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Spatial application mosquito repellents —

Specification —

Part 7 :

Tablets

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In order to match with technological development and to keep continuous progress in industries, standards are subject to periodic review. Users shall ascertain that they are in possession of the latest edition

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Foreword

Rwanda Standards are prepared by Technical Committees and approved by Rwanda Standards Board (RSB) Board of Directors in accordance with the procedures of RSB, in compliance with Annex 3 of the WTO/TBT agreement on the preparation, adoption and application of standards.

The main task of technical committees is to prepare national standards. Final Draft Rwanda Standards adopted by Technical committees are ratified by members of RSB Board of Directors for publication and gazettment as Rwanda Standards.

DRS 393-7 was prepared by Technical Committee RSB/TC 015, *Pharmaceutical Products*.

DRS 393 consists of the following parts, under the general title: *Spatial application mosquito repellents— Specification*:

— *Part 1: Coils*

— *Part 2: Spray*

— *Part 3: Candles*

— *Part 4: Papers*

— *Part 5: Liquid vaporizers*

— *Part 6: Vaporizing mats*

— *Part 7: Tablets*

— *Part 8: Liquid detergents*

Committee membership

The following organizations were represented on the Technical Committee on Pharmaceutical Products (RSB/TC 015) in the preparation of this standard.

National Industrial Research and Development Agency (NIRDA)

National Pharmacy Council (NPC)

University of Rwanda/College of Sciences and Technology (UR/CST)

Pharmacie NOVA

Rwanda Development Board (RDB)

AGROPY LTD

IKIREZI NATURAL PRODUCTS

HORIZON/SOPYRWA

Rwanda Social Security Board (RSSB)

Pharmavie

University of Rwanda/College of Medicine and Health Sciences (UR/CMHS)

Rwanda Biomedical Center/ Malaria and Other Parasitic Diseases Division (RBC/MOPDD)

Society for Family Health (SFH) – Rwanda

Rwanda Biomedical Center/Medical Procurement and Production Division (RBC/MPPD)

Institut d'Enseignement Superieur (INES) - RUHENGERI

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Introduction

Insecticides are used either for killing or controlling harmful insects. The insecticides which are applied for repelling insects are termed as “Repellents". Mosquito is one of the most harmful insects for mankind. To destroy them, many preparations are available on the market in various recipes like pest killer spray, soap, oil, powder, repellent etc. Out of these, mosquito repellent is the most popular as it has germicidal and disinfectant properties and is able to repel mosquitoes and is convenient to use.

The mosquito repellent is used for warding off mosquitoes which is the most harmful insect. Nowadays, mosquito repellents are used for controlling mosquito and are complimenting other mosquito destroyers gradually. With the rise in the standard of living, increasing urbanization and population, the demand of mosquito repellent mat is constantly increasing particularly in tropical places. It is a convenient method for protection against mosquito, so it has a tremendous market potential. Thus, there is a very good scope for development of such units in the country.

Spatial repellents are chemical products designed to be 'active' (requiring heat or electricity) or 'passive' (requiring no heat or electricity) and release volatile chemicals into the air within the treated space. Product examples that are currently available include mosquito coils, spray, candles, papers, liquid vaporizers, vaporizing mats, tablets and liquid detergents, among others. However, many more types of spatial repellent products are waiting to be developed.

Spatial repellents elicit ‘spatial repellency’ which refers to a range of insect behaviours induced by airborne chemicals that result in a reduction in human-mosquito contact. These behaviours include movement away from a chemical stimulus, attraction-inhibition and/or, and feeding inhibition.

Spatial application mosquito repellents — Specification — Part 7: Tablets

1 Scope

This Draft Rwanda Standard prescribes the requirements, sampling and test methods for spatial application mosquito repellents formulated and prepared as tablets.

This document covers, the following types of tablets formulation:

a) Tablets for Direct Application (DT);

b) Water Dispersible Tablets (WT), and

c) Water Soluble Tablets (ST).

