then this claim would be considered as implying "prevents the spread of disease X". Therefore, Health Canada has the responsibility to confirm the validity of such claims either through the evaluation of supportive scientific evidence or by confirming conformance to a prescribed and acceptable standard. A standard has been developed for certain personal domestic use antiseptics in the form of the joint TPD-NHPD Category IV Monograph for *Antiseptic Skin Cleansers.*

However, the lack of guidance for other types of antiseptic products has resulted in a number of undesirable effects and consequences, impacting Health Canada's ability to regulate antiseptic products appropriately. These include:

- industry confusion on submission recommendations and process, resulting in the possibility of non-compliance and an identified need for clarity;

- a high number of Category IV Monograph rejections issued for submissions for professional-use antiseptic products as no guidance is otherwise available;

- less than optimal use of submission review resources as a result of fielding enquiries in the place of a published document, and in processing unnecessary filings;

- consumer and health professional confusion on the availability of appropriate products for use.

It was recognized that Health Canada requires an appropriate tool to effectively manage drug submission applications for antiseptic products.

2 ACRONYMS and DEFINITIONS

ASTM	ASTM International (previously American Society for Testing and Materials)
ATCC	American Type Culture Collection
CDER	Center for Drug Evaluation and Research
CEN	European Committee for Standardization
CFIA	Canadian Food Inspection Agency
CGSB	Canadian General Standards Board
DIN	Drug Identification Number
DINA	Drug Identification Number Application
DINF	Category IV Monograph Drug Identification Number Application
EN	standard developed by the CEN
FDA	Food and Drug Administration, United States of America
FDR	*Food and Drug Regulations*
ICH	International Conference on Harmonization
NCTC	National Collection of Type Cultures
NHP	natural health product
NHPD	Natural Health Products Directorate
NHPR	*Natural Health Products Regulations*
OECD	Organization for Economic Cooperation and Development
TPD	Therapeutic Products Directorate

Persistence: A reduction in skin flora which maintains an extended and low microbial release from the skin due to slow regrowth of the resident microflora. (Fraise et al, 2004)

Resident Organisms: Those organisms normally permanently resident on the skin. Under some circumstances, this may include those that are not permanently resident on normal skin but may be increased in number in the presence of certain skin diseases (e.g. *Klebsiella spp.* on psoriatic skin) or systemic illnesses (diabetes, AIDS, etc). (Fraise et al, 2004)

Transient Organisms: Those organisms picked up by contact with the environment but may remain *in situ* long enough to be transferred (e.g. from patient to patient; from surgeon to patient, etc.). (Fraise et al, 2004)

3 GUIDANCE FOR IMPLEMENTATION

This section describes the:

- different categories of antiseptic products;
- filing processes applicable to antiseptic products;
- general information on filing considerations.

3.1 Categories of Antiseptic Products

The categories of human-use antiseptic products for application on the skin are defined by the intended user and the proposed conditions of use. Such products would be considered drugs under the *Act* if represented for the reduction and/or inactivation of microorganisms on human skin as this implies its use for the prevention of disease or the prevention of disease transmission. Antiseptic products can include both those to be used with water (referred to as washes) or without water (referred to as rubs), and may be presented in different pharmaceutical forms. Antiseptic skin products also include preoperative skin preparations.

Products may be indicated for multiple use categories, provided that each has sufficient data to support the indication, each indication has been authorized by Health Canada, and the product labels contain appropriate information for each use. The statement identifying the environment of use (e.g. For Food Premise Use) may be amended to incorporate all authorized indications.

Below is a list of the categories recognized by Health Canada. Each category is further defined in the appropriate subsection of this guidance document.

3.1.1 Personal Domestic Use

Personal domestic (or household) use products are those used by an individual in a domestic setting to reduce transient organisms on the skin.

3.1.1.1 Monograph Products

A joint TPD-NHPD Category IV Monograph for *Antiseptic Skin Cleansers* is available for products self-selected by a consumer from a retail outlet for their own personal household use as part of a daily skin cleansing routine. These types of products are intended to provide a superficial and non-persistent cleaning effect to reduce domestic transient bacterial and fungal load on hands. Consumers are encouraged to use plain soap and water with vigorous scrubbing of the entire surface of both hands, followed by proper rinsing and drying, as their first option in order to cleanse soiled hands adequately. Antiseptic skin cleansers should be recommended for use on lightly soiled hands only as a second-line approach or when soap and water are not available. The medicinal (active) ingredients and their concentrations, indications, and adequate directions for use (including directions, dosage, and warnings) are restricted to those specified in the Monograph.

The Monograph outlines active ingredients and their concentrations generally recognized as safe and effective in the reduction of transient organisms. The sponsor is required to have the data on file which supports that the finished product is effective when considering the permitted Monograph claims and required directions for use. Products which meet the Monograph specifications are excluded from this guidance, and should be filed with NHPD or TPD in keeping with the Monograph process. This guidance does not apply to products complying with the Monograph unless a change in indication is made by the sponsor after authorization has been received under the Monograph system.

The Monograph does not apply to:

a) antimicrobial products intended to be used by health care professionals or food handlers or in institutions including health care facilities; or
b) antimicrobial products intended to be used in commercial settings (e.g. outside of the home/personal use); or
c) products with claims outside those permitted in the Monograph, such as:
    - efficacy against any specific organisms;
    - persistence claims;
    - log reduction or % reduction (kill) claims;
    - antiviral claims.

3.1.1.2 Non-Monograph Products

Products in this category include any personal-use antiseptic product not captured in the above Monograph. This includes, but may not be limited to, consumer-use first aid antiseptic for application in cleansing minor wounds or self-administered pre-injection preparatory cleanser (e.g. for ear piercing or insulin injections). Products which make such claims are considered outside the scope of this guidance, although some of the same basic principles may apply. A drug application (for pharmaceuticals) or non-traditional NPN application (for natural health products) should be filed with the appropriate supporting data to Health Canada.

3.1.2 Personal Commercial Use

Personal commercial use products are those made available to the general public for occasional use and are intended to reduce transient organisms on the skin in a commercial or institutional setting.

3.1.3 Professional Food Premises

Products for professional food premises are those which are indicated for use by food handlers to reduce transient organisms on the skin in a commercial or institutional setting including food processing plants and also includes restaurants, retail supermarkets, and fast food outlets.

3.1.4 Professional Healthcare Use

Products for professional healthcare use are those which are indicated for use by individuals to reduce transient and/or resident organisms on the skin in a healthcare setting (such as hospitals, nursing homes, clinics, dental offices). Such products are to be used in accordance with applicable hospital protocols.

