ZAMBIA MEDICINES REGULATORY AUTHORITY

GUIDELINES FOR APPLICATION FOR GRANT OF MARKETING AUTHORISATION OF ANTISEPTICS AND DISINFECTANTS

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ACKNOWLEDGEMENTS

ABBREVIATIONS

ASTM	American Society for Testing and Materials
BP	British Pharmacopoeia
CAS number	Chemical Abstracts Service Registry Number CEN European Committee of Standardization
IH	In-House
ISO	International Organisation for Standardisation
JP	Japanese Pharmacopoeia
OECD	Organisation for Economic Corporation Development
Ph. Eur	European Pharmacopoeia
RH	Relative Humidity
USP	United States Pharmacopoeia
ZAMRA	Zambia Medicines Regulatory Authority

FOREWORD

INTRODUCTION

The Zambia Medicines Regulatory Authority (ZAMRA) regulates medicines and allied substances in accordance with the provisions of the Medicines and Allied Substances Act No. 3 of 2013 of the laws of Zambia and the relevant Regulations made thereunder. (Hereafter referred to as "the Act").

These Guidelines for Grant of Marketing Authorisation for Antiseptics and Disinfectants are issued by ZAMRA in pursuant to section 68 of the Medicines and Allied Substances Act, No. 3 of 2013 of the laws of Zambia and will prescribe the information to be incorporated in the applications for grant of marketing authorisation by an applicant who intends to place on the Zambian market Antiseptics and Disinfectants in accordance with Section 39 of the Medicines and Allied Substances Act (No 3) of 2013. The Authority may amend any part of these Guidelines from time to time.

INTERPRETATIONS

In these Guidelines, unless the context otherwise requires -

"Act" means the Medicines and Allied Substances Act No.3 of 2013;

"Active substance" means a biologically or chemically active substance or compound that is used or intended to be used in the manufacture of a product as an active compound (ingredient);

"Antiseptic" means a product that inactivates, reduces, prevents or arrests growth of microorganisms with the inherent intent to mitigate or prevent disease on humans and animals (animates);

"Applicant" means a person who submits an application for grant of marketing authorisation who may be a manufacturer, patent holder or a person responsible for placing the product on the market with Power of Attorney from, or in contract with, the manufacturer or patent holder;

"Authority" means the Zambia Medicines Regulatory Authority;

"Bactericide" means an antimicrobial agent capable of destroying bacteria, but not necessarily bacterial spores or mycobacteria;

"Biocide" means an active substance or preparation containing one or more active substances, put up in a form in which they are supplied to the user, intended to destroy, deter, render harmless, prevent the action of, or otherwise exert a controlling effect on any harmful organism by chemical or biological means;

"Disinfectant" means an antimicrobial agent capable of destroying pathogenic and potentially pathogenic microorganisms on environmental surfaces and inanimate objects;

"Fungicide" means an antimicrobial agent capable of destroying fungi, including their spores;

"Health facility" means "health facility" means any site, fixed or mobile, providing services for the prevention, diagnosis and treatment of disease or illness and includes a diagnostic center, a hospice and a hospital;

"**Holder of Marketing Authorisation"** means a person or company under whom a biocidal product has been issued Marketing Authorisation and is responsible for all aspects of the biocidal product including quality, safety, efficacy and compliance with conditions of Marketing Authorisation;

"Manufacture" means in relation to biocidals, includes any process carried out in the course of making that biocidal, but does not include the process of —

(a) dissolving or dispensing a product in, or diluting or mixing it with, some other substance for purposes of administering it;

"Manufacturer" means a person or firm that is engaged in the manufacture of antiseptic or disinfectant;

"Marketing Authorisation" means the authorisation granted under section thirty-nine of the Act, for the placement of an antiseptic or disinfectant on the market (may be used interchangeably with "registration" in this document);

"Mycobactericide" means an antimicrobial agent capable of destroying mycobacteria

"Persistence" means a claim that the product will deliver a longer action than only the immediate reduction of microorganisms;

"Pharmacopoeia" means current edition of United States Pharmacopoeia (USP), British Pharmacopoeia (B.P.), European Pharmacopoeia (Ph. Eur), The International Pharmacopoeia (Int. Ph) and Japanese Pharmacopoeia;

"Product variant" means a range of products produced by the same manufacturer in the same site, similar in composition and intended for the same use but available in different colours, fragrances and flavours;