2 Normative references

The following documents are referred to in the text in such a way that some or all of their content constitutes requirements of this document. For dated references, only the edition cited applies. For undated references, the latest edition of the referenced document (including any amendments) applies.

RS 191, *Refined pyrethrum concentrate — Specification*

RS ISO 2859-1, *Sampling procedures for inspection by attributes — Part 1: Sampling plans indexed by Quality Level (AQL) for Lot-By-Lot Inspection*.

RS 91, *Labeling and marking of pharmaceutical products — Specification*

AOAC 973.12, *d-trans-Allethrin in pesticides formulations*

CIPAC 741, *Determination of transfluthrin content*

CIPAC 743, *Determination of prallethrin (etoc) content*

CIPAC 993, *Determination of Metofluthrin (S1264)*

CIPAC 742, *Determination of d-allethrin*

CIPAC 977, *Determination of Meperfluthrin*

CIPAC 760, *Determination of picaridin*

CIPAC MT 30.5, *Determination of water content*

CIPAC MT 75.3, *Determination of pH values*

CIPAC MT 191, *Acidity or Alkalinity of formulations*

CIPAC MT 193, *Determination of the attrition of tablets*

CIPAC MT 185, *Wet sieve test*

CIPAC MT 184, *Determination of Suspensibility of formulations forming suspensions*

CIPAC MT 47.2, *Determination of persistent foaming*

CIPAC MT 179, *Dissolution degree and solution stability*

CIPAC MT 46.3, *Accelerated storage stability*

DRS 394-2, *Mosquito repellents — Performance Test Guidelines — Part 2: Spatial repellents*

3 Terms and definitions

For the purposes of this standard, the following terms and definitions apply.

3.1

tablet

small compressed solid substance, typically a measured amount of a medicine or drug

3.2

mosquito

any of numerous arthropod animals of the class mosquito, having an adult stage characterized by three pairs of legs and a body segmented into head, thorax, and abdomen and usually having one or two pairs of wings.

3.3

mosquito repellent

substance applied to skin, clothing, or other surfaces which discourages mosquito (and arthropods in general) from landing or climbing on that surface

3.4

dispersion

the action or process of distributing things or people over a wide area.

3.5

solubility

the property of a solid, liquid or gaseous chemical substance called solute to dissolve in a solid, liquid or gaseous solvent.

3.6

AQL

Acceptable Quality Limit

3.7

Transfluthrin

(1*R*,3*S*)-3-(2,2-Dichlorovinyl)-2,2-dimethyl-1-cyclopropanecarboxylic acid (2,3,5,6-tetrafluorophenyl)methyl ester

3.8

Etoc

Prallethrin. (S)-2-methyl-4-oxo-3-prop-2-ynylcyclopent-2-enyl(1R)- cis, trans-2,2-dimethyl-3-(2-methylprop-1-enyl) cyclopropanecarboxylate

3.9

Metofluthrin

$C_{18}H_{20}F_4O_3$, 2,3,5,6-Tetrafluoro-4-(methoxymethyl)benzyl 2,2-dimethyl-3-(prop-1-en-1-yl)cyclopropanecarboxylate

3.10

d-Alethrin

(RS)-3-allyl-2-methyl-4-oxocyclopent-2-enyl (1R)-cis, trans-chrysanthemate

3.11

Meperfluthrin

$C_{17}H_{16}Cl_2F_4O_3$, [2,3,5,6-tetrafluoro-4-(methoxymethyl)phenyl]methyl (1R,3S)-3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropane-1-carboxylate

4 Types

4.1 ***Tablets for Direct Application (DT)*** intended for application without prior dispersal or dissolution in water.

4.2 ***Water Dispersible Tablets (WT)*** intended for application after disintegration and dispersion in water by conventional spraying equipment.

4.3 ***Water Soluble Tablets (ST)*** intended for application after dissolution in water by conventional spraying equipment. STs contain an active ingredient which is totally soluble in water.