Professional healthcare use antiseptics can be broken down as follows:

Professional hygienic handrub: product used for post-contamination treatment of lightly-soiled hands that involves rubbing hands without addition of water, and which is designed for frequent use.

Professional hygienic handwash: product used for post-contamination treatment that involves washing hands, and which is designed for frequent use.

Surgical handrub: product used for preoperative treatment, which involves rubbing hands without addition of water.

Surgical handwash: product used for preoperative treatment that involves washing hands, either with or without the use of a scrub brush.

Patient preoperative skin preparations: product used to prepare patient skin prior to surgical procedures.

3.2 Filing Applications

Instructions on the data recommendations to support applications for antiseptic products are detailed below in the following Sections. Antiseptic products using drugs from a natural source which meet the definition of Schedule 1 of the *NHPR* are required to submit an application for a Natural Product Number (NPN) to NHPD as per Section 5 of the NHPR. Antiseptic NPN applications are to be submitted to the non-traditional assessment stream in accordance with NHPD's *Product Licensing Guidance Document*. All other applications should be filed with the Therapeutic Products Directorate. Please note that C.08.001 of the *FDR* may apply to drug applications when introducing new ingredients, new indications, etc.

3.2.1 Related Guidances for Filing

Information regarding general submission requirements, contact information, and target performance standards may be found in the Health Canada guidance documents: *Guidance for Industry: Management of Drug Submissions* for pharmaceuticals and *Product Licensing Guidance Document* for natural health products.

3.2.2 Other Related Guidances

This guidance document should be read in conjunction with other associated Health Canada policies and guidance documents including, but not limited to:

- *Preparation of Drug Identification Number Submissions* (1995);
- *Quality Guidance: Applications for Drug Identification Numbers (DINAs) for Pharmaceuticals* (2003);
- *Product Licensing Guidance Document* (2006);
- *Evidence For Quality Of Finished Natural Health Products* (2007);
- *Evidence for Safety and Efficacy of Finished Natural Health Products* (2006).

3.2.3 Pre-Submission Enquiries

The listing of ingredients, data recommendations, and methods in this guidance document is not considered to be exhaustive. Sponsors are advised to contact Health Canada, in writing, if the sponsor wishes to discuss product and/or claim-specific data recommendations, or for applications for products outside the scope of the guidance. Verbal enquiries should be followed-up in writing by the sponsor.

4 DOCUMENTATION

This section outlines the basic data recommended to support all antiseptic product submissions covered in this guidance, including:

- general data for efficacy claims;
- test protocols.

4.1 Common Information for Antiseptic Applications

The following should be included for each drug submission to support efficacy claims and product safety (for any non-Monograph submission):

4.1.1 Efficacy Tests

a) *In vitro* tests:[1]
   - For surrogate and non-surrogate test organisms: one independent[2] test report, which proves the antiseptic activity for a product.

[1] For personal domestic and commercial use products: *In vitro* tests are only recommended for product applications involving fungal and/or viral testing. Note that Health Canada reserves the right to request *in vitro* test results during the course of assessment of other products if such data is determined to be necessary to support an application. Applicants may also choose to voluntarily provide *in vitro* data as secondary supporting evidence to accompany any application.

[2] For the purposes of this guidance, "independent" is defined as a separate legal entity from the market authorization holder. For the purposes of this guidance, all recommended testing should be performed in a laboratory which adheres to Good Laboratory Practices (GLP).

- each test report needs to include only one lot of product;
- the tests are to be done in triplicate to demonstrate reproducibility.

b) *In vivo* tests:
- For non-surrogate test organisms: one independent test report, which proves the antiseptic activity of a product.
- For surrogate test organisms: two[3] independent test reports, which prove the antiseptic activity for a product.
- Each *in vivo* test report should include three separate lots of product.
- Tests should be performed with sufficient subjects[4] per tested product to satisfy the statistical criteria of the clinical trial design.

c) test reports should include at a minimum:
- identification of the standard method used to verify the product efficacy;
- proof of the effectiveness of the neutralizer utilized in the tests for both the reference standard and the test product;
- the relationship of each test to specific area of application;
- the type and level of soil load included in the test along with a rationale;
- the time differential (between application of the test product and the collection of organisms) used in the test and whether the time stated is sufficient to meet the required criteria of specific activity;
- initial number of the test organisms;
- information on the lot number, expiry date, and date of manufacture for each lot tested;
- overview of the statistical plan and assumptions;
- supporting raw data;
- results in tabular form;
- proof of a washout period if a cross-over study is employed, or if a subject is reused;
- proof of glove compatibility for surgical scrub products;
- the minimum inhibitory concentration (MIC) for the product, when available; and
- conclusion, describing whether the product meets the specific criteria relative to the reference method(s) employed.

d) at a minimum, tests must demonstrate that the lower bound of the confidence interval is at the required log reduction; and that a power of 80% and alpha of 5% is used.

e) based on practicality, no product will be accepted if its *in vivo* time-to-effect upon completion of application[5] is greater than 30 seconds (for a leave on product) or 1 minute (for a wash off product)[6].

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[3] In order to meet full validation, surrogate testing should be conducted in independent laboratories located at different sites with different study directors and teams. The laboratories may belong to one single company or organization.

[4] A subject is considered to be a human volunteer. It is not acceptable to interpret a "subject" as a digit on a human hand.

4.1.2 Safety Tests

a) published or unpublished safety data testing local tolerance, such as:
   - irritation and sensitization (in the presence and absence of UV exposure when this is likely to be a risk factor) and preferably conducted in human species;
   - photoallergenicity;
   - photocarcinogenicity, etc.

b) when evidence is not available to show that topically-applied medicinal ingredients are not absorbed systemically to a significant degree, toxicity data should be submitted.

c) safety tests for (a) and (b) should be performed in accordance with relevant internationally-accepted test methods (e.g. OECD, ICH)

4.1.3 Quality Tests

Additional supporting data may be required to support the quality of the finished antiseptic product. The recommended quality data depends on the classification of the proposed product as either a drug or natural health product. Health Canada encourages applicants to verify the quality recommendations with the appropriate Directorate prior to submitting an application.