"Product" means an antiseptic or a disinfectant;

"Resident organisms" means those organisms that normally reside on the skin or mucosa;

"Rubs" means antiseptic products to be used without water;

"Sanitizer" means a product that reduces the level of microorganisms present by significant numbers, e.g. 99.9% or more, or to acceptable levels;

"Specifications" means the combination of physical, chemical, biological and microbiological test requirements that determine whether an antiseptic or disinfectant product is suitable for the intended use;

"Sporicide" means an antimicrobial agent capable of destroying bacterial spores;

"Sterilant" means a chemical agent which is used to sterilize medical devices;

"Transient organisms" means organisms picked up by contact with the environment but may remain in situ long enough to be transferred from a person, an animal or inanimate object;

"Virucide" means an antimicrobial agent capable of destroying viruses;

“Washes” means antiseptic products to be used with water;

1 SECTION 1: GENERAL REQUIREMENTS

1.1 An application for marketing authorisation of a disinfectant or antiseptic shall be made by an applicant who intends to place on the market any disinfectant or antiseptic in Zambia.

1.2 An applicant shall:-

(a) Apply for marketing authorisation of the product to the Authority by submitting-
   (i) A duly completed application form
   (ii) Two (2) samples of smallest commercial packs or an aliquot of the product. Additional samples for analysis may be requested for separately.
   (iii) Product dossier in both hard copy and an electronic, text selectable/editable PDF format in an electronic storage device such as CD –ROM or flash drives;

(b) Submit separate application for each product or product variant.

(c) Any application that is not accompanied by proof of payment shall not be accepted.

All bank charges shall be borne by the applicant. An applicant shall ensure that a remittance advice note is sent to the Authority giving details of the payment, in particular the name of the applicant, the products paid for and amount paid.

1.3 Hard copies of the application should be filed in a spring A4 size file with collapsible edge made of biodegradable material.

Information shall be presented on A4 and 80g/m^2 paper with readily readable letters of at least Times New Roman 12 font size.

Every page shall be numbered sequentially.

Extension sheets, tables, diagrams and other supporting documents shall as far as possible be of the same size, well annotated, numbered and appropriately cross-referenced.

1.4 The Authority may during assessment of applications require the applicant to submit additional samples, documents, and information and give clarification as the case may be.

The processing of an application shall be kept on hold until such samples, documents, information or clarification is provided.

If the applicant fails to respond to the issues within one hundred and twenty (120) days from the date of request, the application shall be closed and the registration of the product shall only be considered upon submission of a new application.

1.5 The Authority may grant marketing authorisation of a product if it is satisfied with that: -

(a) It is of acceptable quality, safety and efficacy; and

(b) It complies with requirements as prescribed.

Where the Authority is satisfied that the product complies with requirements as prescribed it will inform the applicant in writing that the product has been granted marketing authorisation.

1.6 Where the Authority refuses to grant marketing authorisation it shall notify the applicant in writing of such decision and the reason(s) thereof.

1.7 If the applicant is not satisfied with the decision of the Authority, the applicant may, within 30 days from the date of notification appeal to the Minister responsible for Health.

1.8 Marketing Authorisation of a product shall be valid for five (5) years unless suspended or revoked by the Authority.

1.9 The Marketing Authorisation Holder shall pay the prescribed product annual retention fees for the following year by 31st December, of each year.

1.10 If for any reason the marketing authorisation holder changes any matter related to a product that has been granted marketing authorisation including but not limited to change of composition, packaging, labelling or any other change, shall before marketing the changed product, notify and obtain approval of the Authority of the change. The notice to the Authority shall be submitted in a completed application form accompanied by proof of payment or remittance advice.

1.11 The Authority will evaluate reasons provided in the notice referred to under sub section 1.10 and if satisfied with such reasons it will approve the change(s) by issuing approval notice. If not satisfied with the reasons, the Authority will not approve the changes and it will notify the marketing authorisation holder of the decision thereof.

1.12 The marketing authorisation holder may at any time by giving notice in writing to the Authority voluntarily surrender the marketing authorisation.

1.13 An application for renewal of marketing authorisation shall be made in the last year of the validity of the marketing authorisation but at least one hundred and eighty (180) days before the expiry date of the existing marketing authorisation.

1.14 A marketing authorisation holder shall be responsible for: -

(a) All information submitted in support of the application for grant of marketing authorisation and variation thereof.

