



## ICA 10 F

Saltidin® (known as Picaridin in the US)

Issued 10 July 2009

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## 1. Preliminary Remarks

The use of repellents by application to skin and clothing is an important means of human protection against blood-sucking insects and ticks as well as arthropod-borne disease transmission.

Saltidin® belongs to a new generation of synthetic repellents developed as an alternative to DEET.

Developed by Bayer using molecular modelling techniques, Saltidin® showed the best performance among more than 800 substances against a variety of arthropods and the best characteristics as far as safety and compatibility with skin and plastic materials are concerned.

Presently, this molecule is owned by Saltigo GmbH (LANXESS Group) and is marketed by LANXESS Corporation (previously a Division of Bayer Corporation) in the USA and Canada.

Saltidin® is a safe and reliable insect repellent and stands for effective protection against various diseases transmitted by:

- ✓ Mosquitoes
- ✓ Ticks
- ✓ Flies
- ✓ Horseflies
- ✓ Sandflies
- ✓ Biting midges
- ✓ Fleas

Due to its broad spectrum of efficacy, its favourable toxicological and cosmetic properties, Saltidin® can be safely used by consumers.

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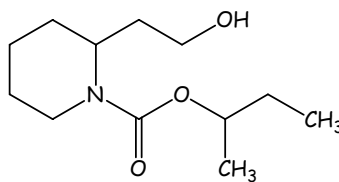
## 2. Physical and Chemical Properties

Chemical Name: 1-PIPERIDINECARBOXYLIC ACID, 2-(2-HYDROXY-ETHYL), 1-METHYLPROPYLESTER

Commercial Name: Saltidin®

Other Names: Icaridin, KBR 3023, Bayrepel™, Picaridin, (US EPA Registration)

Structure:



Empirical Formula:  $C_{12}H_{23}NO_3$

ELINCS Number: 423-210-8

CAS Number: 119515-38-7

Molecular weight: 229.3 g/mol

Melting point:  $< -170\text{ °C}$

Boiling point:  $272\text{ °C}$  at 1013 hPa

Viscosity: 30.7 sec. flow time accord. To DIN 53211, Dynamic: 129 mPa.s at  $20\text{ °C}$

Vapour pressure:  $3.4 \times 10^{-4}$  hPa at  $20\text{ °C}$

$5.9 \times 10^{-4}$  hPa at  $25\text{ °C}$

$7.1 \times 10^{-3}$  hPa at  $50\text{ °C}$

Flash point:  $142\text{ °C}$

Density:  $1.036\text{ g/m}^3$  at  $20\text{ °C}$

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Solubility:	In water:	8.6 g/L at 20 °C
	In propane-2-ol:	> 250 g/L at 20 °C
	In acetone:	> 250 g/L at 20 °C
	In n-heptane:	> 250 g/L at 20 °C
	In xylene:	> 250 g/L at 20 °C
Appearance:	Clear liquid, colourless to brownish	
Odour:	Slightly odorous	
Storage conditions:	Store at room temperature	

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### 3. Formulation

#### ICA 10 F – 10 % Lotion Formulation

##### 3.1 Formulation:

No	Ingredient	CAS Nr	Content %
1	Ethanol abs DBA	64-17-5	29,0
2	Polyethylene glycol 400	Not applicable	14,2
3	Floral D 12889 G	Not applicable	0,5
4	Saltidin®	119515-38-7	10,13
5	G-Water	7732-18-5	46,17

##### 3.2 Preparation

1. Place aqueous Ethanol in a receiver and add the scent under stirring for 5 minutes.
2. Add Saltidin® and stir for another 5 minutes until Saltidin® is dissolved.
3. Dilute the clear solution with water and stir for additional 5 minutes.

##### 3.3 Stability

Short term stability for 6 weeks.

This clear lotion is stable after storage for 6 weeks at 20 °C, 40 °C, 45 °C and at 50 °C.

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#### 4. Toxicological Data

The toxicological properties of the proposed formulation have been assessed on the basis of available data, in accordance with the above intended usages on behalf of Saltigo GmbH (Germany). The studies are described in the report: "ICARIDIN. Tier II Summary Reports for Acute Studies All-Family Insect Repellent Spray (EP)", October 27, 2007.