4.1.4 Additional Data for Professional Food Premise-Use Products

For products that are intended to be used in professional food premises, a duplicate copy of the full submission with the following information should be included:

a) Full disclosure of the chemical formulation of the product. This information should be in the form of a quantitative listing of all ingredients used in its manufacture and in the final product formulation, taking into account that the percentage of the chemical formulation components should add up to 100%. Each ingredient should be identified by its trade name, supplier, and/or proper chemical name and CAS number (if available).

b) Residual data would be requested if necessary: the residual amount of the product that will be found on hands of employees after application of the product and the level that may be expected to be transferred to food products (after precautionary safety approaches were undertaken such as potable water rinse or drainage of excess of product). This information should be in the form of actual analytical data or theoretical estimates based on the proposed use level of the product.

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[5] To be calculated once the product has been fully applied according to the proposed directions for use, and should not include application time.

[6] A supporting scientific and clinically-relevant rationale should be provided if the time-to-effect is longer than recommended.

c) Type of foods that are processed in the plants where this product is proposed to be used at (if known).

During the review sponsors may also be asked to provide the following additional information, pending assessment by the Food Directorate (FD):

i) The worst case Estimated Dietary Intake (EDI) resulting from the use of the product. This should include any information that is used to estimate the dietary exposure such as type of foods, residual levels, etc.; and

ii) Any available data (full reports) on the mammalian oral toxicity of the product.

4.2 Test Protocol Recommendations

a) *In vitro* and *in vivo* studies submitted for review to support the proposed product and/or claim should:
- utilize the specific microorganism(s) for which antimicrobial claims are to be made (or a suitable surrogate thereof when appropriate);
- use the proposed Canadian formulation (including same concentration of active ingredients);[7]
- if a reference standard is not specified in the test method, then the following reference standards should be used:
  - Personal use products: 2-propanol;
  - Professional use products: 1-propanol.
- if the test method requires that a soap and water prewash be used immediately prior to baseline measurements and there are no test organisms added to the skin (that is [i.e.] assessment of volunteer's personal microbial load), the log reduction value for the test product may be shown to be not significantly worse than the reference product.

b) *In vivo* studies submitted for review to support the proposed product and/or claim should also:
- use the proposed Canadian conditions of use recommended in the labelling, including:
  - same pharmaceutical form (e.g. lotion, gel, wipe, etc.);
  - same contact times;
  - volume to be used;
  - directions for use;
  - presence or absence of organic load;
  - surgical scrubs should assess glove compatibility;
  - the determination of infective titre should be performed using a direct method (e.g. plaque assay technique for plaque-forming viruses); and
  - for all products, any other factor/s which may influence the effectiveness of the product.

[7] Health Canada will allow minor variation in formulation without receipt of new data to support product efficacy ***only*** for personal use products when variations are made to the fragrance or colour. Manufacturers should demonstrate product efficacy to Health Canada for all other reformulations as they may affect the product's performance.

4.3 Standard Test Methodologies

The guidance is based on standard European (CEN) and North American (ASTM) test methods and represents current scientific knowledge. The EN and ASTM norms were selected as the basis for the data recommendations because these were deemed to:

- be conducive to determination of a products' efficacy against specific organism claims;
- provide both *in vivo* and *in vitro* test methodology;
- allow for virucidal testing;
- use ATCC identifiable organisms.

Each standard test method specifies the recommendations and criteria the product must comply with in order to support the claims of the specific microbiocidal activity, with the purpose of:

- enabling the manufacturers to select appropriate test methodology to furnish data in support of the claims for the specific use;
- ensuring that the users of the antiseptic products will be able to select the most appropriate product for a specific purpose;
- eliminating methodology bias and objectively comparing product efficacies since the testing is performed under identical conditions.

Claims for antiseptic products include statements of efficacy, persistence, organism-specificity, and category of product (e.g. professional use, commercial use, etc.) Each claim must be supported by evidence in the form of specific tests that have been carried out to demonstrate the efficacy of the product. As test results may be formulation-dependent, it cannot be assumed that the presence of an active ingredient confers equal efficacy across a range of products.

It is recommended that a modular approach be taken to first test the formulation *in vitro*, then proceed to *in vivo* testing if the *in vitro* testing is successful. It is not generally considered acceptable to label a product for effectiveness against certain microorganisms based only on *in vitro* studies as there is not usually a correlation between data generated *in vitro* and effectiveness observed *in vivo*. *In vitro* studies are usually considered only secondary supportive evidence.

For personal domestic and commercial use products, only *in vivo* data need be submitted for assessment except where otherwise specified for fungal and viral testing (see specifics under Common Information for Antiseptic Applications). Ultimately *in vivo* studies should be provided as the primary evidence for claims. For professional use products, both *in vitro* and *in vivo* tests are required to demonstrate efficacy against a broader range of organisms, however the *in vivo* tests will be limited to representative organisms only.

Please note that Phase I test methods have not been included in the guidance. Such data may be submitted with an application; however it is only considered secondary supporting evidence and is not sufficient on its own to support a therapeutic indication.

Step 1: *In vitro* testing

ASTM E 1052-96 Standard Test method for Efficacy of Antimicrobial Agents Against Viruses in Suspension.

EN 13624 Chemical disinfectants and antiseptics. Quantitative suspension test for the evaluation of fungicidal activity of chemical disinfectants for instruments used in the medical area. Test method and requirements (phase 2, step 1)

EN 13727 Chemical disinfectants and antiseptics - Quantitative suspension test for the evaluation of bactericidal activity of chemical disinfectants for instruments used in the medical area - Test method and requirements (phase 2, step 1)

EN 14348 Chemical disinfectants and antiseptics Quantitative suspension test for the evaluation of mycobactericidal activity of chemical disinfectants in the medical area including instrument disinfectants Test methods and requirements (phase 2, step 1)

EN 14476 Chemical disinfectants and antiseptics. Virucidal quantitative suspension test for chemical disinfectants and antiseptics used in human medicine. Test method and requirements (phase 2, step 1)

Step 2*: In vivo* testing on volunteers

EN 1499 Chemical disinfectants and antiseptics. Hygienic handwash. Test method and requirements (phase 2/step 2)

EN 1500 Chemical disinfectants and antiseptics. Hygienic handrub. Test method and requirements (phase 2/step 2)

EN 12791 Chemical disinfectants and antiseptics. Surgical hand disinfection. Test method and requirement (phase 2/step2)

ASTM E 1115-02 Standard Test Method for Evaluation of Surgical Hand Scrub Formulations. USA, 2002.

ASTM E 1173-01e1 Standard Test Method for Evaluation of a Preoperative, Precatheterization, or Preinjection Skin Preparations

ASTM E 1174-06 Standard Test Method for Evaluation of the Effectiveness of Health Care Personnel Handwash Formulations.