(b) Ensuring safety, quality and efficacy of the registered product and that the product at all times complies with all prescribed requirements.

(c) Effective voluntary and compulsory product recall whenever necessary including vigilance activities.

(d) Compliance to current Good Manufacturing Practices

2 SECTION 2: ANTISEPTIC PRODUCTS

2.1 Introduction

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 diseases. For the purpose of these guidelines, microorganisms are defined as bacteria, yeast, fungi, and viruses.

2.2 Scope

These Guidelines apply to antiseptic skin products that are intended for use in professional and personal settings. 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 dosage forms. Antiseptic skin products also include preoperative skin preparations.

The Guidelines refer to antiseptic products without medicinal claims for external use or application in animals and humans.

2.3 Category of antiseptic use

2.3.1 Personal use antiseptics

2.3.1.1 Antiseptics for domestic use

Domestic (or household) use antiseptic products are those used by an individual in a domestic setting to reduce transient organisms on the skin. This includes, but may not be limited to, consumer-use first aid antiseptics for application in cleansing cuts and abrasions, self-administered pre-injection or body piercing.

2.3.1.2 Antiseptics for use in a commercial or institutional setting

Commercially or institutionally used antiseptics 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.

2.3.2 Professional use antiseptics

2.3.2.1 Food premises use antiseptics

Antiseptic products used at 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, restaurants, supermarkets, and fast food outlets.

2.3.2.1 Professional healthcare use antiseptics

Antiseptic 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 health facility.

Professional healthcare use antiseptics can be broken down as follows: -

(a) Professional hygienic hand rubs: products used for post-contamination treatment of lightly-soiled hands that involves rubbing hands without addition of water;
(b) Professional hygienic hand wash: products used for post contamination treatment that involves washing hands;
(c) Surgical hand rubs: products used for preoperative treatment, which involves rubbing hands without addition of water;
(d) Surgical hand wash: products used for preoperative treatment that involves washing hands, either with or without the use of a scrub brush; or
(e) Patient preoperative skin preparations: products used to prepare patient skin prior to surgical procedures.

2.4 Documentation requirements for registration

An applicant shall submit documents that demonstrate quality, safety and efficacy of the product including the material safety data sheet.

2.4.1 Manufacturing and marketing authorisation (Certificates and Licenses)

An applicant shall submit the following:

(a) A valid Manufacturing license for the manufacturing site for the product;
(b) A valid GMP certificate issued not older than 24 months from the last date of inspection; and
(c) Documentary proof of marketing authorisation (where applicable) for the submitted product in the country of origin, in any other country(s) and specifically those in the SADC region.

2.4.2 Chemistry, Manufacturing and Controls

2.4.2.1 Chemistry

2.4.2.1.1 Active ingredient(s)

An applicant shall provide the following:

(a) Information related to the active substance(s) where the active substance shall be identified by its non-proprietary name, chemical name and Chemical Abstract Service (CAS) number (if available);

(b) A copy of a certificate of analysis for the active substance(s) from the manufacturer of the active substance(s); and

(d) A copy of a certificate of analysis for the active substance(s) from the manufacturer of the finished product(s).

2.4.2.1.2 **Non active substance(s)**

An applicant shall provide the following:

(a) Information related to the non-active substance(s) were the non-active substance shall be identified by its non-proprietary name, chemical name and Chemical Abstract Service (CAS) number. Where the non-active ingredient does not have a CAS number, reasons should be stated in the application;

(b) A copy of a certificate of analysis for the non-active substance(s) from the manufacturer of the non-active substance(s); and

(c) A copy of a certificate of analysis for the non-active substance(s) from the manufacturer of the finished product(s).

2.4.2.2 **Raw material (active and non-active substances) Quality control**

2.4.2.2.1 **Specifications and analytical methods**

Summarised specifications for the active and non-active substance shall be provided, that is the acceptable limits of the entire physical-chemical parameters.

Justification for the specifications should be provided. Specification shall include but not be limited to: -

(a) Description;

(b) Identity - test method should be specific for active substance(s);

(c) Related substances or impurities; and

(d) Assay - test method should be specific and stability indicating for active substance(s).

A full description of the analytical and other control procedures carried out to ascertain the final product specifications stated above should be provided.

An applicant shall provide one (1) copy of typical batch certificate of analysis for at least one (1) batch for each active or inactive substance(s).