<b>Extrapolated Acute Toxicity and Precautionary Signal Words for ICA 10 F (10 % Lotion Formulation)</b>			
<b>Study type</b>	<b>Species</b>	<b>Results</b>	<b>EU Classification</b>
<b>Acute Oral</b>	Rat LD <sub>50</sub>	Male and Females = > 5050 mg/kg	Not classified
<b>Acute Dermal</b>	Rat LD <sub>50</sub>	Male and Females = > 5020 mg/kg	Not classified
<b>Acute Inhalation</b>	Rat LC <sub>50</sub>	> 30.2 mg/L (4-hours)	Not classified
<b>Eye Irritation</b>	Rabbit	No Eye Irritation	Not classified
<b>Skin Irritation</b>	Rabbit	No Skin Irritation	Not classified
<b>Dermal Sensitization</b>	Guinea Pig	Non Sensitizing	Not classified

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## 5. Efficacy Studies

The efficacy of the proposed formulation has been assessed on the basis of available data, in accordance with the above intended usages on behalf of Saltigo GmbH (Germany). Reported here below are efficacy data against mosquitoes, flies and sandflies obtained with formulations containing 10 % of Saltidin®. The studies are summarized in the report: "ICARIDIN. Summary Report of Efficacy Data", Report N° 07-LX-12, October 20, 2007.

### 5.1 Effectiveness Against Mosquitoes

Saltidin® has been shown to be a safe and effective repellent against various species of mosquitoes (e. g., *Aedes aegypti*, *Aedes albopictus*, *Culex quinquefasciatus*, and *Anopheles dirus*). Two types of protocols were used for testing the efficacy of Saltidin® on Mosquitoes: cage tests on human volunteers and field tests on human volunteers.

Cage tests on human volunteers were conducted during the development of the product to estimate the efficacy of the product and to compare different formulations of the product under standardized conditions.

The tests by Yap et al. (1997) were conducted in screened cages (1 x 1 x 1m) with circular openings (15 cm in diameter) fitted with cloth sleeves. Eight volunteers (6 male and 2 females) were involved in the experiment. The application rate was 150 µL/90 cm<sup>2</sup>. The applied product was left to dry before covering it with a rubber sleeve with an opening window of 25 cm<sup>2</sup> as a surface for landing/biting activities of mosquitoes. Both hands of the volunteers were covered with thick rubber gloves up to the wrists to prevent unwanted bites.

In the study by Luepkes (2005), the test protocol was similar to the Yap protocol: the cages measured 90 x 30 x 40 cm and the application rate was 150 µg/90 cm<sup>2</sup>.

The results showed that the 10 % formulation provided 4 - 8 hours protection compared to 4 - 6 hours for DEET (Table 1).

ICA 10F formulation was tested with the same protocol above described (cages measured 90 x 30 x 40 cm and the application rate was 150 µl/90 cm<sup>2</sup>) by Luepkes (2009), obtaining 5.4 hours protection.

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Table 1: Efficacy (Protection time = PT) of 10 % Saltidin® and DEET formulation against mosquitoes in cage tests.

Test Species	Test Location (Time of test)	Saltidin®		DEET		Study ID/Reference
		(%)	PT (h)	(%)	PT (h)	
<i>Aedes aegypti</i>	University Sains, Malaysia	10.0	4.0	10.0	<4.0	Yap et al., 1997 <sup>[1]</sup>
<i>Aedes aegypti</i>	BioGenius, Germany	10.0	4.6	Not determined		Luepkes, 2005 <sup>[2]</sup>
<i>Anopheles dirus</i>	University Sains, Malaysia	10.0	8.0	10.0	6.0	Yap et al., 1997 <sup>[1]</sup>
<i>Aedes aegypti</i>	BioGenius, Germany	10.0	5.4	Not determined		Luepkes, 2009 <sup>[3]*</sup>

\* tests carried out on ICA 10F formulation

Field tests were designed to determine the efficacy of products under real life conditions. It is common knowledge that cage tests are more conservative and that often the protection time for the cage tests is lower than in field tests. Therefore, field studies are important in order to establish the efficacy of the product. For this reason, this report will focus on field studies and on the more relevant data obtained from the cage tests using animals and human volunteers.

