Health Canada Santé Canada

GUIDANCE DOCUMENT
Disinfectant Drugs (2018)

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Health Canada is responsible for helping Canadians maintain and improve their health. It ensures that high-quality health services are accessible, and works to reduce health risks.

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Ligne directrice – Désinfectants assimilés aux drogues

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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.

Document Revision History

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Version	Location of Change	Change Made	Effective Date
1	Not applicable	Initial Issuance of Guidance	2014/01
2	Some revisions throughout document	Removal of references to contact lens disinfectants, and high-level disinfectants and sterilants for use on reusable semi-critical and critical medical devices	2018/01

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INTRODUCTION

Most chemical products represented for use in Canada as disinfectants on environmental surfaces and inanimate objects, or represented for use to reprocess non-critical medical devices are regulated as drugs under the *Food and Drugs Act,* due to either their uses in mitigating or preventing the transmission of human or animal disease, or due to their uses in premises where food is manufactured, prepared or kept. The Natural and Non-prescription Health Products Directorate is the regulatory body within Health Canada[1] that assesses applications for products that are represented for use as:

- disinfectants for use on non-critical medical devices and hard non-porous environmental surfaces and inanimate objects in domestic, industrial/institutional, hospital, food processing and/or barn premises, referred to as "hard surface disinfectants", and that additionally may indicate hard non-porous food and non-food contact surface sanitizer claims on their labelling, in which case they are referred to as "disinfectant-sanitizers".

This guidance document provides an overview of the regulation of disinfectant drugs in Canada, outlines the general information considered necessary to support their safety, efficacy and quality, and sets out the labelling requirements for these products as per the *Food and Drugs Act* and *Regulations*.

Specific safety and efficacy requirements for hard surface disinfectants are addressed in a separate guidance document:

- Safety and Efficacy Requirements for Hard Surface Disinfectant Drugs (2014)

An overview of the application streams applicable to disinfectant drugs is available in the following guidance document:

- Management of Disinfectant Drug Applications (2018)

1.1 Policy Objectives

The objective of this guidance document is to provide disinfectant drug applicants the necessary information to comply with the *Food and Drugs Act* and *Regulations.*

1.2 Policy Statements

Applicants must provide Health Canada with sufficient information to support the safety, efficacy and quality of a disinfectant drug when used in accordance with the label's recommended conditions of use before market authorization can be granted.

[1] As of July 1, 2013, the review of over-the-counter drugs and disinfectant drugs applications transferred from the Therapeutic Products Directorate to the Natural and Non-prescription Health Products Directorate.

Health Canada must evaluate this information and determine whether a drug identification number (DIN) should be issued.

1.3 Scope and Application

This guidance document applies to products regulated as drugs under the *Food and Drugs Act* and *Regulations* that are represented for use as:

- disinfectants for use on non-critical medical devices and hard non-porous environmental surfaces and inanimate objects in domestic, industrial/institutional, hospital, food processing and/or barn premises, referred to as "hard surface disinfectants", and that additionally may indicate hard non-porous food and non-food contact surface sanitizer claims on their labelling, in which case they are referred to as "disinfectant-sanitizers".

All disinfectant drug applications must support the general safety, efficacy, and quality requirements outlined in this guidance document, except where otherwise noted, as well as the labelling requirements set out by the *Food and Drugs Act* and *Regulations*. In addition, applications must meet the specific safety and efficacy requirements outlined in the guidance document:

- Safety and Efficacy Requirements for Hard Surface Disinfectant Drugs (2014)

An overview of the application streams applicable to disinfectant drugs, information regarding the regulatory frameworks for chemical products intended for use on environmental surfaces and inanimate objects (e.g., cleaners, sanitizers and disinfectants), and the associated contact information for the responsible regulatory bodies is available in the following guidance document:

- Management of Disinfectant Drug Applications (2018)

1.4 Background

In Canada, chemical products represented for use on environmental surfaces and inanimate objects (e.g., cleaners, sanitizers and disinfectants) are regulated according to their represented use or purpose, and not based on their chemical compositions (i.e., the presence or concentration of a recognized antimicrobial active ingredient as part of a product's formulation does not dictate how it is regulated). As a result, these products may be regulated under a number of different frameworks.

In general, two key factors determine which regulatory framework is applicable to a product:

1. the intended use as represented by the expressed or implied claims on its label; and
2. the type of surface or object to which it is intended to be applied.

Therefore, a chemical product claiming antimicrobial activity on its label could be regulated as a sanitizer or disinfectant, depending on the expressed or implied level of antimicrobial activity, whereas if the same chemical product did not make an expressed antimicrobial claim on its label it would be regulated as a cleaner.

Most chemical products represented for use in Canada as disinfectants on environmental surfaces and inanimate objects, or represented for use to reprocess non-critical medical devices are regulated by Health Canada as drugs under the *Food and Drugs Act* and *Regulations.* Disinfectant drugs require a pre-market assessment and assignment of a drug identification number (DIN) prior to being sold in Canada.

As part of the pre-market assessment for disinfectant drugs, the efficacy, safety and quality of the product may be evaluated, and as a condition of market authorization applicants are required to submit draft labelling which complies with the *Food and Drugs Act* and *Regulations.* For a DIN to be issued for a disinfectant regulated as a drug, the product must be established by the Natural Health Products Directorate to be safe and effective for its intended use. The extent of the pre-market assessment is based on the relative risk associated with the use of the product, which varies depending on the knowledge of the active ingredients and the intended use of the product.

1.4.1 Definitions

Antimicrobial agent: Defined in section C.01A.001 of the *Food and Drug Regulations* as:

> *a drug that is capable of destroying pathogenic micro-organisms and that is labelled as being for use in the disinfection of environmental surfaces or medical devices, as defined by the Medical Devices Regulations, that*
> *(a) are not invasive devices as defined in those Regulations; and*
> *(b) that are intended to come into contact with intact skin only*.

Bactericide: A substance, or mixture of substances, capable of destroying vegetative bacteria, but not necessarily bacterial spores or mycobacteria, present on environmental surfaces and inanimate objects. Disinfectants with efficacy at a minimum against vegetative bacteria can be registered as limited disinfectants, general disinfectants or hospital disinfectants.

Bacteriostat: A substance, or mixture of substances, that inhibits the growth of vegetative bacteria on environmental surfaces and inanimate objects.

Biofilm: A dynamic accumulated mass of bacteria and extracellular material that is tightly adhered to a surface and cannot be easily removed, and which may protect bacteria within from being destroyed by disinfectants.

Broad-spectrum virucide: A substance, or mixture of substances, capable of destroying or irreversibly inactivating at a minimum one representative hard to kill non-enveloped virus, and

which is expected to inactivate other enveloped and non-enveloped viruses present on environmental surfaces and inanimate objects.

Cleaner: A substance, or mixture of substances, that physically removes foreign material (e.g., soil, inorganic and organic material) from environmental surfaces and inanimate objects due to the detergent or enzymatic properties of the formulation.

Contact time: The length of time a disinfectant drug must be in contact with a target surface or device to achieve the desired efficacy result.

Disinfectant: A substance, or mixture of substances, capable of destroying or irreversibly inactivating pathogenic (disease-causing) and potentially pathogenic (opportunistic) microorganisms, but not necessarily bacterial spores, present on environmental surfaces and inanimate objects due to the antimicrobial action of the active ingredient(s).

Disinfectant-sanitizer: A chemical product represented for use as a sanitizer on hard non-porous environmental surfaces and inanimate objects which is also represented for use as a hard surface disinfectant.