2.4.2.2.2 **Final Product Quality control**

a) **Unit and Batch composition**

An applicant shall be required to provide unit and batch composition as guided by the table below:

Table No.1: Unit and Batch composition

S.No	Name of Ingredient	Reference Method	Quantity/Unit	Quantity/ Batch	Reason for Inclusion

b) **Specifications and analytical methods**

Summarized specifications for both release and shelf-life of the final product shall be provided, that is the acceptable limits for the entire physical-chemical parameters.

Justification for the specifications should be provided.

Specifications should include but not be limited to: -

(a) Description;

(b) Identity - test method shall be specific for active substance(s);

(c) Assay - test method shall be specific and stability indicating for active substance(s); and

(d) Additional specifications and test methods for liquid preparation shall include pH and Specific Gravity.

A full description of the analytical and other control procedures carried out to ascertain the final product specifications stated above should be provided.

Three (3) copies of typical batch certificates of analysis for at least three (3) batches of finished product shall be submitted.

2.4.1.3 Manufacturing process

An applicant shall submit appropriate document(s) that:

(a) Describe all stages involved in the manufacture of the finished product. This shall be in the form of a detailed narrative and a simplified flow diagram accompanied by a list of equipment, including their capacities, used at each stage. Basic principles involved shall be clearly set out from dispensing to packaging. All stages shall be illustrated that is filling, weight checking, labelling, packaging and sealing. All steps involved and their operations shall be carefully described including the conditions subjected to each operation that is temperature, pH adjustments and processing time;

(b) Provide in-process control checks (sampling and testing at critical points); and

(c) Provide the actual batch manufacturing and packaging records for one production scale batch.

2.4.2.4 Stability studies

An applicant shall submit data on accelerated stability testing at conditions (40±2ºC/75±5 % R H) and long-term study at conditions (30±2ºC/65±5 %R H) for three batches for the finished product. In - use stability studies shall be provided where applicable.

For more details please refer to Guidelines on Stability Studies, available at http://www.zamra.co.zm

2.4.2.5 **Efficacy and Safety**

An applicant shall furnish the Authority with efficacy and safety data. The data shall be used to prove the efficacy of the product against the target organism when used normally under the claimed conditions of use. Published and/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 conducted in human and animal species; photo-allergenicity; photo-carcinogenicity shall be provided.

The efficacy and safety studies shall be carried out according to national guidelines or standards (where these are available and applicable) or internationally recognized guidelines or standards such as: -

(a) Individual manufacturer standard method approved by the Authority;
(b) Data from the actual development of the product approved by the Authority; or
(c) CEN, OECD, ASTM International Standards or any other internationally recognized standards.

The demonstration of efficacy, both *in vitro* and *in vivo* study reports shall be submitted taking into consideration the requirements stipulated in Table 2 below:

Table 2: Study reports required to support efficacy of the product

	1-In vitro test	**2 - In vivo test**
Test report which proves the antiseptic activity of the product	For surrogate and non-surrogate test organisms: one independent report.	For non-surrogate test organisms: one independent report.
		For surrogate test organisms: two independent reports.

Test reports shall include at a minimum: -

(a) Identification of the standard method used to verify the product efficacy;
(b) Proof of the effectiveness of the neutralizer utilized in the tests for both the reference standard and the test product;
(c) The relationship of each test to specific area of application;
(d) The type and level of soil load included in the test;
(e) 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;
(f) Initial number of the test organisms;
(g) Information on the batch number, expiry date, and date of manufacture for the batch tested;
(h) Proof of a washout period if a cross-over study is employed or if a subject is reused;

(i) Proof of glove compatibility for surgical scrub products;
(j) The minimum inhibitory concentration (MIC) for the product, when available; and
(k) Conclusion, describing whether the product meets the specific criteria relative to the reference method(s) employed.

Note:

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

2.4.3 Data to support specific claims

2.4.3.1 Antiseptic products used in professional food premises

For products that are intended to be used in professional food premises, data to demonstrate 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 shall be provided (after precautionary safety approaches are undertaken such as rinsing of hands with water or drainage of excess of the product).

An applicant shall provide data on Estimated Dietary Intake (EDI) resulting from the use of the product. This shall include any information that is used to estimate the dietary exposure such as, residual levels.

The applicant shall provide data on the mammalian oral toxicity of the product.