In the study by Yap et al. (1998), the trials against *Aedes albopictus* were conducted outdoors in a plantation on Penang Island during the day in order to coincide with the day-time biting activities. The trials against *Culex quinquefasciatus* were conducted in the living rooms of residential houses during the night to coincide with peak biting activities. The dosages tested for the repellents formulation were 1 ml on the leg and 0.5 ml on the hand.

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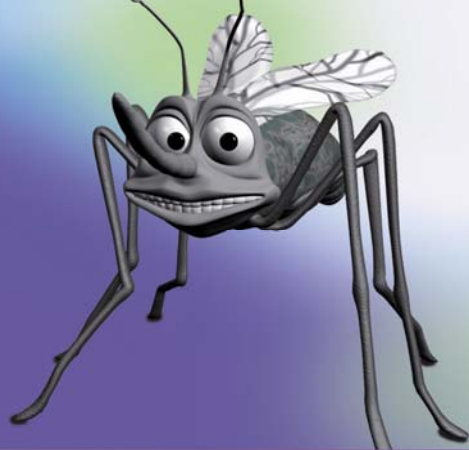


Table 2: Efficacy (Protection time = PT) of 10 % Saltidin® and DEET formulation against mosquitoes in field tests.

Test Species	Test Location (Time of test)	Saltidin®		DEET		Study ID/ Reference
		(%)	PT (h)	(%)	PT (h)	
<i>Aedes albopictus</i>	Residential-Mainland Peninsular, Malaysia (Day)	10.0	4.0	10.0	4.0	Yap et al., 1998 <sup>[4]</sup>
<i>Culex quinquefasciatus</i>	Residential-Mainland Peninsular, Malaysia (Night)	10.0	8.0	10.0	8.0	Yap et al., 1998 <sup>[4]</sup>

From the results of all the laboratory and field tests carried out by various researchers and in various parts of the world, it may be concluded that the formulation containing 10 % Saltidin® provides 8 - 9 hours of protection (Table 2). It can also be concluded that the performance of Saltidin® proves to be similar to DEET in comparative studies.

## 5.2 Effectiveness Against Flies

In the efficacy tests carried out against flies, LANXESS used a low quantity of Saltidin® (7.5 - 12.0). The repellence against this kind of insect is high even with this amount and even higher with a 20 % Saltidin® content.

Efficacy of formulations containing 7.5 % Saltidin® was determined against tabanids under field conditions. The study was conducted in Austria by Prof. Muelhofer (1993) at the LHS - Labor fuer Hygiene and Sicherheit (Laboratory for Hygiene and Safety). The following abundance of various species was present: *Tabanus bovinus*, 35 %; *Haematopota pluvialis*, 30 %; *Stomoxys calcitrans*, 20 %; and *Chrysops relictus*, 15 %.

Ten volunteers (5/product) wearing protective sleeves with a 10 x 10 cm<sup>2</sup> opening were used in the test. 200 µl of the tested product were applied to each volunteer. The exposure time was 30 minutes and the test was repeated every hour. The test was stopped when one bite occurred over a 30 minute test period. The overall protection time

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(average of all insect densities) for 7.5 % Saltidin® was five hours and for DEET was six hours (Table 3). At normal insect densities, protection time for 7.5 % Saltidin® was 6 hours and for 10 % DEET was 7 hours. At high insect densities, the corresponding values were 4 and 6 hours. Under extreme insect pressure, the efficacy declined to 4 hours for Saltidin® and to 5 hours for DEET.

Table 3: Efficacy (Protection time = PT) of 7.5 % Saltidin® and 10 % DEET formulations against flies in field tests.

Test Species	Test Location	Saltidin®		DEET		Study ID/ Reference
		(%)	PT (h)	(%)	PT (h)	
<i>Tabanus bovinus</i> , 35 %; <i>Haematopota pluvialis</i> , 30 %; <i>Stomoxys calcitrans</i> , 20 %; <i>Chrysops relictus</i> , 15 %.	Austria	7.5	5.0	10.0	6.0	Muelhofer, 1993 <sup>[5]</sup>

In a cage test by Nentwig (1997), a formulation containing 12 % Saltidin® was tested against *Stomoxys calcitrans*. The insects were placed in cages (90 x 30 x 40 cm, with gauze side walls) equipped with two cloth sluices. 90 cm<sup>2</sup> of each forearm of a volunteer was treated with 150 ul of the test product. A sleeve with an opening of 25 cm<sup>2</sup> was fastened around the arm: the opening was positioned over the treated area. Both arms were introduced into the cage through the cloth sluice and the number of bites per arm in a three minutes test period was registered.