Drug: Defined in section 2 of the *Food and Drugs Act* as:

> *any substance or mixture of substances manufactured, sold or represented for use in*
> *(a) the diagnosis, treatment, mitigation or prevention of a disease, disorder, or abnormal physical state, or its symptoms, in human beings or animals;*
> *(b) restoring, correcting or modifying organic functions in human beings or animals; or*
> *(c) disinfection in premises where food is manufactured, prepared or kept.*

Drug Identification Number (DIN): A computer-generated eight-digit number assigned by Health Canada to a drug product which has been granted market authorization in accordance with the *Food and Drugs Act* and *Regulations*. The DIN uniquely identifies the product and must appear on the marketed product label for all drugs authorized for sale in Canada.

Establishment Licence: A licence issued to a person in Canada which indicates that a building has been inspected and assessed as compliant to conduct any of these licensable activities: fabricate, package/label, test, import, distribute or wholesale a drug, as set out in Part C, Division 1A of the *Food and Drug Regulations*.

Food contact surface sanitizer: A substance, or mixture of substances, that reduces the bacterial population on environmental surfaces and inanimate objects which may come into direct contact with food or beverages (e.g., eating and drinking utensils, cutting boards, countertops, food processing equipment) by significant numbers (e.g., a minimum 3 $\log_{10}$ reduction), but which does not destroy all bacteria.

Fungicide: A substance, or mixture of substances, capable of destroying fungi (including yeast) and fungal spores, pathogenic to humans or other animals present on environmental surfaces and inanimate objects.

Fungistat: A substance, or mixture of substances, that inhibits the growth of fungi on environmental surfaces and inanimate objects (e.g., prevents/controls the growth of mould and mildew). Also referred to as *mildewstat*.

General disinfectant: A substance, or mixture of substances, capable of destroying both Gram-positive bacteria and Gram-negative bacteria present on environmental surfaces and inanimate objects. Also referred to as a *broad-spectrum disinfectant*, however applicants are encouraged to use the preferred term *general disinfectant* on their labelling.

Germicide: A substance, or mixture of substances, capable of destroying or irreversibly inactivating pathogenic (disease-causing) and potentially pathogenic (opportunistic) microorganisms, but not necessarily bacterial spores, present on environmental surfaces and inanimate objects. Applicants are encouraged to use the preferred term *disinfectant* on their labelling.

Germ: A term commonly used in public health communications in reference to pathogenic (disease-causing) microorganisms, such as bacteria, fungi and viruses. Disinfectants with efficacy at a minimum as a general disinfectant, or a hospital disinfectant can be registered with "Kills germs" claims on their label.

Good Laboratory Practice (GLP): The organizational process and conditions under which laboratory studies are planned, performed, monitored, recorded, archived and reported. They are intended to promote the quality and validity of test data and improve the international acceptance of data generated in adherence to its principles.

Good Manufacturing Practices (GMP): The part of quality assurance that ensures that drugs are consistently produced and controlled in such a way to meet the quality standards appropriate for their intended use, as required by the marketing authorization, as set out in Part C, Division 2 of the *Food and Drug Regulations*

Hard surface disinfectant: A substance, or mixture of substances, capable of destroying or irreversibly inactivating, at a minimum, vegetative bacteria present on non-critical medical devices, environmental surfaces and inanimate objects.

High-level disinfectant: A substance, or mixture of substances, capable of destroying or irreversibly inactivating all microbial pathogens, but not necessarily large numbers of bacterial spores.

Hospital disinfectant: A substance, or mixture of substances, capable of destroying both Gram-positive bacteria and Gram-negative bacteria present on non-critical medical devices, environmental surfaces and inanimate objects, and that is represented for use in hospitals, medical clinics, dental offices or any other healthcare-related facility.

Incidental additive: Chemical products used in food processing facilities which are often not intended to come into direct contact with food but which may potentially become residues in food.

Intermediate-level disinfectant: A substance, or mixture of substances, capable of destroying or irreversibly inactivating all microbial pathogens, including mycobacteria but not bacterial spores.

Limited disinfectant: A substance, or mixture of substances, capable of destroying Gram-positive bacteria or Gram-negative bacteria, but not both.

Low-level disinfectant: A substance, or mixture of substances, capable of destroying or irreversibly inactivating, at a minimum, vegetative bacteria.

Market authorization: A legal document issued by Health Canada, authorizing the sale of a drug based on the requirements of the *Food and Drugs Act* and *Regulations*. The marketing authorization may be in the form of a Notice of Compliance or a Drug Identification Number. Also referred to as *pre-market authorization*.

Microbicide: A substance, or mixture of substances, capable of destroying or irreversibly inactivating pathogenic (disease-causing) and potentially pathogenic (opportunistic) microorganisms, but not necessarily bacterial spores, present on environmental surfaces and inanimate objects due to the antimicrobial action of the active ingredient(s). Applicants are encouraged to use the preferred term *disinfectant* on their labelling.

Mycobactericide: A substance, or mixture of substances, capable of destroying or irreversibly inactivating mycobacteria present on environmental surfaces and inanimate objects. Also referred to as a *tuberculocide*, however applicants are encouraged to use the preferred term *mycobactericide* on their labelling.

New drug: Regulated under Part C, Division 8 of the *Food and Drug Regulations* as:

a) *a drug that contains or consists of a substance, whether as an active or inactive ingredient, carrier, coating, excipient, menstruum or other component, that has not been sold as a drug in Canada for sufficient time and in sufficient quantity to establish in Canada the safety and effectiveness of that substance for use as a drug;*
b) *a drug that is a combination of two or more drugs, with or without other ingredients, and that has not been sold in that combination or in the proportion in which those drugs are combined in that drug, for sufficient time and in sufficient quantity to*

establish in Canada the safety and effectiveness of that combination and proportion for use as a drug; or

c) *a drug, with respect to which the manufacturer prescribes, recommends, proposes or claims a use as a drug, or a condition of use as a drug, including dosage, route of administration, or duration of action and that has not been sold for that use or condition of use in Canada, for sufficient time and in sufficient quantity to establish in Canada the safety and effectiveness of that use or condition of use of that drug.*

New Drug Submission (NDS): Refers to the submission process applicable to drugs defined under Part C, Division 8 of the *Food and Drug Regulations* as a new drug. The pre-market assessment process includes the review of supporting efficacy, safety and quality data, and leads to the issuance of both a DIN and a NOC.

Notice of Compliance (NOC): A notification, issued pursuant to Division 8 of the *Food and Drug Regulations*, which is issued to the sponsor of a new drug submission following the satisfactory review of the supporting efficacy, safety and quality data.

Non-Medicinal Ingredient (NMI): A substance, other than the active ingredient, that is added to a drug formulation during the manufacturing process and that is present in the finished drug product (e.g., solvents, stabilizer, surfactants), also referred to as *inactive ingredient* or *inert ingredient*.

Non-critical medical devices: Devices that contact intact skin but not mucous membranes during routine use (e.g., stethoscopes, blood pressure cuffs, wheelchairs), and for which reprocessing using low-level or intermediate-level disinfectants are commonly recommended.

Non-food contact surface sanitizer: A substance, or mixture of substances, that reduces the bacterial population on environmental surfaces and inanimate objects which do not come into direct contact with food or beverages (e.g., floors, walls, furniture) by significant numbers (e.g., minimum 3 $\log_{10}$ reduction), but which does not destroy all bacteria.

One-step cleaner/disinfectant: a substance, or mixture of substances, that has been tested and found to be effective in the presence of light to moderate amounts of soil (e.g., a 5% organic soil load), and therefore may be used without a pre-cleaning step for light to moderate amounts of soil in the labelled directions for use.

Prion: Proteinaceous infectious particles that are transmissible and pathogenic agents and which cause a variety of progressive neurodegenerative diseases of the central nervous system in humans and animals, collectively called transmissible spongiform encephalopathies (TSEs or prion disesases) (e.g., bovine spongiform encephalopathy in cattle, and Creutzfeld-Jakob disease in humans). Prions are unlike any other infectious pathogens because they are composed of abnormal folding conformations of a normal, ubiquitous cellular protein, the “cellular” prion

protein (PrP^C). Prions demonstrate a high level of resistance to inactivation by sterilization processes and disinfectants.