Data on claims made against a specific organism, antiviral claims, or those relating to persistence, sterility, time kill, % reduction and/or log-reduction shall be provided.

2.4.4.1 Log reduction claims

An Applicant claiming that a product has log reduction values (for example kills 99.9% of bacteria) shall submit data to support such claims for the specific formulation and using the recommended test methods.

For products intended for use in professional food premises and professional health care setting, a minimum log reduction in vivo should be demonstrated.

2.4.4.2 Persistence claims

Any claim for Persistence can only be made relative to an organism and this shall be supported by scientific data.

Professional-use surgical scrubs and preoperative patient skin preparations shall be required to demonstrate a minimum persistence of at least six (6) hours.

2.4.4.3 Time kill claims

Antiseptic products are expected to have a minimum time-to-effect of 30 seconds (for waterless hand rubs) to 1 minute (for washes or scrubs using water) upon completion of application according to the proposed directions for use. Applicants who submit products with claims of fast-action shall be required to submit data supporting this claim.

2.4.4.4 Sterility

An applicant who submits any products claiming to have a sterilizing effect shall submit supporting data.

2.4.5 Container closure system(s) and other packaging

The suitability of the container closure systems (primary and secondary) used for the final product shall be discussed.

The discussion shall include choice of materials, protection from moisture and light, compatibility of the materials of construction with the dosage form (including sorption to container and leaching) and performance.

A detailed description of the container closure system(s), including any liner or wadding, and details of the composition of each component shall be provided.

An applicant shall provide the specifications for any part of the container closure system(s), which comes into contact with the product or its protective including at least one (1) certificate of analysis. The specifications shall include parameters of description, identification and dimensions.

2.4.4 Labelling

Antiseptics intended to be placed on the Zambian market shall be labelled in English and shall have appropriate symbols in accordance with the Globally Harmonized Systems (GHS) of Classification and labelling of Chemicals. The applicant shall submit a proposed mock-up packaging label for the antiseptic including artwork.

A label shall contain a minimum of the following information: -

(a) Name of the product;
(b) Active substance(s): the identity and concentration of each active substance;
(c) Net contents (volume or weight/mass);
(d) Batch number;
(e) Name and address of the manufacturing site;
(f) Inclusion of appropriate symbols and cautionary statements such as for pressurized metal cans;
(g) Manufacturing date;
(h) Expiry date;
(i) Storage conditions (including the actual storage temperature);
(j) Precautions and warnings:

i. For external use only. Do not ingest **(labelled in red)**;
ii. Avoid contact with the eyes;
iii. Discontinue use and consult a health care practitioner if irritation and redness develops;
iv. Keep out of reach of children and animals; and
v. If swallowed, immediately seek medical attention.

(k) Other labelling information:

i. Labels which include the authorized claims shall also describe the intended area of application and specific attributes of the product, such as: bactericidal, fungicidal, mycobactericidal or virucidal;
ii. The label shall clearly reflect the same conditions of use as employed in the tests used to demonstrate efficacy (for example directions for use and warnings);
iii. Products with more than one indication or claim, label shall include the full warnings and adequate directions for use for each indication;
iv. If surrogates were used in testing this shall be stated on the labels;
v. Dispensing units that contain an antiseptic product shall be labelled as prescribed;
vi. Antiseptic products intended for commercial use shall bear the following statements on the label: -
    (a) For commercial use only;
    (b) For hand wash: "Use ….mL and lather in hands with water for at least 30 seconds. Rinse well"; or
    (c) For hand rub: "Use …mL and rub thoroughly into hands for at least 30 seconds. Allow to dry".
vii. Antiseptic products intended for professional food premises shall bear the following statements on the label: -
    (a) For use in food premises only;
    (b) To reduce bacteria, mycobacteria, fungi, and viruses on skin;
    (c) Avoid food contamination during use and storage;
    (d) Do not refill container;
    (e) This product may not be effective against parasites;
    (f) For hand wash: "Use …mL and lather in hands with water for at least 30 seconds. Rinse well";
    (g) For hand rub: "Use …mL and rub thoroughly into hands for at least 30 seconds. Allow to dry";
    (h) For volatile products: "after use of this product, food handlers' hands are to be dry and free of product residue prior to handling food products"; and
    (i) For non-volatile products: "after use of this product food handlers' are to rinse their hands with portable water prior to handling food products".