5 Requirements

5.1 General requirements

5.1.1 The Product shall consist of a homogeneous mixture of active ingredients, in the form of tablets, together with carriers.

5.1.2 The formulation shall be of dry, unbroken, free-flowing tablets and shall be free from visible extraneous matter.

5.2 Active ingredient

5.2.1 Natural repellents

5.2.1.1 Active ingredients used in natural repellents shall be natural plant based active ingredients such as essential oils or any other plant extract approved as mosquito repellents.

5.2.1.2 The manufacturer shall provide adequate data on the repellence/efficacy of such ingredients/product.

5.2.1.3 The manufacturer shall have adequate data justifying the proportion of ingredient(s) for which claims are made, used in the product.

5.2.1.4 The essential oils and other plant extracts used in natural repellents shall be, but not limited to:

a) Cedarwood oil;

b) Tea tree oil;

c) Geranium oil;

d) Rosemary oil;

e) Lemongrass oil;

f) Citronella oil;

g) Soybean oil;

h) Eucalyptus oil;

i) Cinnamon oil; and

j) Neem oil

5.2.1.5 The proportion of single or blended essential oil in natural repellent shall be set by the manufacturer in accordance with specific standard (s) of the essential oil used and records shall be availed.

5.2.1.6 Pyrethrum extracts such as pyrethrins shall be considered in natural repellents. The limits of pyrethrins in natural repellents shall not be less than 0.5 % and the extract used shall meet the requirements of RS 191.

5.2.2 Synthetic repellents

5.2.2.1 Synthetic repellents shall contain synthetic chemical compounds which are able to discourage mosquitoes and send them flying or crawling away.

5.2.2.2 If the synthetic chemical compound is blended with other active ingredient (s), either natural or synthetic, the proportion shall be set by the manufacturer based on scientific research and records shall be availed.

5.2.2.3 Active ingredients and their content in synthetic repellents shall meet the requirements prescribed in table 1.

Table 1 — Active ingredients content for synthetic repellents

S/N	Active ingredient % w/w	Limits	Identification method
1	DEET	5 – 50	Annex A
2	Permethrin, max	13	Annex B
3	Transfluthrin, max	1	CIPAC 741
4	Etoc	0.5 – 1.5	CIPAC 743
5	Metofluthrin (S1264), max	1.82	CIPAC 993
6	d-Alethrin (Pynamin Forte), max	5	CIPAC 742
7	Meperfluthrin , max	0.05 – 0.1	CIPAC 977

5.2.2.4 Synthetic repellents and their active ingredients shall be approved and registered by competent authority.

5.3 Specific requirements

5.3.1 Specific requirements for DT

5.3.1.1 The product shall be in the form of tablets for direct application.

5.3.1.2 The product shall comply with the quality requirements given in table 2.

Table 2 —Specific requirements for DT

S/N	Parameters		Requirements	Test methods
i.	Tablet dose uniformity		AQL of 3.5	ISO 2859
ii.	Uniformity of mass, % w/w (deviation in 20 tablets)	Less than 80 mg	± 10, minimum 18 tablets	International pharmacopoeia
			± 20, maximum 2 tablets	
		80 mg to 250 mg	± 7.5, minimum 18 tablets	
			± 15, maximum 2 tablets	
		More than 250 mg	± 5, minimum 18 tablets	
			± 10, maximum 18 tablets	
iii.	Water content, g/kg		20	CIPAC MT 30.5
iv.	pH		5 – 7	CIPAC 75.3
v.	Acidity as H_2SO_4, g/kg, max		4	CIPAC 191
vi.	Alkalinity as NaOH, g/kg, max		8	
vii.	Table integrity		No broken tablets	Visual
viii.	Tablet hardness, kg/cm^2		3.0 - 4.2	International pharmacopoeia
ix.	Degree of attrition, % by mass, max		1	CIPAC MT 193