Residual self-sanitizer: A substance, or mixture of substances, that provides residual sanitizing action (e.g., significant reduction in numbers of infectious microorganisms which may be present or subsequently deposited) on treated hard, non-porous environmental surfaces.

Sanitizer: A substance, or mixture of substances, that reduces the bacterial population on environmental surfaces and inanimate objects by significant numbers (e.g., a minimum 3 $\log_{10}$ reduction) due to the antimicrobial action of the active ingredient(s), but which does not destroy all bacteria.

Spaulding Classification system: Categorizes medical devices used in patient care based on the invasiveness of the procedure that the device will be used for. The system divides these devices into three categories according to the degree of risk for infection involved in the use of the items: 1) non-critical; 2) semi-critical; and 3) critical. Based on these categories, there are four recommended levels of disinfectant activity that could be applicable to reprocessing these devices: 1) low-level disinfectants; 2) intermediate-level disinfectants; 3) high-level disinfectants; or 4) sterilants. Of note, a certain level of flexibility is required in implementing this classification system as not all medical devices clearly fit into one device category, and therefore public health guidelines and infection prevention and control protocols may recommend different levels of disinfectant activity for some medical devices (e.g., the reprocessing of flexible endoscopes, disinfection of hydrotherapy tanks).

Sporicide: A substance, or mixture of substances, capable of destroying or irreversibly inactivating bacterial endospores (also referred to as *bacterial spores*) present on environmental surfaces and inanimate objects.

Sterilant: A substance, or mixture of substances, capable of destroying or irreversibly inactivating all forms of microbial life present on inanimate objects, including all forms of vegetative bacteria, bacterial spores, fungi, fungal spores, and viruses, present on inanimate objects. These are also referred to as *chemical sterilants* or *chemosterilants*, and include substances which at the time of use are liquids, gases or vapours (e.g., ethylene oxide, hydrogen peroxide gas plasma).

Tuberculocide: A substance, or mixture of substances, capable of destroying or irreversibly inactivating mycobacteria, specifically tubercle bacilli (i.e., *Mycobacterium tuberculosis*), present on environmental surfaces and inanimate objects. Applicants are encouraged to use the preferred term *mycobactericide* on their labelling.

Virucide: A substance, or mixture of substances, capable of destroying or irreversibly inactivating viruses present on environmental surfaces and inanimate objects. Disinfectants with efficacy at a minimum against any specific virus can be registered as a virucide.

GUIDANCE FOR IMPLEMENTATION

2.1 General Efficacy Considerations for all Disinfectant Drugs

The information in the following sections provides applicants with the information considered necessary to support the efficacy of a disinfectant drug and provides an overview of the general efficacy requirements applicable to all disinfectant drugs, except where otherwise noted.

Specific safety and efficacy data requirements recommended by Health Canada for the different categories of disinfectant drugs are specified in the guidance document:

- Safety and Efficacy Requirements for Hard Surface Disinfectant Drugs (2014)

2.1.1 Submission of Efficacy Data

The submission and evaluation of efficacy data is required as part of the application process for all disinfectant drugs that are outside the scope of a monograph. Applicants are responsible for ensuring that the efficacy data submitted in support of a disinfectant drug application is representative of the intended uses or purposes of the product as represented on the label and when used in accordance with the label's recommended conditions for use.

2.1.2 Acceptable Test Methods

In general, Health Canada supports the use of internationally recognized disinfectant and sanitizer test methods and protocols published by standards organizations or by other international regulators, including:

- AOAC International
- ASTM International
- Australian Therapeutic Goods Administration (TGA)
  - Guideline for the evaluation of sterilants and disinfectants.
- European Committee for Standardization (CEN)
- Organisation for Economic Co-Operation and Development (OECD)
  - Quantitative test method for hard surface disinfectants.
- United States Environmental Protection Agency (U.S. EPA)
  - 810.2000, 810.2100, 810.2200 and 810.2300 product performance guidelines, which are applicable to hard surfaces disinfectants.

The test methods, organisms, batch replication requirements, number of carriers or replicates, microbial counts and the performance criteria recommended by Health Canada for efficacy testing are specified in the separate guidance documents for the different categories of disinfectant drugs. While the efficacy testing requirements recommended within these guidance documents are primarily applicable to test methods published by the AOAC International and ASTM International, other appropriately validated test methods and protocols published by the above standards organizations or as recommended by other international regulators may also be considered acceptable by Health Canada to support the efficacy of a disinfectant. Applicants

seeking to market disinfectants tested using alternate efficacy test methods are encouraged to contact Health Canada in advance of submitting an application to verify whether these test methods would be considered acceptable to support the efficacy of the product. In general, when alternate efficacy test methods are used, the prescribed test requirements specific to those methods or as recommended by other international regulators should be followed (e.g., the test organisms, number of carriers or replicates, microbial counts and the performance criteria).

Similarly, while Health Canada primarily recommends the use of test organism stocks available for purchase through the American Type Culture Collection (ATCC), efficacy testing using microorganism stocks purchased through alternate suppliers is also acceptable provided that they meet quality assurance standards and are appropriate for the chosen efficacy test method.

Health Canada expects that applicants will use the current official version of all test methods, and applicants should note that it is not considered acceptable to apply requirements from different test methods unless there is a suitable rationale for the mixing of their requirements (e.g., modifications to test methods commonly recommended by other international regulators to test alternate organisms or product forms).

2.1.2.1 Considerations for Efficacy Claims against Bacteriostats and Fungistats

Applicants seeking to market disinfectants with bacteriostatic or fungistatic claims (e.g., "prevents the growth of mould and mildew" or "controls the growth of mould and mildew") do not require efficacy data to be submitted to support the claims, provided that no specific bacteria or fungi are associated with the claims.

2.1.2.2 Considerations for Efficacy Claims against Biofilms

Applicants seeking to market disinfectants with claims to destroy or control biofilms are encouraged to contact Health Canada in advance of submitting an application to determine the data requirements that may be considered acceptable to support the claims. The following ASTM biofilm test methods may be considered acceptable: E2196, E2562, E2647, E 2799 or E2871.

2.1.2.3 Considerations for Efficacy Claims against Prions

Applicants seeking to market disinfectants with claims to reduce the infectivity of prions on inanimate objects are encouraged to contact Health Canada to determine the data requirements that may be considered acceptable to support the claims. Health Canada recommends that applicants reference the United States Environmental Protection Agency 810.2700 product performance test guideline for general efficacy and labelling considerations for prion-related products.

2.1.2.4 Considerations for Products with Residual Self- Sanitizer Claims

Applicants seeking to market disinfectants with residual self-sanitizing claims are encouraged to contact Health Canada in advance of submitting an application to determine the data requirements that may be considered acceptable to support the claims.