(l) Antiseptic products intended for professional health use, shall bear the following statements on the label: -

i. Allow product to evaporate completely prior to use in electrocautery procedures **[Note: only for alcohol-based products];**

ii. For healthcare hand wash only: Use … mL and lather in hands with water for at least 30 seconds. Rinse well;

iii. For healthcare hand rub only: Use … mL and rub thoroughly into hands for at least 30 seconds. Allow to dry;

iv. Do not refill container;

v. For professional hand wash or hand rub: "For Hospital and Healthcare Professional Use. To reduce bacteria, mycobacteria, fungi, and viruses on skin.";

vi. Surgical hand rub and hand wash: "For Hospital and Healthcare Professional Use. Preoperative antiseptic hand rub or surgical hand rub. To reduce bacteria and fungi on skin to diminish the risk of surgical site infection. Reapply every 6 hours or if hands are re-contaminated."; and

vii. Patient preoperative skin preparation: "For Hospital and Healthcare Professional Use. Preoperative antiseptic skin preparation. To reduce bacteria and fungi on skin to diminish the risk of surgical site infection. Reapply every 6 hours or if skin is re-contaminated".

(m) For antiseptic products containing ethanol or isopropanol only: -

i. Flammable;

ii. Keep away from open flame and sources of heat; and

iii. Keep container tightly closed.

(n) For all types of antiseptic products, the following statements may be allowed to be used on the labels: -

i. Antiseptic cleanser;

ii. Medicated cleanser; and

iii. Kills harmful bacteria or germs.

(o) For products containing povidone-iodine the following statement may be made for wound cleansing: "Apply to wound once or twice daily".

(p) For products intended as hand sanitizers the following statement shall be stated on the label: "Rub product onto hands and allow to dry".

3 SECTION 3: DISINFECTANTS

3.1 Introduction

The term "disinfectant" as defined and interpreted in these Guidelines is considered to include bactericides, fungicides, virucides, sporicides, sterilants, antiprotozoals, parasiticides or combinations of these.

3.2 Scope

These Guidelines apply to substances or mixture of substances manufactured, sold or presented for use in disinfecting premises in which food and medicines are manufactured, prepared or kept, health facilities, veterinary clinics, equipment and farm structures including domestic use.

3.3 Classification of Disinfectants

3.3.1 Classes of Disinfectants

Table 3

CLASSES OF CHEMICAL DISINFECTANTS	ALCOHOLS	ALDEHYDES	CHLORINE COMPOUNDS	IODOPHOR	OXIDIZING AGENTS	PHENOLIC COMPOUNDS	QUATERNARY AMMONIUM COMPOUNDS (QUATS)
Aqueous Concentration	70%	Variable	10% (500 to 5000 mg/L)	0.1-0.2%	3-6%	0.5 to 3%	
Activity Level	Intermediate	High to Intermediate	Intermediate	Intermediate to Low	High to Intermediate	Intermediate to low	Low

3.3.2 Classification of Disinfectants according to risk

For the purpose of these Guidelines, disinfectants are classified based on the risk level of the device and hard non-porous inanimate surfaces or inanimate objects on which the product is intended to be used on as shown in the table below:

Table No. 4: Classifications of disinfectants according to risk

Disinfectant class	**Risk level of device**	**Device definition**	**Definition of disinfectant class**
Gaseous sterilant and critical device sporicide, also referred to as critical sporicide	Critical	Present a high risk of infection if they are not sterile, that is contaminated with any organism, including spores. Routinely penetrate the skin or mucus membranes into normally sterile areas of the body (e.g., implants, scalpels, needles, surgical instruments, laparoscopes), or come into direct contact with recalculating body fluids, (e.g., kidney dialysis tubing and dialyzers, or blood oxygenators).	A disinfectant which helps achieves sterilization.
High-level Disinfectant.	Semi critical	Contact with mucous membranes during use but do not usually penetrate	A disinfectant that kills all microbial pathogens,
		Normally sterile areas of the body, e.g. endoscopes, anesthesia breathing circuits, respiratory therapy equipment, dental mirrors, etc…	except Large numbers of bacterial endospores according to labeling.
Intermediate level.	Non critical	Contact only intact skin during routine Use, e.g. stethoscopes, bedpans, etc...	A disinfectant that kills all microbial pathogens, except bacterial endospores, when used according to labelling.

3.4 Documentation requirements for registration

An applicant shall submit documents that demonstrate quality, efficacy and safety of the product including the material safety data sheet.