ASTM E 2011-09 Standard Test Method for Evaluation of Hygienic Handwash and Handrub Formulations for Virus-Eliminating Activity Using the Entire Hand.

ASTM E 2276-03 Standard Test Method for Determining the Bacteria-Eliminating Effectiveness of Hygienic Handwash and Handrub Agents Using the Fingerpads of Adult Subjects.

ASTM E 2613-08 Standard Test Method for Determining Fungus-Eliminating Effectiveness of Hygienic Handwash and Handrub Agents Using Finger Pads of Adults

Note that the most recent validated test method must be used in case of an update.[8] Alternate test methodologies may also be considered acceptable for an antiseptic product submission application, provided that they are scientifically justified and appropriately validated. The use of alternate approaches should be discussed in advance with Health Canada to ensure that the proposed methodology will generate the required data. In such a case, a presubmission meeting is highly recommended.

4.4 Test Organisms

The test organisms recommended for personal domestic and commercial use products are based on the selected test methods. The test organisms recommended for professional use food premise and healthcare products were selected because these were determined to be common organisms of concern in these environments, including those that are recognized to contribute to nosocomial infections. Surgical use products - including patient preoperative skin preparations - are not required to demonstrate efficacy against mycobacteria and viruses as currently only bacteria and fungi are recognized as frequent causative agents of surgical site infections.

4.5 Label Recommendations

The general recommendations for labelling of drug products are outlined in the *Food and Drugs Act* as well as the *Food and Drug Regulations* and *Natural Health Products Regulations.*

4.5.1 For all labels

Labels which include the authorized claims should also describe the intended area of application and specific attributes of the product, such as: bactericidal, fungicidal, mycobactericidal or virucidal. The label should also clearly reflect the same conditions of use employed in the tests used to demonstrate efficacy (e.g. directions for use, warnings, etc.).

Products may carry more than one indication or claim, as long as each has been authorized by Health Canada. In such an instance, the label must include the full warnings and adequate directions for use for each indication, should these differ.

If surrogates were used in testing this should be stated on the labels (e.g. “murine norovirus used as a surrogate for human norovirus”) in order to ensure transparency and clarity for the end user.

[8] Products authorized using an older test method must ensure that they still meet the method if it is updated.

Note: dispensing units are also considered labels when they contain a drug product, and should be labelled in accordance with regulatory requirements.

See category-specific sections for detailed labelling recommendations.

5 PERSONAL USE PRODUCTS

5.1 Scope

Personal use products are those self-selected for use by an individual in a domestic setting. The majority of personal use products are subject to the Antiseptic Skin Cleanser Monograph. This Human-Use Antiseptic Drugs guidance document applies only to those personal use products which do not meet the scope of the Monograph. All personal use products are expected to demonstrate efficacy against bacteria and fungi at a minimum (whether through the Monograph stream or outside), but such data is maintained on file with the sponsor unless additional claims are made (e.g. log reduction) or the product contains a new active ingredient or new combination of active ingredients. Claims for mycobacteria and/or viruses are considered to require additional supporting data.

5.2 Test recommendations

For personal domestic use products, only *in vivo* data need be submitted for assessment except where otherwise specified for fungal and viral testing (see specifics under Common Information for Antiseptic Applications).

5.2.1 In Vitro

Table 1:

Claim*		***In vitro* Test**		**Minimum Acceptable Log Reduction**	**Organisms**	**Code**
		CEN‡	**ASTM‡**			
Antimycobacterial	Mycobacteria	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable
Antiviral/Kills viruses	Viruses [a]	EN 14476	E 1052	4	Polio virus type 1 - SabinMahoney - Pette strain	VR-1562
					Adenovirus (Human Type 2)	VR-2
					Herpes simplex Type I	VR-733
Log or % Reduction	Bacteria	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable
	Mycobacteria	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable
	Fungi	EN 13624	Not applicable	4	*Candida albicans*	ATCC 10231

					Aspergillus niger	ATCC 16404
	Viruses [a]	EN 14476	E 1052	4	Polio virus type 1 - SabinMahoney - Pette strain	VR-1562
					Adenovirus (Human Type 2)	VR-2
					Herpes simplex Type I	VR-733
New active ingredient/new combination of active ingredients[b]	Bacteria	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable
	Fungi	EN 13624	N/A	4	*Candida albicans*	ATCC 10231
					Aspergillus niger	ATCC 16404
Organism Specific[c]	Bacteria	Same as for Log Reduction claims			Organisms highlighted on labelling: see 5.2.3.	
	Mycobacteria					
	Fungi					
	Viruses [a]					
Persistence[d]	Bacteria	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable

***** Premarket assessment of supporting data is required for the personal use categories only if these claims are made for the product (e.g. claims not covered by a Monograph).

[t] Either the CEN or ASTM test method are acceptable for testing when both are listed. Organisms listed in the table are to be used in either case.

[a] The Polio virus has been chosen as representative of virucidal activity as it is the most difficult to eradicate. A product with demonstrated activity against the recommended virus would most likely be effective against enveloped viruses as well. Should a sponsor wish to make claims **only** against specific enveloped viruses for personal domestic or personal commercial-use products, then sufficient testing against and labelling of this virus would be considered as an organisms-specific data submission.

[b] If claims are made for mycobacteria and/or viruses additional organism testing as outlined in the Log Reduction section would also be required. Note that for pharmaceutical drugs additional data may be necessary to meet New Drug requirements (Division 8 of the *Food and Drug Regulations*).

[c] The test methods may need to be adapted and a rationale provided dependent on the organism selected by the sponsor.

[d] Persistence claims can only be made relative to bacteria. Should a sponsor wish to make persistence claims against other organisms, a presubmission meeting with a strong supporting scientific rationale outlining an appropriate test method would be necessary.