2.1.3 Good Laboratory Practice

Efficacy testing submitted in support of a disinfectant drug should be conducted in accordance with Good Laboratory Practice (GLP) principles endorsed by Health Canada to ensure that the data is of high quality and reliable. Acceptable standards include those published by the Organisation for Economic Co-Operation and Development (OECD), and the United States Environmental Protection Agency (U.S. EPA). Applicants should reference the following guidance document for information on providing evidence to Health Canada that efficacy studies adhere to the principles of Good Laboratory Practice:

- Guidance Document Non-Clinical Laboratory Study Data Supporting Drug Product Applications and Submissions: Adherence to Good Laboratory Practice

2.1.4 Efficacy Data Reporting

Efficacy data submitted in support of a disinfectant drug should be presented in a report format, and should include the following information:

- The identification of the testing laboratory or organization (i.e., the name and address) and the dates on which the study was initiated and completed, terminated or discontinued;
- A statement of Good Laboratory Practice (GLP) compliance;
- The test method used, and any deviations or modifications made to the standard test parameters or methodologies;
- For alternate test methods not expressly recommended by Health Canada (i.e., for in-use testing or simulated-use testing), complete testing protocols should be submitted, including an overview of the materials and procedures employed in testing;
- The test organisms used, including identification of the specific strain and stock supplier (e.g., the American Type Culture Collection identifier);
- The product name or identification number, and the number of batches tested;
- The concentration of the active ingredient(s) for each batch tested, and if any were aged or stressed, for how long and under what conditions;
- For products that are diluted from a concentrated formulation, how the dilution was prepared;
- The level of water hardness used in the test, if the test product was diluted;
- The type and level of soil load used in the test;
- The initial inoculums of the test organisms;
- The number and type of carriers or replicates used in the test;
- The identification of all material or procedural options employed, where such choice is provided for or recommended in the test method selected (e.g., growth media, drying time for inoculated carriers, neutralization confirmation and/or subculture media, secondary sub-culturing);
- The test exposure conditions used in the test (i.e., contact time, temperature, and relative humidity);
- The inoculum counts or carrier counts required to validate the test;
- Any control data essential to establish the validity of the test;

- An overview of the statistical plan and assumptions for analyzing the data;
- The raw data obtained, in tabular form (i.e., the numerical test results obtained through the study should be submitted for assessment; the submission of test summaries alone is not considered acceptable) and;
- A conclusion, describing whether the product meets the specific performance criteria relative to the test method(s) employed.

2.1.5 Lower Active Ingredient Limit and Lower Certified Limit

Efficacy testing should be conducted using a test product that has been formulated at or below the lower active ingredient limit or lower certified limit for each of the active ingredients within the formulation. Applicants should declare in their application which type of lower limit has been used for efficacy testing.

In situations where it may not be technically feasible to test a product formulated at the exact lower active ingredient limit or lower certified limit, a rationale should be provided to Health Canada to support efficacy testing not conducted at the exact lower limits (e.g., for reactive chemistries with a degradation profile, multiple active ingredients, formulations with inversely related active ingredients).

2.1.5.1 Lower Active Ingredient Limit

Health Canada encourages applicants to formulate their product used for efficacy testing at the lower active ingredient limit (i.e., 87.0-90.0% of the labelled nominal active ingredient concentrations), as testing at this lower limit is considered adequate to support the efficacy of the product for the duration of its shelf life.[2]

2.1.5.2 Lower Certified Limit

Alternatively, an applicant may formulate the product used for efficacy testing at the lower certified limit, determined by the product's labelled nominal active ingredient concentrations. The standard certified limits outlined in Table 1 should be met, unless an applicant proposes, and justifies, alternate limits. In this situation, an explanation should be provided to Health Canada to indicate how the alternate limits were established (e.g., sample analysis or a quantitative estimate based upon the production process). Health Canada recommends that applicants reference the United States Environmental Protection Agency 830.1750 product properties test guideline for information relevant to the establishment and declaration of certified limits for disinfectant products.

[2] As set out in section C.01.062(1) of the *Food and Drug Regulations, "*no manufacturer shall sell a drug in dosage form where the amount of any medicinal ingredient therein, determined using an acceptable method is (a) less than 90.0 per cent of the amount of the medicinal ingredient shown on the label".

Table 1. Standard Certified Limits

Nominal Concentrations of Ingredients	Upper Limit	Lower Limit
N ≤ 1.0%	N + 10% N	N – 10% N
1.0% < N ≤ 20.0%	N + 5% N	N – 5% N
20.0% < N ≤ 100.0%	N + 3% N	N – 3% N

2.1.6 Batch Replication

Efficacy testing using multiple batches of a test product may be required to demonstrate the consistency of efficacy results for a disinfectant. In general, Health Canada requires efficacy testing to be conducted using the following numbers of batches, unless otherwise specified:

- For bactericide, broad-spectrum virucide, sporicide and sanitizer claims: 3 batches per representative test organism
- For fungicide, virucide and mycobactericide claims: 2 batches per representative test organism

2.1.7 Diluent

Products that are intended to be diluted prior to their use should be tested using the type of diluent specified in the directions for use (e.g., distilled, soft or hard water) and at the use-dilution specified in the directions for use. Unless the label of the test product specifies otherwise, water with a minimum hardness of 100 ppm (parts-per-million), expressed as the amount of calcium carbonate ($CaCO_3$) present, is recommended to be used for testing.

2.1.8 Addition of Activator

Products that are intended to have an activator added prior to their use should be tested using batches of the test product which have been activated as specified in their directions for use.

2.1.9 Organic Burden

Products that are represented for use in the presence of light to moderate amounts of soil (e.g., labelled as a one-step cleaner/disinfectant), should have an appropriate organic soil load included in their efficacy testing for all disinfectant and sanitizer claims. A minimum of a 5% v/v (volume-per-volume) representative organic soil load, such as blood or bovine serum or another scientifically accepted equivalent type of soil load, is recommended.

2.1.10 Temperature

The temperature used during the course of efficacy testing (e.g., during the inoculation of carriers, exposure of carriers to the test substance, and during neutralization confirmation), should be according to the labelled directions for use. A default temperature of 18-25^{o}C should be used unless the label of the test product specifies otherwise.

2.1.11 Contact Time

The contact time used for efficacy testing should be according to the contact time specified in the directions for use of the test product. While many of the efficacy test methods recommended by Health Canada prescribe a specific contact time to be used (e.g., commonly 10 minutes for

disinfectant testing), it is acceptable to modify the contact time used for efficacy testing to that specified on the label for a test product (e.g., the contact time may be shorter than the contact time prescribed in a recommended test method). However, the modification of the contact time used in a chosen test method may be restricted by the manipulative limitations inherent to the test method.

2.1.12 Neutralization

Neutralization procedures should be employed at the completion of the contact time for all efficacy tests in order to preclude residual effects of the active ingredients in the subculture medium. Health Canada recommends the ASTM E1054 method be used to validate the neutralizers used for disinfectant and sanitizer tests for all microorganisms except for viruses. For virucidal tests, the ASTM E1482 method should be used.

2.1.13 Microbial Counts

For suspension test methods, the quantitative determination of the microbial count of the inoculum is required to determine the level of microbial challenge in the test. For carrier test methods, the enumeration of the microbial counts on untreated dried control carriers following the application of the test inoculum is required to determine the validity of the test results obtained with the treated carriers. For either type of test method, the microbial levels must be within the prescribed limits for the test method for the test results to be considered valid.

2.1.14 Towelette Products

Single-use pre-saturated or impregnated towelette products should be tested using the towelette itself. An acceptable test method should include within its methodology detailed procedures for wiping the surface of inoculated test carriers with the towelette, and then subculturing the carriers after the specified contact time. In general, one towelette should be used to treat ten carriers, or alternatively one carrier with a surface area equivalent to ten 1x1 inch carriers may be used for testing one towelette per carrier set per batch.

Alternatively, efficacy testing may be conducted using the liquid expressed from a towelette, in which case the active ingredients in the liquid expressed from the towelette should be present at the same concentration as in the towelette.

Health Canada will allow applicants of a hard surface disinfectant towelette product to bridge the efficacy claims for the towelette product using the efficacy data generated for a liquid product. Confirmatory data against the representative test organisms for each microbial category claimed on the label of the towelette product is required (e.g., a liquid product represented for use as a general disinfectant with a fungicidal claim would require confirmatory testing using the towelette product against the representative bacteria and fungi originally tested in support of the claims). This confirmatory testing allows for the bridging of all additional specific claims approved for the liquid product (e.g., all other claims against bacteria and fungi would be considered acceptable without the submission of efficacy data). For viruses, confirmatory testing using 2 batches of the test product and 10 carriers per batch against the hardest to kill virus on

the product label is required (e.g., a small-sized non-enveloped virus, if applicable), which allows for the bridging of all additional virus claims without the submission of efficacy data. In order for the bridging of efficacy claims from a liquid product to a towelette product to be considered acceptable, the following requirements are applicable:

- the ingredients in the liquid expressed from the towelette must be identical and present at the same concentration as in the liquid product;
- the same testing conditions (e.g., contact time, soil load, temperature) must be used for testing the towelette as were used for testing the liquid product; and
- the batch replication requirements specified in Section 2.1.6 must be met for the representative test organisms for each microbial category claimed on the label of the towelette product.