5.3.2 Specific requirements for WT

5.3.2.1 The product shall be in the form of tablets for use after disintegration and dispersion in water.

5.3.2.2 The product shall conform to the quality requirements given in table 3.

Table 3 — Specific requirements for WT

S/N	Parameters	Requirements	Test methods
i.	Water content, g/kg, max	20	CIPAC MT 30.5
ii.	pH	5 – 7	CIPAC MT 75.3
iii.	Acidity as H_2SO_4, g/kg, max	4	CIPAC MT 191
iv.	Alkalinity as NaOH, g/kg, max	6	
v.	Disintegration time, minutes, max	3	International pharmacopoeia
vi.	Wet sieve test (75 µm test sieve), % w/w, max	95	CIPAC MT 185

vii.	Suspensibility, % w/w, min.	70	CIPAC MT 184
viii.	Persistent foam (after 1 min), mL, max.	50	CIPACMT 47.2
ix.	Degree of attrition, % w/w, max.	2	CIPAC MT 193

5.3.3 Specific requirements for ST

6.3.3.1 The product shall be in the form of tablets for use after disintegration and dissolution in water.

6.3.3.2 The product shall comply with the quality requirements given in table 4.

Table 4 — Specific requirements for ST

S/N	Parameters		Requirements	Test methods
i.	Water content, g/kg, max		100	CIPAC MT 30.5
ii.	pH		5 – 7	CIPAC 75.3
iii.	Acidity as H_2SO_4, g/kg, max		4	CIPAC MT 191
iv.	Alkalinity as NaOH, g/kg, max		6	
v.	Disintegration time, minutes, max		3	International pharmacopoeia
vi.	Degree of dissolution and solution stability, % by mass, max.	after 5 min on a 75 µm test sieve	Tite	CIPAC MT 179
		after 18 h on a 75 µm test sieve	Tite	
vii.	Wet sieve test (75 µm sieve test), % w/w, max.		2	CIPAC MT 185
viii.	Persistent foam (after 1 min), mL, max.		50	CIPAC MT 47.2
ix.	Tablet integrity		No broken tablets	Visual
x.	Degree of attrition, % w/w, max.		2	CIPAC MT 193

5.4 Storage stability

Stability at elevated temperature: After storage at 54 ± 2ºC for 14 days, the determined average active ingredient content shall not be lower than 95% relative to the determined average content found before storage and the formulation shall continue to conform to the requirements of the product. The storage stability shall be tested in accordance with CIPAC MT 46.3.

5.5 Biological efficacy

5.5.1 When tested in accordance with DRS 394-2, the product shall repel 100 % of the mosquitoes available in space, within protection time indicated by the manufacturer.

5.5.2 The protection time of the product shall be indicated on the label.

6 Sampling

Random samples of the product shall be drawn for test in accordance with RS ISO 2859-1 from the market, factory or anywhere else.

7 Packaging and labelling

7.1 Packaging

The product shall be packaged in a container which offers protection and maintains the integrity of the product.

7.2 Labelling

The containers shall be securely closed and in addition to the labelling requirements of RS 91, the following information shall be legibly and indelibly marked on the container:

a) name of the product;

b) indication of the source of manufacture;

c) batch number;

d) date of manufacture;

e) date of expiration;

f) total number of tablets in the container;

g) name and content of active ingredient (s);

h) protection time;

i) directions for use;

j) special population whose exposure is prohibited (children and pregnant women) ; and

k) storage conditions.

Annex A
(normative)

Determination of DEET content

A.1 General

The sample is dissolved in carbon disulfide and the difference in absorbance at 14.18 µm and at 14.48 µm is determined. The quantity of meta-isomer is obtained from this value by means of a calibration curve prepared by the use of a reference standard.

A.2 Apparatus

F.2.1 Double-beam infrared spectrophotometer. Perkin-Elmer model 21 or equivalent.

F.2.2 Two equivalent infrared absorption cells, with sodium chloride windows and a path length of approximately 0.4 mm.