5.2.2 In Vivo

Table 2:

Claim*		***In vivo* Test**		**Minimum Acceptable Log Reduction†**	**Organisms**	**Code**
		CEN‡	**ASTM‡**			
Antimycobacterial	Mycobacteria	Wash: EN 1499 Rub: EN 1500	E 2276	2	*Mycobacterium terrae*	ATCC 15755
					Mycobacterium avium	ATCC 15769
Antiviral/Kills viruses	Viruses [a]	Not applicable	E 2011	2	Human Rotavirus Wa	VR-2018
					Rhinovirus Type 37 **or** 14	VR-I 147 **or** VR-284
					Hepatitis A	VR-1402
					Murine norovirus[a]	
					Adenovirus (Human Type 5)	VR-1516
Log or % Reduction	Bacteria	Wash: EN 1499 Rub: EN 1500	E 2276	2	*Serratia marcesens*	ATCC 14756
					Escherichia coli K 12	NCTC 10538
					Staphylococcus aureus	ATCC 6538
					Staphylococcus. epidermidis	ATCC 14990
	Mycobacteria	Wash: EN 1499 Rub: EN 1500	E 2276	2	*Mycobacterium terrae*	ATCC 15755
					Mycobacterium avium	ATCC 15769
	Fungi	Not applicable	E 2613	2	*Candida albicans*	ATCC 10231
					Aspergillus niger	ATCC 16404
	Viruses [b]	Not applicable	E 2011	2	Human Rotavirus Wa	VR-2018
					Rhinovirus Type 37 **or** 14	VR-I 147 **or** VR-284
					Hepatitis A	VR-1402
					Murine norovirus[a]	
					Adenovirus (Human Type 5)	VR-1516

New active ingredient/new combination of active ingredients[c]	Bacteria	Wash: EN 1499 Rub: EN 1500	E 2276	2	*Serratia marcesens*	ATCC 14756
					Escherichia coli K 12	NCTC 10538
					Staphylococcus aureus	ATCC 6538
					Staphylococcus. epidermidis	ATCC 14990
	Fungi	Not applicable	E 2613	2	*Candida albicans*	ATCC 10231
					Aspergillus niger	ATCC 16404
Organism Specific[d]	Bacteria Mycobacteria Fungi Viruses[b]	Same as for Log Reduction claims			Organisms highlighted on labelling: see 6.2.3.	
Persistence[e]	Bacteria	EN 12791	E 1115	CEN: Not significantly worse than the reference product ASTM: 3	Test performed against volunteer's resident organisms	

***** Premarket assessment of supporting data is required for the personal use categories only if these claims are made for the product (e.g. claims not covered by a Monograph).

[†] If the reference product demonstrates higher results, then the proposed product must demonstrate the minimum log reduction or not significantly worse than the reference product.

[t] Either the CEN or ASTM test method are acceptable for testing when both are listed. Organisms listed in the table are to be used in either case.

[a] Note that based on current scientific understanding, Health Canada prefers the use of murine norovirus as a surrogate for human norovirus pending further scientific innovation in this area. Sponsors are discouraged from using the less similar organism feline calcivirus as a representative organism.

[b] The Polio virus has been chosen as representative of virucidal activity as it is the most difficult to eradicate. A product with demonstrated activity against the recommended virus would most likely be effective against enveloped viruses as well. Should a sponsor wish to **only** make claims against specific enveloped viruses for personal domestic or personal commercial-use products, then sufficient testing against and labelling of this virus would be considered as an organisms-specific data submission.

[c] If claims are made for mycobacteria and/or viruses additional organism testing as outlined in the Log Reduction section would also be required. Note that for pharmaceutical drugs additional data may be necessary to meet New Drug requirements (Division 8 of the *Food and Drug Regulations*).

[d] The test methods may need to be adapted and a rationale provided dependent on the organism selected by the sponsor.

[e] Persistence claims can only be made relative to bacteria. Should a sponsor wish to make persistence claims against other organisms, a presubmission meeting with a strong supporting scientific rationale outlining an appropriate test method would be necessary.

5.2.3 Organism-Specific Claims

The following organisms are recognized as potentially appropriate to be labelled on personal use products, and this list is intended as a reference only for the ATCC/NCTC codes only. The presence in this table does not convey automatic acceptance of the suitability of a highlighted organism for any given product. A rationale and supporting clinical data for highlighting a specific organism is required.

Table 3:

Type	**Organism**	**Code**
Bacteria	*Staphylococcus aureus*	ATCC 6538/ATCC 29213
	Enterococcus faecium	ATCC 6057
	Enterococcus hirae	ATCC 10541
	Escherichia coli K 12	NCTC 10538
	Proteus mirabilis	ATCC 14153
	Pseudomonas aeruginosa	ATCC 15442/ATCC 27583
Fungi/Yeast	*Candida albicans*	ATCC 10231
	Aspergillus niger	ATCC 16404
Mycobacteria	*Mycobacterium terrae*	ATCC 15755
	Mycobacterium avium	ATCC 15769
Viruses[a]	Hepatitis B virus - surrogate Duck Hepatitis B virus (DHBV)	
	Hepatitis A virus	VR-1402
	Hepatitis C virus - surrogate Bovine Viral Diarrhea virus (BVDV)	
	Herpes simplex virus type 1	
	Herpes simplex virus type 2	
	Human adenovirus type 4	
	Norovirus - surrogate Murine Norovirus (MNV) [b]	
	Polio virus type 1 - SabinMahoney -Pette strain	VR-1562
	Respiratory syncytial virus	
	Rotavirus	
	Rhinovirus	
	Papovavirus SV 40	
	Influenza A virus	
	Influenza B virus	

[a] The list of the viruses is not exhaustive and other viruses can be considered for testing when necessary. Consideration must be given to careful selection of the viruses which represent the intended area of application. When a corresponding claim is sought, the *in vivo* ASTM E 2011 test performed under practical conditions should utilize surrogate markers such as DHBVuck Hepatitis B virus , BVDV, Murine Norovirus or Poliovirus type 1 virus Sabin Mahoney-Pette strain due to the lack of infectivity or because of immunity due to vaccination (Poliovirus 1 type 1).

[b] Note that based on current scientific understanding, Health Canada prefers the use of murine norovirus as a surrogate for human norovirus pending further scientific innovation in this area. Sponsors are discouraged from using the less similar organism feline calcivirus as a representative organism.

5.3 Indications

5.3.1 Highlighting Specific Organisms for Personal Domestic Use Product

If it has been successfully determined that the proposed formulation is effective against an organism using the recommended test methods, that organism may be named on the labels. A generalized claim that a product is bactericidal/fungicidal/virucidal etc. (or likewise "antibacterial…") cannot be determined by one organism alone nor can this representative class be considered authorization to highlight any other untested or specific organism.

Health Canada reserves the right to determine when an organism-specific claim would likely result in the product being used for professional purposes, for example when claiming for organisms identified to be of high risk in healthcare settings (e.g. severe acute respiratory syndrome (SARS), methicillin-resistant staphylococcus aureus (MRSA), H1N1, etc). In such instances, the sponsor will be expected to meet the recommendations for professional use products. Sponsors are encouraged to verify the applicability of organism-specific claims for personal use products prior to testing and/or submitting an application.