2.1.15 Vapour or Gas Products

Disinfectants which at the time of use are vapours or gases (e.g., those recommended for use in a fogging machine, or used in combination with a specific device for non-critical medical device reprocessing) should be tested under conditions that are representative of the uses specified in the product's labelling (i.e., through simulated-use testing), and when relevant (e.g., for fogging applications), in a setting that is representative in type and size of the labelled use areas.

Applicants seeking to market disinfectants with represented fogging disinfection applications are encouraged to contact Health Canada to determine what data requirements may be considered necessary to support the efficacy of the product.

All testing of vapour or gas products should ensure that key parameters for efficacy (e.g., active ingredient concentration, temperature, relative humidity and contact time) are accurately monitored throughout the enclosed space. The total mass of vapour or gas released into the use area and the maximum volume of space that can be disinfected should be determined and tested. Appropriate controls should be employed, and the method of monitoring and determining the efficacy of the disinfection process should be described. The test data should demonstrate that the active ingredient concentration can be maintained throughout the entire use area for the duration of the labelled contact time, and that the product's efficacy is demonstrated on surfaces that have a mild to moderate soil load.

2.1.16 Diluted or Activated Products

Products represented as being effective for an extended period of time following dilution or activation (i.e., the label indicates that the diluted solution remains effective for a defined number of days after preparation) should have data submitted to support the efficacy of the product at the end of the stated period of time. Alternatively, a scientific rationale should be submitted to justify the claim.

2.1.17 Reusable Products

Products represented as being effective for an extended period of time for reuse applications (e.g., disinfectants for reusable immersion applications that indicate on their labelling a claim

that the product remains effective for a certain number of days) should have data submitted to support the efficacy of the product at the end of the stated period of time. Alternatively, a scientific rationale should be submitted to justify the claim.

2.1.18 Re-Testing for False Positives

Health Canada will accept re-testing of a particular batch for which a test laboratory deems the results of any failures per batch to be possibly attributable to false positives. All re-testing should be conducted under identical conditions as the original test (i.e., contact time, soil load, temperature, level of water hardness, type of carriers).

2.1.19 Confirmatory Efficacy Data Requirements

Health Canada will allow applicants to submit confirmatory efficacy data for a market authorized hard surface disinfectant with reduced batch replication requirements in support of modifications to the product's conditions of use (e.g., different contact time, level of organic soil) or in support of significant changes to the inert ingredients which may have an effect on the efficacy of the product. Confirmatory efficacy testing of the product at the same use concentration as originally tested and approved is required against the representative test organisms for each microbial category claimed on the label (e.g., a product represented for use as a general disinfectant with a fungicidal claim would require confirmatory testing against the representative bacteria and fungi originally tested in support of the claims). The following reduced batch replication requirements are applicable:

- For bactericide, broad-spectrum virucide, sporicide and sanitizer claims: 2 batches per representative test organism.
- For fungicide, virucide and mycobactericide claims: 1 batch per representative test organism.

Additionally, Health Canada will allow the number of carriers or replicates used for the confirmatory efficacy testing to be reduced (e.g., for bactericide testing using an AOAC Use-Dilution method, only 10 carriers per bacterium is required; for sporicide testing using the AOAC 966.04 method, only 30 carriers for each of the two prescribed types of surfaces per bacterial spore is required; and for virucide testing using the ASTM E1053 method, testing using only 1 carrier is required).

Disinfectants that are tested as per these confirmatory efficacy data requirements are permitted to bridge all of the additional specific claims approved for the product without the submission of efficacy data (e.g., a product with bactericide and fungicide confirmatory data would be permitted to bridge all other claims against bacteria and fungi). For viruses, confirmatory testing using the hardest to kill virus on the product label is required (e.g., a small-sized non-enveloped virus, if applicable), which allows for the bridging of all additional virus claims without the submission of efficacy data.

2.2 General Safety Considerations for all Disinfectant Drugs

The information in the following sections provides applicants with an overview of the general safety considerations applicable to all disinfectant drugs, except where otherwise noted.

Specific safety data considerations (e.g., chronic toxicity, material compatibility and processing residues) recommended by Health Canada for the different categories of disinfectant drugs are specified in the guidance document:

- Safety and Efficacy Requirements for Hard Surface Disinfectant Drugs (2014)

2.2.1 Submission of Safety Data

Applicants are responsible for ensuring that the labelling of all disinfectant drugs specifies information that is representative of the potential safety hazards associated with a product when used and stored in accordance with the label's recommended conditions of use.

The submission and evaluation of safety data is not mandatory as part of the application process for hard surface disinfectants that are regulated under Division 1 of the *Food and Drug Regulations*; however, applicants may voluntarily choose to submit safety data for assessment by Health Canada to support the appropriate labelling of a product based on the identified toxicity hazards and physical and chemical hazards. Note that Health Canada may request the submission of safety data or a scientific rationale to support the safety of a disinfectant drug product, as determined on a case-by-case basis.

The submission and evaluation of safety data is required as part of the application process for all disinfectants that meet the definition of a "new drug", as set out in Division 8 of the *Food and Drug Regulations*.

All safety data testing submitted in support of a disinfectant drug should be conducted in accordance with Good Laboratory Practice (GLP) principles endorsed by Health Canada to ensure that the data is of high quality and reliable. Acceptable standards include those published by the Organisation for Economic Co-Operation and Development (OECD), and the United States Environmental Protection Agency (U.S. EPA). Applicants should refer to the guidance document referenced in Section 2.1.3 for information on providing evidence to Health Canada that safety studies adhere to the principles of Good Laboratory Practice.

2.2.2 Acute Toxicity Hazards

In developing appropriate labelling for disinfectant drugs, the potential acute toxicity hazards associated with their use should be considered. As neither the *Food and Drugs Act* nor the *Food and Drug Regulations* specify acute toxicity hazard classification or evaluation criteria for disinfectant drugs, it is recommended that applicants consider referencing the *Consumer Chemicals and Containers Regulations* and the *Controlled Products Regulations* for guidance on how to evaluate the hazards of a product. In general, the safety evaluation of a disinfectant should be based on the product as sold in its marketed container (e.g., the concentrated form of the product for disinfectants that are intended to be diluted before use), however, depending on

the intended use of the product and the ingredients within the product formulation, the hazard profile of the use-dilution may also be considered in order to appropriately address the acute toxicity hazards associated with the use of the product.

In lieu of conducting acute toxicity testing for a disinfectant drug, Health Canada may consider existing acute toxicity hazard reviews or information from other published scientific sources for similar formulations to be adequate evidence to support the safety of a disinfectant, provided that these sources address the potential toxicity hazards of both the active and inert ingredients within the product's formulation. Additionally, applicants may choose to reference acute toxicity hazard information prepared for other purposes (e.g., specified in a Material Safety Data Sheet) for a proposed product. As a result, the submission of a rationale to support the safety of a disinfectant drug based on the extrapolation of acute toxicity hazard information from these sources is generally considered acceptable. However, for disinfectant drugs that require the submission and evaluation of safety data as part of their application process, applicants are encouraged to contact Health Canada in advance of submitting an application to determine the specific safety data requirements that may be considered necessary.