A.3 Preparation of calibration curve

F.3.1 Weigh (to the nearest 0.1 mg) into four volumetric flasks sufficient amounts of the reference DEET standard of known purity to give concentrations of approximately 20, 40, 60 and 80 g/L when dissolved in carbon disulfide.

F.3.2 Fill the reference cell with carbon disulfide and the sample cell with each of the standard solutions in turn, and record the spectra. The spectrum may be scanned rapidly, except for the region 12 – 15 µm, where a normal speed should be used. Carry out a blank measurement with carbon disulfide to correct for any inequality in the paired cells and to determine whether a cell correction is required.

F.3.3 Measure the absorbance at 14.18 µm and at 14.48 µm and calculate the difference between these values, ΔA, for each of the solutions. Plot the values of ΔA against the concentration (g/l) of the meta-isomer.

F.3.4 If a cell correction is required, the value of ΔA is determined from the formula:

$$\Delta A = [A_{14.18} - A_{14.48}]_{ref.} - [A_{14.48}]_{blank}$$

Where ref. = determination with reference standard
blank = determination on CS_2 blank

A.4 Procedure

Weigh (to the nearest 0.1 mg) about 0.5 g of the sample, transfer quantitatively to a 10 mL volumetric flask, and make up to the mark with carbon disulfide. Measure the infrared absorption at 14.18 µm and 14.48 µm using the same conditions as described in section A.3. Determine the concentration of meta-isomer by comparing this value with the calibration curve. A standard sample should be run each day to check the calibration of the instrument.

A.5 Calculation

DEET content (g/kg) = $\frac{C1\ x\ P}{C2}$

Where,

C_1 = concentration (g/L) of standard DEET found from calibration curve

C_2 = concentration (g/L) of sample taken

P = purity (g/kg) of the reference standard.

Annex B
(normative)

Determination of permethrin

Permethrin as one of the active ingredients in this product may be determined using HPLC by injecting a solution of analyte into a chromatograph, followed by separation and comparison of peak areas of the analyte in the sample with that of an external standard.

B.1 Reagents

Cis – Permethrin, 99%

Trans - Permethrin, 99%

Methanol HPLC grade

Water, HPLC grade

B.2 Apparatus

An HPLC equipped with an autosampler, a variable wavelenght detector (or equivalent) and a column (phenomena x, 250 x 4.6mm Luna Phenyl 5µ Reverse phase (or equivalent)

B.3 Operating conditions

Flow rate	1.0mL/min
Solvent composition	60% : 40% (Methanol: Water)
Elution	Isocratic
Column temperature	40oC
Wavelength	240nm
Injection volume	25 µL
Stop time	50 minutes
Post time	2 minutes

B.4 Procedure

B.4.1 Preparation of standard solution

Weigh about 0.001g (to the nearest 0.0001g) Permethrin standard in beaker, use methanoldissolved and transfer them into a separate volumetric flasks (50 ml), dilute to the mark and mix well.

B.4.2 Preparation of Solution

Weigh about 0.02 g (to the nearest 0.0001g) Permethrin test sample into beaker, use methanol dissolved and transfer them into a separate volumetric flasks (50 ml), dilute to the mark and mix well.

B.4.3 Determination

After the chromatograph is stable, make a minimum of three injections of the standard as well as for the sample and average the area counts. The relative standard deviation between injections should be within 2%.

B.5 Calculation

The % of either cis or trans isomers is calculated as follows;

$$\%cisortranspermethrin = \frac{Averagesamplearea \times weightofstd \times purity(in\%)}{\text{Average std area} \times \text{weight of sample}}$$

Report the concentration of permethrin as the total of Cis and Trans.

Bibliography

[1] Manual on development and use of FAO and WHO specifications for pesticides, November 2010, 2nd Edition.

[2] Official Methods of Analysis of AOAC International, 19th Edition, 2012, volume I

[3] The International Pharmacopoeia, Seventh edition, 2017

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