5.3.2 Log or % Reduction Claims

Personal domestic use products claiming log or % reduction values (e.g. kills 99.9% of bacteria) are required to submit data to support the claim for the specific formulation and using the recommended test methods. General log reduction claims need only demonstrate efficacy against bacteria and fungi unless claims are also made against mycobacteria and/or viruses.

5.3.3 Persistence Claims

Persistence is defined as a claim that the product will deliver a longer action than only the immediate reduction of microorganisms on hands (see Definitions). Persistence claims for personal use products can only be made relative to bacteria. Should a sponsor wish to make persistence claims against other organisms, a presubmission meeting with a strong supporting scientific rationale outlining an appropriate test method would be necessary.

5.3.4 Time Kill Claims

Antiseptic products are expected to have a minimum time-to-effect of 30 seconds (for waterless handrubs) to 1 minute (for washes or scrubs using water) upon completion of application according to the proposed directions for use. As this is considered the norm for antiseptics, a claim that a product is fast-acting would have to demonstrate both a significantly shorter time-to-effect and still maintain clinical relevance, and should use the test methods outlined for log reduction testing (organisms dependent on indications, with bacteria/fungi as a minimum).

5.3.5 Sterile

Any pharmaceutical product claiming sterility of any component of an antiseptic product must also undergo a chemistry and manufacturing review. Sponsors are recommended to consult the Health Canada guidance document on supporting data requirements for sterility claims: *Stability Testing of Existing Drug Substances and Products* and *Quality Guidance: Applications for Drug Identification Numbers (DINAs) for Pharmaceuticals*.

A product license application for a non-traditional natural health antiseptic product includes a chemistry and manufacturing review portion for all products, including those claiming sterility.

5.4 Labelling

Labelling for personal/domestic use products is restricted to that permitted in the Antiseptic Skin Cleanser Monograph, except where data has been reviewed resulting in Health Canada authorization of altered or additional claims.

6 COMMERCIAL USE PRODUCTS

6.1 Scope

Personal commercial use products are those made available to the general public for occasional use and are intended to reduce transient organisms on the skin in a commercial or institutional setting. This includes, but may not be limited to, antiseptic products dispensed in washrooms in public buildings (such as daycares and schools) or used in workplaces other than healthcare or food-handling premises These products are commonly used to reduce transient organisms on hands, including those organisms that may not necessarily be encountered in a domestic setting. They are intended to provide a superficial and non-persistent cleaning effect to reduce microbial load on hands to either augment the effect of soap and water cleaning or for use when soap and water are not available.

Personal commercial use products do not include those intended to be used by professionals or in healthcare facilities and food processing plants.

Personal commercial products making general statements such as those outlined in the Monograph for *Antiseptic Skin Cleansers* are not considered Monograph applications as the directions for use are inappropriate; however, they may be filed as a DINA (form) for pharmaceuticals or as a non-compendial application for natural health products. **No additional supporting clinical data need be filed if the claims, ingredients, and concentrations are the same as those found in the Monograph for *Antiseptic Skin Cleansers*.**

All personal use products are expected to demonstrate efficacy against bacteria and fungi at a minimum (whether through the Monograph stream or outside) but such data is maintained on file with the sponsor unless additional claims are made (e.g. log reduction) or the product contains a new active ingredient or new combination of active ingredients. Claims for mycobacteria and/or viruses are considered to require additional supporting data.

This guidance outlines the data recommendations for supporting an application for personal commercial use wherein claims are made against a specific organism, antiviral claims, or those relating to persistence, sterility, and/or % or log-reduction.

6.2 Test recommendations

For personal commercial use products, only *in vivo* data need be submitted for assessment except where otherwise specified for fungal and viral testing.

6.2.1 In Vitro

Table 4:

Claim*		***In vitro* Test**		**Minimum Acceptable Log Reduction**	**Organisms**	**Code**
		CEN‡	**ASTM‡**			
Antimycobacterial	Mycobacteria	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable
Antiviral/Kills viruses	Viruses [a]	EN 14476	E 1052	4	Polio virus type 1 - SabinMahoney - Pette strain	VR-1562
					Adenovirus (Human Type 2)	VR-2
					Herpes simplex Type I	VR-733
Log and % Reduction	Bacteria	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable
	Mycobacteria	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable
	Fungi	EN 13624	Not applicable	4	*Candida albicans*	ATCC 10231
					Aspergillus niger	ATCC 16404
	Viruses [a]	EN 14476	E 1052	4	Polio virus type 1 - SabinMahoney - Pette strain	VR-1562
					Adenovirus (Human Type 2)	VR-2
					Herpes simplex Type I	VR-733

New active ingredient/new combination of active ingredients[b]	Bacteria	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable
	Fungi	EN 13624	Not applicable	4	*Candida albicans*	ATCC 10231
					Aspergillus niger	ATCC 16404
Organism Specific[c]	Bacteria	Same as for Log Reduction claims			Organisms highlighted on labelling: see 6.2.3.	
	Mycobacteria					
	Fungi					
	Viruses [a]					
Persistence[d]	Bacteria	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable

* Premarket assessment of supporting data is required for the personal use categories only if these claims are made for the product (e.g. claims not covered by a Monograph).

[t] Either the CEN or ASTM test method are acceptable for testing when both are listed. Organisms listed in the table are to be used in either case.

[a] The Polio virus has been chosen as representative of virucidal activity as it is the most difficult to eradicate. A product with demonstrated activity against the recommended virus would most likely be effective against enveloped viruses as well. Should a sponsor wish to make claims **only** against specific enveloped viruses for personal domestic or personal commercial-use products, then sufficient testing against and labelling of this virus would be considered as an organisms-specific data submission.

[b] If claims are made for mycobacteria and/or viruses additional organism testing as outlined in the Log Reduction section would also be required. Note that for pharmaceutical drugs additional data may be necessary to meet New Drug requirements (Division 8 of the *Food and Drug Regulations*).

[c] The test methods may need to be adapted and a rationale provided dependent on the organism selected by the sponsor.

[d] Persistence claims can only be made relative to bacteria. Should a sponsor wish to make persistence claims against other organisms, a presubmission meeting with a strong supporting scientific rationale outlining an appropriate test method would be necessary.