Common short-term exposure endpoints which should be evaluated for all disinfectant drugs include the following, with recommended test protocols published by the Organisation for Economic Co-Operation and Development referenced:

- Acute Oral Toxicity (LD_{50}) (OECD 420, 423 or 425)
- Acute Dermal Toxicity (LD_{50}) (OECD 402)
- Acute Inhalation Toxicity (LC_{50}) (OECD 403)
- Acute Dermal Irritation (OECD 404)
- Acute Eye Irritation (OECD 405)
- Dermal Sensitization (OECD 406 or 429)

2.2.3 Physical and Chemical Hazards

In developing appropriate labelling for disinfectant drugs, the potential physical and chemical hazards associated with their use and storage should be considered (e.g., flammability, explodability, potential for chemical incompatibility). As neither the *Food and Drugs Act* nor the *Food and Drug Regulations* specify physical or chemical hazard classification and evaluation criteria for disinfectant drugs, it is recommended that applicants consider referencing the *Consumer Chemicals and Containers Regulations* and the *Controlled Products Regulations* for guidance on how to evaluate the hazards of a product. In general, the safety evaluation of a disinfectant should be based on the product as sold in its marketed container (e.g., the concentrated form of the product for disinfectants that are intended to be diluted before use), however, depending on the intended use of the product and the ingredients within the product formulation, the hazard profile of the use-dilution may also be considered in order to appropriately address the physical and chemical toxicity hazards associated with the use of the product.

In lieu of conducting physical or chemical hazard testing for a disinfectant drug, Health Canada may consider existing hazard reviews or information from other published scientific sources for similar formulations to be adequate evidence to support the safety of a disinfectant. Additionally, applicants may choose to reference physical or chemical hazard information prepared for other purposes (e.g., specified in a Material Safety Data Sheet) for a proposed product. As a result, the submission of a rationale to support the safety of a disinfectant drug based on the extrapolation of physical and chemical hazard information from these sources is generally considered acceptable. However, for disinfectant drugs that require the submission and evaluation of safety data as part of their application process, applicants are encouraged to contact Health Canada in advance of submitting an application in to determine the specific safety data requirements that may be considered necessary.

2.3 Quality Considerations for all Disinfectant Drugs

The information in the following sections provides applicants with an overview of the general quality considerations applicable to all disinfectant drugs, except where otherwise noted.

2.3.1 Submission of Quality Data

Applicants are responsible for ensuring that all disinfectant drugs are produced in a high quality manner to ensure the safety and efficacy of a product when used and stored in accordance with the label's recommended conditions of use.

The submission and evaluation of safety data is not mandatory as part of the application process for disinfectants that are regulated under Division 1 of the *Food and Drug Regulations.*

The submission and evaluation of quality data is required as part of the application process for disinfectants that meet the definition of a "new drug", as set out in Division 8 of the *Food and Drug Regulations*.

2.3.1.1 Quality Data Requirements for New Drugs

In support of a drug application for a "new drug", at a minimum the following quality documents must be submitted:

- a completed Quality Overall Summary - Chemical Entities (QOS-CE);
- a completed Certified Product Information Document - Chemical Entities (CPID-CE); and
- compliance certificates for Good Manufacturing Practices (GMP) and establishment licence requirements, if applicable.

Applicants are encouraged to contact Health Canada in advance of submitting an application to determine the specific quality data requirements that may be considered necessary.

2.3.2 Good Manufacturing Practices and Establishment Licence Requirements

Good Manufacturing Practices (GMP) requirements for drugs are set out in Division 2 of the *Food and Drug Regulations.* Basic GMP requirements include the mandatory declaration of the manufacturing process of a drug, the requirement for record keeping that enables the complete

history of a production batch of the drug to be traced, the requirement for a drug's expiration date (i.e., shelf-life) to be determined prior to marketing and the requirement for a continuing stability program to be developed to ensure compliance with the approved shelf-life specifications of a drug.

Establishment licence requirements for drugs are set out in Division 1A of the *Food and Drug Regulations*. A drug establishment licence is required for any person in Canada who is conducting any of six licensable activities: fabricating, packaging, labelling, testing, importing, distributing, or wholesaling a drug. The holder of an establishment licence must ensure that the licensable activities are being conducted in compliance with GMP requirements.

2.3.2.1 Hard Surface Disinfectants

Fabricators, packagers/labellers, distributors, importers and testers of disinfectants which meet the definition of an "antimicrobial agent" (i.e., disinfectants represented for use on non-critical medical devices, environmental surfaces and inanimate objects) are not required to obtain an establishment licence or meet GMP compliance requirements. However, they are still expected to meet the provisions of section 8 of the *Food and Drugs Act*, which denotes the prohibition on selling drugs manufactured under unsanitary conditions or that are adulterated. To support compliance with this regulatory requirement, a voluntary standard was developed by Health Canada:

- Standard for the Fabrication, Control and Distribution of Antimicrobial Agents for Use on Environmental Surfaces and Certain Medical Devices, Version 2 (Guide-0049)

2.3.3 Colouring Agent Regulatory Restriction

Any colouring agent may be used in disinfectant drugs, as set out in section C.01.040.2(5) of the *Food and Drug Regulations*, unless there is a safety issue related to its use. While only disinfectants represented for use on medical devices, in health care facilities, and in premises in which food is manufactured, prepared or kept have been specifically exempt from colouring agent restrictions, this section of the *Food and Drug Regulations* has been interpreted by Health Canada to also be applicable to disinfectants represented for use in domestic, industrial/ institutional and barn premises.

Information regarding the permitted variation of colours and fragrances for marketed drug products may be found in the following Health Canada policy document:

- Drug Identification Number: A Brand Name Product with Different Fragrances, Flavours or Colours

2.3.4 Highest Degree of Purity

Health Canada considers the highest degree of purity requirement specified in section C.01.011(4) of the *Food and Drug Regulations* not to be applicable to disinfectant drugs.

2.3.5 Upper Active Ingredient Limit Regulatory Requirement

The extension of the upper active ingredient limit beyond 110.0% is considered acceptable for liquid disinfectants containing sodium hypochlorite as their active ingredient due to their rapid degradation and inherent instability. For these products, an over formulation not exceeding 25.0% of the nominal active ingredient concentration claimed on the label is permitted, which is expected to ensure that the product remains effective for the duration of the product's shelf life (i.e., a minimum of 1 year).[3] The extension of the upper active ingredient limit beyond 110.0% may be considered acceptable for other active ingredients, as determined on a case-by-case basis where supporting scientific data is provided.

2.4 Regulatory Labelling Requirements

The information in the following sections provides applicants with the labelling requirements for all disinfectants drugs as set out in the *Food and Drugs Act* and *Regulations*.

Optional labelling considerations for disinfectants are found in Appendix 2; however, these are **recommendations only**, and are **not** regulatory requirements.

2.4.1 Brand Name

The brand name (i.e., product name) under which a disinfectant drug is to be sold or advertised must be indicated on the label. The product name must not create an erroneous or misleading impression of the product.

To verify the uniqueness of a proposed product name prior to submitting an application, applicants may conduct a search for the proposed product name through the Drug Product Database, accessible through the Health Canada website.

2.4.2 Name and Address of the Manufacturer

The name and address of the manufacturer of a disinfectant drug must be indicated on the label. If the address of the manufacturer is not in Canada, then the name of the importer (i.e., the person responsible for the import and sale of the product in Canada) and the address of their principal place of business in Canada must be indicated on the label.

2.4.3 Active Ingredient(s)

The identity and percent nominal concentration of each active ingredient, expressed as a percentage on a weight-per-weight basis (%w/w), in a disinfectant drug must be indicated on the label. This labelling requirement permits the calculation of the concentration of the active ingredients, expressed as parts-per-million (ppm), in the product when used in accordance with the label directions.

[3] As set out in section C.01.062(1) of the *Food and Drug Regulations, "*no manufacturer shall sell a drug in dosage form where the amount of any medicinal ingredient therein, determined using an acceptable method is (a) less than 90.0 per cent of the amount of the medicinal ingredient shown on the label; or (b) more than 110.0 per cent of the amount of the medicinal ingredient shown on the label".