3.4.1 Manufacturing and marketing authorisation (Certificates and Licenses)

An applicant shall submit the following:

(a) A valid Manufacturing license for the manufacturing site of the product;

(b) A valid GMP certificate issued not older than 24 months from the last date of inspection; and

(c) Documentary proof of marketing authorisation (where applicable), for the submitted product(s) in the country of origin or any other country(s) and specifically those in the SADC region.

3.4.2 Chemistry, Manufacturing and Controls

3.1.1.1 Chemistry

3.4.2.1.1 Active ingredient(s)

An applicant shall provide the following:

(a) Information related to the active substance(s) where the active substance shall be identified by its non-proprietary name, chemical name and Chemical Abstract Service (CAS) number (if available);

(b) A copy of a certificate of analysis for the active substance(s) from the manufacturer of the active substance(s); and

(c) A copy of a certificate of analysis for the active substance(s) from the manufacturer of the finished product(s).

3.4.2.1.2 Non active substance(s)

An applicant shall provide the following:

(a) Information related to the active substance(s) where the active substance shall be identified by its non-proprietary name, chemical name and Chemical Abstract Service (CAS) number (if available);

(b) A copy of a certificate of analysis for the active substance(s) from the manufacturer of the active substance(s); and

(c) A copy of a certificate of analysis for the active substance(s) from the manufacturer of the finished product(s).

3.4.2.1.3 **Raw material (active and non-active substances) Quality control Specifications and analytical methods**

Summarized specifications for the active and non-active substance shall be provided, i.e. the acceptable limits of the entire physical-chemical parameters.

Justification for the specifications shall be provided.

Specification shall include but not be limited to:-

(a) Description;
(b) Identity - test method should be specific for active substance(s);
(c) Related substances/Impurities; and
(d) Assay - test method shall be specific and stability indicating for active substance(s).

A full description of the analytical and other control procedures carried out to ascertain the final product specifications stated above shall be provided.

An applicant shall provide one (1) copy of typical batch certificate of analysis for at least one (1) batch of active/inactive substance(s).

3.4.2.1.4 **Final Product Quality control**

Unit and Batch composition

An applicant shall be required to provide unit and batch composition as guided by the table below.

Table No.5: Unit and Batch composition

S.No	**Name of Ingredient**	**Reference Method** (IH, Pharmacopoeial)	**Quantity/Unit**	**Quantity/Batch**	**Reason for Inclusion**

Specifications and analytical methods

Summarized specifications for both release and shelf-life of the final product shall be provided, i.e. the acceptable limits of the entire physical-chemical parameters.

Justification for the specifications shall be provided.

Specifications shall include but not be limited to:-

(a) Description;
(b) Identity - test method shall be specific for active substance(s);
(c) Assay - test method shall be specific and stability indicating for active substance(s); and
(d) Additional specifications and test methods for liquid preparation shall include pH and Specific Gravity.

A full description of the analytical and other control procedures carried out to ascertain the final product specifications stated above shall be provided.

Three (3) copies of typical batch certificates of analysis for at least three (3) batches of the finished product(s) shall be provided.

3.1.1.2 **Manufacturing process**

An applicant shall:

(a) Describe all stages involved in the manufacture of the finished product. This shall be in the form of a detailed narrative and a simplified flow diagram accompanied by a list of equipment, including their capacities, used at each stage. Basic principles involved shall be clearly set out from dispensing to packaging. All stages shall be illustrated i.e. filling, weight checking, labelling, packaging and sealing. All steps involved and their operations shall be carefully described including the conditions subjected to each operation i.e. temperature, pH adjustments and processing time;

(b) Provide documentation on in-process control checks (sampling and testing at critical points); and

(c) Provide copies of batch manufacturing and packaging records for one production scale batch.

3.4.2.3 **Stability studies**

An applicant shall submit data on accelerated stability testing at conditions (40±2ºC/75±5 % RH) and long-term study at conditions (30±2ºC/65±5 %RH) for three batches for the finished product. In use stability studies shall be provided where applicable.

For more details please refer to Guidelines on Stability Studies, available at http://www.zamra.co.zm

3.4.3 **Efficacy and Safety**

An applicant shall furnish the Authority with efficacy and safety data. The data shall be used to prove the efficacy of the product against the target organism when used normally under the claimed conditions of use.