6.2.2 In Vivo

Table 5:

Claim*		***In vivo* Test**		**Minimum Acceptable Log Reduction[†]**	**Organisms**	**Code**
		CEN[‡]	**ASTM[‡]**			
Antimycobacterial	Mycobacteria	Wash: EN 1499 Rub: EN 1500	E 2276	2	*Mycobacterium terrae*	ATCC 15755
					Mycobacterium avium	ATCC 15769
Antiviral/Kills viruses	Viruses [a]	Not applicable	E 2011	2	Human Rotavirus Wa	VR-2018
					Rhinovirus Type 37 **or** 14	VR-I 147 **or** VR-284

					Hepatitis A	VR-1402
					Murine norovirus[a]	
					Adenovirus (Human Type 5)	VR-1516
Log and % Reduction	Bacteria	Wash: EN 1499 Rub: EN 1500	E 2276	2	*Serratia marcesens*	ATCC 14756
					Escherichia coli K 12	NCTC 10538
					Staphylococcus aureus	ATCC 6538
					Staphylococcus. epidermidis	ATCC 14990
	Mycobacteria	Wash: EN 1499 Rub: EN 1500	E 2276	2	*Mycobacterium terrae*	ATCC 15755
					Mycobacterium avium	ATCC 15769
	Fungi	Not applicable	E 2613	2	*Candida albicans*	ATCC 10231
					Aspergillus niger	ATCC 16404
	Viruses[b]	Not applicable	E 2011	2	Human Rotavirus Wa	VR-2018
					Rhinovirus Type 37 **or** 14	VR-I 147 **or** VR-284
					Hepatitis A	VR-1402
					Murine norovirus[a]	
					Adenovirus (Human Type 5)	VR-1516
New active ingredient/new combination of active ingredients[c]	Bacteria	Wash: EN 1499 Rub: EN 1500	E 2276	2	*Serratia marcesens*	ATCC 14756
					Escherichia coli K 12	NCTC 10538
					Staphylococcus aureus	ATCC 6538
					Staphylococcus. epidermidis	ATCC 14990
	Fungi	Not applicable	E 2613	2	*Candida albicans*	ATCC 10231
					Aspergillus niger	ATCC 16404
Organism Specific[c]	Bacteria/ Mycobacteria	Same as for Log Reduction claims			Organisms highlighted on labelling: see 7.2.3.	
	Fungi					
	Viruses[b]					

Persistence[d]	Bacteria	EN 12791	E 1115	CEN: Not significantly worse than the reference product ASTM: 3	Test performed against volunteer's resident organisms

* Premarket assessment of supporting data is required for the personal use categories only if these claims are made for the product (e.g. claims not covered by a Monograph).
[†] If the reference product demonstrates higher results, then the proposed product must demonstrate the minimum log reduction or not significantly worse than the reference product.
[t] Either the CEN or ASTM test method are acceptable for testing when both are listed. Organisms listed in the table are to be used in either case.
[a] Note that based on current scientific understanding, Health Canada prefers the use of murine norovirus as a surrogate for human norovirus pending further scientific innovation in this area. Sponsors are discouraged from using the less similar organism feline calcivirus as a representative organism.
[b] The Polio virus has been chosen as representative of virucidal activity as it is the most difficult to eradicate. A product with demonstrated activity against the recommended virus would most likely be effective against enveloped viruses as well. Should a sponsor wish to make claims **only** against specific enveloped viruses for personal domestic or personal commercial-use products, then sufficient testing against and labelling of this virus would be considered as an organisms-specific data submission.
[c] If claims are made for mycobacteria and/or viruses additional organism testing as outlined in the Log Reduction section would also be required. Note that for pharmaceutical drugs additional data may be necessary to meet New Drug requirements (Division 8 of the *Food and Drug Regulations*).
[d] The test methods may need to be adapted and a rationale provided dependent on the organism selected by the sponsor.
[e] Persistence claims can only be made relative to bacteria. Should a sponsor wish to make persistence claims against other organisms, a presubmission meeting with a strong supporting scientific rationale outlining an appropriate test method would be necessary.

6.2.3 Organism-Specific Claims

The following organisms are recognized as potentially appropriate to be labelled on personal use products, and this list is intended as a reference only for the ATCC/NCTC codes only. The presence in this table does not convey automatic acceptance of the suitability of a highlighted organism for any given product. A rationale and supporting clinical data for highlighting a specific organism is required.
Table 6:

Type	**Organism**	**Code**
Bacteria	*Staphylococcus aureus*	ATCC 6538/ATCC 29213
	Enterococcus faeciu	ATCC 6057
	Enterococcus hirae	ATCC 10541
	Escherichia coli K 12	NCTC 10538
	Proteus mirabilis	ATCC 14153
	Pseudomonas aeruginos	ATCC 15442/ATCC 27583
Fungi/Yeast	*Candida albicans*	ATCC 10231
	Aspergillus niger	ATCC 16404
Mycobacteria	*Mycobacterium terrae*	ATCC 15755
	Mycobacterium avium	ATCC 15769
Viruses[a]	Hepatitis B virus - surrogate Duck Hepatitis B virus (DHBV)	VR-1402
	Hepatitis A virus	
	Hepatitis C virus - surrogate	

	Bovine Viral Diarrhea virus (BVDV)	VR-1562
	Herpes simplex virus type 1	
	Herpes simplex virus type 2	
	Human adenovirus type 4	
	Norovirus - surrogate Murine Norovirus (MNV)[b]	
	Polio virus type 1 - SabinMahoney -Pette strain	
	Respiratory syncytial virus	
	Rotavirus	
	Rhinovirus	
	Papovavirus SV 40	
	Influenza A virus	
	Influenza B virus	

[a] The list of the viruses is not exhaustive and other viruses can be considered for testing when necessary. Consideration must be given to careful selection of the viruses which represent the intended area of application. When a corresponding claim is sought, the in vivo ASTM E 2011 test performed under practical conditions should utilize surrogate markers such as DHBVuck Hepatitis B virus , BVDV, Murine Norovirus or Poliovirus type 1 virus Sabin Mahoney-Pette strain due to the lack of infectivity or because of immunity due to vaccination (Poliovirus 1 type 1).

[b] Note that based on current scientific understanding, Health Canada prefers the use of murine norovirus as a surrogate for human norovirus pending further scientific innovation in this area. Sponsors are discouraged from using the less similar organism feline calcivirus as a representative organism.

6.3 Indications

6.3.1 Highlighting Specific Organisms for Personal Commercial Use Product

If it has been successfully determined that the proposed formulation is effective against an organism using the recommended test methods, that organism may be named on the labels. A generalized claim that a product is bactericidal/fungicidal/virucidal etc. (or likewise "antibacterial…") cannot be determined by one organism alone nor can this representative class be considered authorization to highlight any other untested or specific organism.