For disinfectant drugs marketed as single-use pre-saturated or impregnated towelettes, the percent nominal concentration of each active ingredient declared on the label as the amount of the active ingredients present in the liquid that can be expressed from the towelette.

2.4.4 Net Content

The net amount of a disinfectant drug in its marketed packaging (i.e., net content) must be indicated on the label in a unit that is appropriate for the declared dosage form of the drug (e.g., disinfectants packaged as liquids should be expressed using metric volume units; disinfectants packaged as powders, solids and aerosol sprays should be expressed using metric mass units; and disinfectants packaged as towelettes and tablets should be declared by count).

2.4.5 Lot Number

The indication of a lot number is required on the label, or alternatively stamped onto the marketed container or packaging, of a disinfectant drug to permit the tracing and identification of a production batch through its manufacture and distribution. The use of alternate lot number designations other than those specified in the *Food and Drug Regulations* is considered acceptable provided that they allow products to be traced and identified.

2.4.6 Expiration Date

The indication of an expiration date is required on the label, or alternatively stamped onto the marketed container or packaging, of a disinfectant drug to communicate the shelf-life stability of the product (i.e., the maintenance of the product's labelled potency, purity and physical characteristics) when stored in accordance with the labelled directions, and represents the date after which the manufacturer recommends that the product not be used.

2.4.6.1 Expiration Date Requirement for Domestic Use Products

Health Canada will consider the omission of an expiration date to be acceptable for disinfectants represented for use on non-critical medical devices and hard non-porous environmental surfaces and inanimate objects in domestic premises (i.e., for private/household use), provided that their formulations do not change significantly over time (i.e., a minimum 1-year shelf-life) when the marketed container or packaging is stored in accordance with the label directions. These products should be represented for use in domestic premises only.

2.4.7 Drug Identification Number

The drug identification number (DIN) assigned for a disinfectant drug must be indicated on the label.

2.4.8 Directions for Use

Adequate directions for all intended uses of the disinfectant drug must be indicated on the label to ensure the safety and efficacy of the product when used in accordance with the label directions.

2.4.9 Pressurized Metallic Containers

Disinfectant drugs packaged for sale in pressurized metallic containers must indicate a hazard symbol, signal word and appropriate hazard statement on the label, including:

- The hazard symbol for "Explosive" accompanied by the signal word "Caution"; and
- The hazard statement: "Container may explode if heated".

The following hazard statements must also be indicated on the label, as appropriate:

- Contents under pressure. Do not place in hot water or near radiators, stoves or other sources of heat. Do not puncture or incinerate container or store at temperatures over 50^{o}C; and
- Do not use in open flame or spark.

EFFECTIVE DATE

This guidance document will come into effect 90 days following the date of publication. All disinfectant drug submissions received after the effective date are expected to be filed with the updated supporting data requirements. Data reports which have been signed off as completed prior to the effective date of this guidance document will be assessed at Health Canada's discretion for their acceptability under the updated data requirements.

Appendices

Appendix 1: References

AOAC: *960.09 Germicidal and Detergent Sanitizing Action of Disinfectants. In* Official Methods of Analysis of AOAC International: Chapter 6 – Disinfectants. USA, Current edition.

ASTM: *E1054 Method: Standard Test Methods for Evaluation of Inactivators of Antimicrobial Agents*. *In* Annual Book of ASTM Standards. USA; Current edition.

ASTM: *E1482 Method: Standard Test Method for Neutralization of Virucidal Agents in Virucidal Efficacy Evaluations. In* Annual Book of ASTM Standards. USA; Current edition.

ASTM: *E2196 Method: Standard Test Method for Quantification of Pseudomonas aeruginosa Biofilm Growth with Medium Shear and Continuous Flow using Rotator Disk Reactor. In* Annual Book of ASTM Standards. USA; Current edition.

ASTM: *E2562 Method: Standard Test Method for Quantification of Pseudomonas aeruginosa Biofilm Growth with High Shear and Continuous Flow using CDC Biofilm Reactor. In* Annual Book of ASTM Standards. USA; Current edition.

ASTM: *E2647 Method: Standard Test Method for Quantification of Pseudomonas aeruginosa Biofilm Growth using Drip Flow Biofilm Reactor with Low Shear and Continuous Flow. In* Annual Book of ASTM Standards. USA; Current edition.

ASTM: *E2799 Method: Standard Test Method for Testing Disinfectant Efficacy against Pseudomonas aeruginosa Biofilm using MBEC Assay. In* Annual Book of ASTM Standards. USA; Current edition.

ASTM: *E2871 Method: Standard Test Method for Evaluating Disinfectant Efficacy against Pseudomonas aeruginosa Biofilm Growth in the CDC Biofilm Reactor using the SingleTtube Method. In* Annual Book of ASTM Standards. USA; Current edition.

OECD (1987): Organisation for Economic Co-operation and Development. *Test No. 402: Acute Dermal Toxicity.* OECD Guidelines for the Testing of Chemicals, Section 4: Health Effects. Paris, France; 1987.

OECD (1992): Organisation for Economic Co-operation and Development. *Test No. 406: Skin Sensitisation.* OECD Guidelines for the Testing of Chemicals. Paris, France; 1992.

OECD (2001): Organisation for Economic Co-operation and Development. *Test No. 420: Acute Oral Toxicity – Fixed Dose Procedure.* OECD Guidelines for the Testing of Chemicals. Paris, France; 2001.

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OECD (2002): Organisation for Economic Co-operation and Development. *Test No. 405: Acute Eye Irritation/Corrosion.* OECD Guidelines for the Testing of Chemicals. Paris, France; 2002.

OECD (2009): Organisation for Economic Co-operation and Development. *Test No. 403: Acute Inhalation Toxicity.* OECD Guidelines for the Testing of Chemicals. Paris, France; 2009.

OECD (2002): Organisation for Economic Co-operation and Development. *Test No. 404: Acute Dermal Irritation/Corrosion.* OECD Guidelines for the Testing of Chemicals. Paris, France; 2002.

OECD (2010): Organisation for Economic Co-operation and Development. *Test No. 429: Skin Sensitisation.* OECD Guidelines for the Testing of Chemicals. Paris, France; 2010.

TGA (1998): Therapeutic Goods Administration. *Guidelines for the evaluation of sterilants and disinfectants.* Department of Health and Ageing, Therapeutic Goods Administration. Australia, February 1998.

U.S. EPA (1996): United States Environmental Protection Agency. *OPPTS 830.1750:* Certified Limits. Product Properties Test Guidelines. Office of Pesticide Programs. USA; 1996.

U.S. EPA (2012): United States Environmental Protection Agency. *OPPTS 810.2000: General Considerations for Uses of Antimicrobial Agents.* Product Performance Test Guidelines. Office of Pesticide Programs, Antimicrobials Division. USA; 2012.

U.S. EPA (2012): United States Environmental Protection Agency. *OPPTS 810.2100: Sterilants – Efficacy Data Recommendations.* Product Performance Test Guidelines. Office of Pesticide Programs, Antimicrobials Division. USA; 2012.

U.S. EPA (2012): United States Environmental Protection Agency. *OPPTS 810.2200: Disinfectants for Use on Hard Surfaces – Efficacy Data Recommendations.* Product Performance Test Guidelines. Office of Pesticide Programs, Antimicrobials Division. USA; 2012.

U.S. EPA (2012): United States Environmental Protection Agency. *OPPTS 810.2300: Sanitizers for Use on Hard Surfaces – Efficacy Data Recommendations.* Product Performance Test Guidelines. Office of Pesticide Programs, Antimicrobials Division. USA; 2012.

U.S. EPA (2013): United States Environmental Protection Agency. *OPPTS 810.2700: Products with Prion-Related Claims.* Product Performance Test Guidelines. Office of Pesticide Programs, Antimicrobials Division. USA; 2013.