The efficacy and safety studies shall be carried out according to national guidelines or standards (if these are available and applicable) or internationally recognized guidelines or standards such as:-

(a) Individual manufacturer standard method approved by the Authority;
(b) Data from the actual development of the product approved by the Authority; or
(c) CEN, OECD, ASTM International Standards or any other internationally recognized standards.

3.4.3 **Container Closure System(s)**

The suitability of the container closure systems (primary and secondary) used for the final product shall be discussed. The discussion shall include choice of materials, protection from moisture and light, compatibility of the materials of construction with the dosage form (including sorption to container and leaching) and performance. A detailed description of the container closure system(s), including any liner or wadding, and details of the composition of each component shall be provided. An applicant shall provide the specifications for any part of the container closure system(s), which comes into contact with the product or it's protective including at least one (1) certificate of

analysis. The specifications shall include parameters of description, identification and dimensions.

3.4.4 **Labelling**

Disinfectants intended to be placed on the Zambian market shall be labelled in English and shall have appropriate symbols in accordance with the Globally Harmonized Systems (GHS) of Classification and labelling of Chemicals. An applicant shall submit a proposed mock-up packaging label for the disinfectant including artwork.

A label shall contain as a minimum the following: -

(a) Name of the product;
(b) Active substance(s): the identity and concentration of each active substance;
(c) Net contents (volume or weight/mass);
(d) Batch number;
(e) Name and address of the manufacturing site;
(f) Inclusion of appropriate symbols and cautionary statements such as for pressurized metal cans;
(g) Manufacturing date;
(h) Expiry date;
(i) Storage conditions (including the actual storage temperature); and
(j) Intended use:
    i. Claims (for example as a disinfectant, sterilant, sporicidal); and
    ii. Site of use (premises where food is manufactured, processed or kept, health care facilities) and the types of inanimate objects (for example, work surfaces, floors, walls in patient care areas) or medical devices (e.g., bronchoscopes, bedpans, contact lenses) to be disinfected. In addition, for contact lenses, the type of lens (for example soft, hard, gas permeable) should be specified.
(k) Directions for use:
    i. The label shall provide specific instructions to the user for preparing the in-use dilution of the product in order to achieve the intended antimicrobial effect. More than one dilution may be specified if several different applications are intended. In use period shall also be stated;
    ii. Contact time: More than one contact time shall be specified if several different applications are intended;
    iii. If the product is to be used at a specified temperature, that temperature shall be specified and the label shall indicate that heating or cooling to the specific temperature is required for efficacy;
    iv. Where applicable, the volume and directions for the use of an activator shall be indicated;
    v. The labelling for products not labelled for single use shall clearly indicate their expiry date after activation and/or dilution and reuse conditions as appropriate;
    vi. Disinfectants intended for use on medical devices shall include the statement: “Thoroughly clean the device prior to its disinfection”;
    vii. Appropriate rinse procedures to ensure the absence of unacceptable residues:

(a) Dilution containers; and

(b) Device surfaces before and after disinfection or sterilization are required.

viii. For products labelled with efficacy claims against blood borne viral pathogens such as HIV, HBV and HCV, the following additional labelling criteria should be included: -

(a) A term like "HIV" is acceptable, but shall also be identified as "human immunodeficiency virus". Similarly, the terms HBV and HCV are acceptable, but should also be respectively identified as “hepatitis B virus” and “hepatitis C virus”;

(b) Direction for use shall indicate that the product is intended for use against the blood borne pathogens listed on the label, for example, HIV, HBV, HCV, in settings where these microorganisms would be expected to be encountered, such as settings where contamination by blood or body fluids is likely; and

(c) Directions for use should also provide specific decontamination procedures, including: -

1. The need for surfaces to be cleaned prior to disinfection;
2. Personnel that clean items soiled with blood or body fluids: “wear appropriate barrier protection, such as disposable gloves, gowns, and masks”; and
3. Directions for the disposal of cleaning materials and waste.

(l) Precautionary statements, for example.

i. Warnings (labelled in red):-

(a) Keep out of reach of children;

(b) For External use only;

(c) Use in ventilated area; and

(d) Avoid contact with eyes.

ii. Use appropriate personal protective equipment (PPE), for example safety glasses, gloves, gowns;

iii. In case of contact, flush with water immediately and contact a doctor; and

iv. If swallowed, immediately seek medical attention.