Health Canada reserves the right to determine when an organism-specific claim would likely result in the product being used for professional purposes, for example when claiming for organisms identified to be of high risk in healthcare settings (e.g. severe acute respiratory syndrome (SARS), methicillin-resistant staphylococcus aureus (MRSA), H1N1, etc). In such instances, the sponsor will be expected to meet the recommendations for professional use products. Sponsors are encouraged to verify the applicability of organism-specific claims for personal use products prior to testing and/or submitting an application.

6.3.2 Log and % Reduction Claims

Personal use products claiming log reduction values (e.g. kills 99.9% of bacteria) are required to submit data to support the claim for the specific formulation and using the

recommended test methods. General log reduction claims need only demonstrate efficacy against bacteria and fungi unless claims are also made against mycobacteria and/or viruses.

6.3.3 Persistence Claims

Persistence is defined as a claim that the product will deliver a longer action than only the immediate reduction of microorganisms on hands (see Definitions). Persistence claims for personal use products can only be made relative to bacteria. Should a sponsor wish to make persistence claims against other organisms, a presubmission meeting with a strong supporting scientific rationale outlining an appropriate test method would be necessary.

6.3.4 Time Kill Claims

Antiseptic products are expected to have a minimum time-to-effect of 30 seconds (for waterless handrubs) to 1 minute (for washes or scrubs using water) upon completion of application according to the proposed directions for use. As this is considered the norm for antiseptics, a claim that a product is fast-acting would have to demonstrate both a significantly shorter time-to-effect and still maintain clinical relevance, and should use the test methods outlined for log reduction testing (organisms dependent on indications, with bacteria/fungi as a minimum).

6.3.5 Sterile

Any pharmaceutical product claiming sterility of any component of an antiseptic product must also undergo a chemistry and manufacturing review. Sponsors are recommended to consult the Health Canada guidance document on supporting data requirements for sterility claims: *Stability Testing of Existing Drug Substances and Products* and *Quality Guidance: Applications for Drug Identification Numbers (DINAs) for Pharmaceuticals*.

A product license application for a non-traditional natural health antiseptic product includes a chemistry and manufacturing review portion for all products, including those claiming sterility.

6.4 Labelling

All products intended for use in a commercial setting should be labelled “For commercial use” on the front panel of the inner and outer labels, and may only use an acceptable indication from the list outlined in the Monograph for *Antiseptic Skin Cleansers* unless data is submitted to support additional claims. Further, the inner and outer labels shall also carry the following warning statements and directions for use, clearly identified with appropriate headings:

- For external use only. Do not ingest.
- Avoid contact with the eyes.
- Discontinue use and consult a health care practitioner if irritation and redness develops.
- Keep out of reach of children.

- (For handwash): Use XmL and lather in hands with water for at least 30 seconds. Rinse well.[a]
- (For handrub): Use XmL and rub thoroughly into hands for at least 30 seconds. Allow to dry.[a]

[a] Where "XmL" is equivalent to the dose required to achieve effect, as measured in *in vivo* efficacy trials.

7 PROFESSIONAL FOOD HANDLER USE PRODUCTS

7.1 Scope

Products for professional food premises are those which are indicated for use by food handlers and are used frequently to reduce transient organisms on the skin in a commercial or institutional setting including food processing plants, restaurants, retail supermarkets, and fast food outlets. The intent of such products is to both protect food handlers as well as to reduce the likelihood of transmission of disease through food.

This guidance provides information regarding the data necessary for Health Canada to conduct a premarket evaluation prior to the authorization of these products for sale in Canada. A product indicated for use by food handlers should be safe and effective when applied (and frequently reapplied) to human skin. When applied to bare hands that will come into direct contact with food, the product's chemical composition is not to be detrimental or transfer residue to the food, when the product is used or stored in a food processing facility, where food is prepared, packed or stored. To this end, the FD will be consulted by NHPD or TPD to carry out the premarket safety assessment of an antiseptic product for use in food processing facilities.

There are additional considerations for federally-registered food establishments. The CFIA requires a further assessment of the acceptability for use in establishments operating under the authority of the Agency prior to marketing the product. FD and the CFIA require full disclosure of product's chemical composition listing its ingredients by percentage or quantitatively and a product label, with specific directions for use in a food plant. The premarket review directorates of Health Canada will be responsible for this assessment, and will inform FD and the CFIA of when a product has been authorized for use in food premises. Further information regarding the *Reference Listing of Accepted Construction Materials, Packaging Materials, and Non-Food Chemical Products* is available at the CFIA Web site (http://www.inspection.gc.ca/english/fssa/reference/refere.shtml)

7.2 Test recommendations

For professional use products, both *in vitro* and *in vivo* tests are required to demonstrate efficacy against a broader range of organisms, however the *in vivo* tests will be limited to representative organisms only unless a specific organism is highlighted. Products intended for use by food handlers should also demonstrate efficacy in the presence of organic soil such as food ingredients and fats, in order to adequately represent likely conditions of use. Additional consideration must be given to the proposed product formulation, as these must be appropriate for use in food premises. Given the acknowledged potential for spread of enteric viruses, products for use by food handlers should also demonstrate efficacy against viruses in addition to other

microorganisms. All *in vivo* tests should demonstrate a minimum log reduction in microorganisms.

Products for use in professional food premises should also include the additional data for assessment outlined in Section 4.1.4.

Professional-use antiseptic hand rubs and hand washes for use in food premises should have supporting data demonstrating efficacy against all of the following organisms in using the recommended test methods.

7.2.1 In Vitro

Table 7:

Claim		***In vitro* Test**		**Minimum Acceptable Log Reduction**	**Organisms**	**Code**
		CEN‡	**ASTM‡**			
Food Premise Use [a]	Bacteria	EN 13727*	Not applicable	5	*Campylobacter jejuni*	
					Enterococcus faecium	ATCC 6057
					Enterococcus hirae	ATCC 10541
					Escherichia coli	ATCC 11229
					Escherichia coli O157:H7	
					Listeria monocytogenes	ATCC 43256
					Pseudomonas aeruginosa	ATCC 15442
					Salmonella spp	Typhimurium code ATCC 14025
					Shigella spp	Sonnei code ATCC 25931 and Flexneri code ATCC12022
					Staphylococcus aureus	ATCC 6538
					Yersinia enterocolitica	ATCC 55075
	Mycobacteria	EN 14348	Not applicable	5	*Mycobacterium terrae*	ATCC 15755
					Mycobacterium avium	ATCC 15769
	Fungi	EN 13624	Not applicable	4	*Candida albicans*	ATCC 10231
					Aspergillus niger	ATCC 16404