Appendix 2: General Labelling Considerations for Disinfectant Drugs

This appendix is intended to assist applicants in preparing appropriate labelling for all categories of disinfectant drugs; however, these are labelling **recommendations only** and are **not** regulatory requirements. These labelling considerations are intended to address the regulatory requirement for adequate directions for all intended uses of a disinfectant drug to be indicated on its labelling.

Specific labelling considerations applicable to disinfectant drugs are addressed in a separate guidance document:

- Safety and Efficacy Requirements for Hard Surface Disinfectants (2014)

1.0 Intended Uses or Purposes

Disinfectant drug labels should clearly and prominently indicate their intended uses or purposes on the primary panel of their labelling (e.g., disinfectant, sanitizer, bactericide, fungicide, virucide, mycobactericide, sporicide, high level disinfectant).

2.0 Non-Therapeutic Claims

Non-therapeutic claims indicated on disinfectant drug labels must not be false, misleading, or likely to create an erroneous impression of the product; therefore, applicants are responsible for ensuring that all proposed non-therapeutic claims are appropriate for the intended uses of the product and that the product performs as represented. Common types of non-therapeutic claims include, but are not limited to: physical or sensory characteristics, such as colour and smell; market characteristics; cleaning claims; laundry whitening claims; deodorization claims; soap scum removal claims; and mould and mildew control claims.

Information regarding the broad principles relating to marketing practices in Canada is available through the Competition Bureau, who is responsible for the administration and enforcement of the *Competition Act.*

Applicants labelling disinfectant drugs with "green" claims should consult the following Competition Bureau document, developed in partnership with the Canadian Standards Association:

- Environmental Claims: A Guide for Industry and Advertisers

3.0 Dilution Instructions

Products that are intended to be diluted into a secondary container prior to their use should specify clear directions to the user on how to dilute the product. Metric units of measurement (e.g., millilitres per litre) or ratios (e.g., 1:256) should be used. When the type and temperature of diluent is not specified in the directions for use, the use of 18-25^{o}C tap water may be assumed. The dilution directions specified should correspond with those used for efficacy testing.

Additionally, the amount of time that a diluted solution may be stored or used without a decrease in efficacy should be specified. Disinfectants that are intended to be diluted and stored for an extended period of time in a secondary container (i.e., the label indicates that the diluted solution remains effective for a defined number of days after preparation), should have efficacy data or a scientific rationale approved to support the claim. Otherwise, a statement to the effect of the following is recommended:

- Prepare a fresh solution for each use; or
- Prepare a fresh solution at least daily or when use solution becomes visibly dirty.

4.0 Addition of Activator

Products that are intended to have an activator added prior to their use should specify the volume and directions for the addition of the activator.

Additionally, the amount of time that an activated solution may be stored or used without a decrease in efficacy should be specified. Disinfectants that are intended to be activated and stored for an extended period of time (i.e., the label indicates that the activated solution remains effective for a defined number of days after preparation) should have efficacy data or a scientific rationale approved to support the claim. Otherwise, the labelling should clearly specify that the product is to be activated immediately before being used.

5.0 Temperature

When an ambient temperature is not specified in the directions for use of products represented for use on environmental surfaces, a temperature of 18-25^{o}C may be assumed. Products that have been tested and found to be effective at temperatures other than 18-25^{o}C (e.g., disinfectants for use in heated immersion baths) should specify in their directions for use that heating or cooling to the specified temperature is required prior to disinfection or sanitization.

6.0 Contact Time

The contact times specified on the label should correspond with those used for efficacy testing. The directions for use should specify that a target surface is to be exposed to the product for the duration of the contact time. A statement to the effect of the following is appropriate for disinfectants intended to be applied to environmental surfaces and inanimate objects:

- Allow surface to remain wet for (X) minutes.

7.0 Re-Use Applications

Products which are intended for re-use applications (e.g., disinfectants intended for immersion applications) should specify the duration of time that they may be re-used without a decrease in efficacy. Products that are represented as being effective for an extended period of time for reuse applications (i.e., the label indicates that the solution remains effective for a defined number of days for re-use) should have efficacy data or a scientific rationale approved to support the claim. Otherwise, a statement to the effect of the following is recommended:

- Replace solution at least daily or when use solution becomes visibly dirty.

8.0 Hazard Classification Criteria and Precautionary Statements

Neither the *Food and Drugs Act* nor the *Food and Drug Regulations* specify hazard classification criteria or precautionary statements for disinfectant drugs, with the exception of the regulatory requirements for labelling pressurized metallic containers. It is recommended that applicants consider referencing the *Consumer Chemicals and Containers Regulations* for guidance on hazard classification criteria and the associated precautionary and hazard statements which may be appropriate for disinfectant drugs.

Appropriate precautionary statements should be clearly and prominently specified on the labelling of disinfectant drugs to ensure the safety of the product when it is used in accordance with the label directions. The precautionary statements must be relevant to the potential acute toxicity exposure hazards of the product.

8.1 Warning Statements

Disinfectant drug labels should indicate the following statements:

- Read the label before using; and
- Keep out of reach of children.

8.2 Signal Words and Primary Hazard Statements

Appropriate signal words (e.g., Danger, Poison, Warning, and Caution) and primary hazard statements (e.g., Corrosive, Irritant) should be indicated on disinfectant drug labels, as appropriate for the potential acute toxicity hazards of the product.

8.3 Hazards to Humans and Domestic Animals

Specific hazard statements should be indicated on disinfectant drug labels, as appropriate for the potential acute toxicity hazards to humans and domestic animals of the product (e.g., Fatal if swallowed; Corrosive – Causes severe eye damage; Causes skin irritation – Do not get on skin or on clothing).

8.4 Personal Protective Equipment

Personal protective equipment statements should be indicated on disinfectant drug labels, as appropriate for the potential acute toxicity hazards of the product, in order to ensure the safety of the product when it is used in accordance with the label directions. The type of personal protective equipment specified should be appropriate to the potential hazard to a user, and

include: protective clothing, protective footwear, chemical-resistant gloves, protective eyewear, and respiratory protective devices.

8.5 First Aid Statements

First aid statements should be indicated on disinfectant drug labels, as appropriate for the potential acute toxicity hazards of the product (e.g., for accidental ingestion, inhalation, eye contact, skin contact, and for accidental injuries requiring medical attention).

8.6 Physical and Chemical Hazard Statements

Physical and chemical hazard statements should be indicated on disinfectant drug labels, as appropriate to the potential physical and chemical hazards of the product (e.g., flammability, explodability, and chemical incompatibility). For products with known chemical incompatibilities, a hazard statement may be appropriate on the label (e.g., sodium hypochlorite forms toxic chlorine gas when mixed with acids or ammonia compounds).

9.0 Storage Instructions

Storage instructions appropriate for the level of hazard and packaging of a disinfectant should be indicated on the label, and should address the factors which might alter the shelf-life of the product (e.g., temperature extremes, excessive moisture, heat or humidity, sunlight). One or more statements to the effect of the following may be appropriate:

- Storage at room temperature / Store at 15-30^{o}C.
- Store in a cool, dry place.
- Store tightly closed in a cool, dry place in original container away from sunlight.
- Do not freeze.

10.0 Disposal Instructions

Disposal instructions appropriate for the level of hazard and packaging of the disinfectant should be indicated on the label, and should provide sufficient information on how to appropriately dispose of the product container and any unused product. Applicants should contact municipal/provincial/territorial product stewardship organization(s) for information on how to manage the life cycle of their chemical products. One or more statements to the effect of the following may be appropriate:

- For information on disposal of unused, unwanted product, contact the manufacturer or the appropriate municipal/provincial/territorial agency or product stewardship organization.
- Rinse the emptied container thoroughly prior to disposal.
- Non-refillable container / Do not reuse or refill this container.
- Dispose of the empty container in accordance with municipal/provincial/territorial requirements. Offer for recycling, if available.