The protection time for the Saltidin® formulation was 7 hours compared to 4 hours for DEET (Table 4).

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Table 4: Efficacy (Protection time = PT) of 12.0 % Saltidin® and 17.0 % DEET formulations against flies in cage tests.

Test Species	Test Location	Saltidin®		DEET		Study ID/Reference
		(%)	PT (h)	(%)	PT (h)	
<i>Stomoxys calcitrans</i>	Bayer Laboratory, Monheim, Germany	12.0	7.0	17.0	4.0	Nentwig, 1997 <sup>[6]</sup>

### 5.3 Effectiveness Against Sandflies

The efficacy of the formulations was tested on the laboratory bred strain of *Phlebotomus (Phlebotomus) duboscqi* in human volunteers (Perrotey *et al.*, 2002, laboratory report and Pesson and Perrotey, 2005, published short communication). A 50 % DEET formulation was also tested for comparative purposes.

In the test, a group of 30 unfed female insects were released into gauze cages (20 x 20 x 20 cm). The test was carried out with six human volunteers (three males and three females). The repellents were applied to the back of the hand and wrist. During the test, a latex glove was worn with a square opening (4 x 4 cm) permitting skin exposure of only a part of hand and wrist. The treated surfaces were exposed in the cage for 5 minutes at hourly intervals until one bite was recorded, terminating the test.

The results of laboratory test with human volunteers showed that Saltidin® formulation had a high degree of repellence against *P. duboscqi* (8.8 hours). The formulation containing 50 % DEET provided 8.4 hours protection. It can be concluded that Saltidin® is highly effective against Sandflies (Table 5).

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Table 5: Efficacy (Protection time = PT) of 10.0 % Saltidin® and 50.0 % DEET formulations against sandflies in cage tests.

Test Species	Test Location	Saltidin®		DEET		Study ID/ Reference
		(%)	PT (h)	(%)	PT (h)	
<i>Phlebotomus</i> ( <i>Phlebotomus</i> ) <i>duboscqi</i>	Parasitology laboratory, Strasbourg, France	10.0	8.8	50.0	8.4	Perrotey et al., 2002 <sup>[7]</sup>  Pesson and Perrotey, 2005 <sup>[8]</sup>

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## 6. References

- [1] Yap, H.H. et al. (1997) Progress report of the various tests some of which were published.
- [2] Luepkes, K. H. (2005) Mosquito Repellent Effects of Various Formulations Based on Bayrepel/KBR 3023 against Yellow Fever Mosquito *Aedes aegypti*. Unpublished LANXESS report.
- [3] Luepkes, K. H. (2009) Repellent Effect of Various Formulations. Mosquito repellent effect of two formulations against Yellow Fever Mosquito *Aedes aegypti*. Unpublished LANXESS report.
- [4] Yap, H. H., Jahangir, K., Chong, A. C. S., Adanan, C. R., Malik, Y. A., and Rohaizat, B. (1998) Field Efficacy of a New Repellent, KBR 3023, against *Aedes albopictus* (SKUSE) and *Culex quinquefasciatus* in a Tropical Environment. *Journal of Vector Ecology* 23(1): 62-68.
- [5] Muehlhofer (1993) LHS- Labor fuer Hygiene and Sicherheit (Laboratory for Hygiene and Safety, Austria). Unpublished LANXESS report.
- [6] Nentwig (1997) Efficacy of a formulation with 12 % KBR 3023 in comparison to a formulation with 17 % Deet on human arms against three different blood sucking diptera. Bayer Report No. 018032.
- [7] Perrotey, S, Madulo-Leblond, G., and Pesson, B. (2002) Laboratory testing of the insect repellent KBR 3023 against *Phlebotomus duboscqi* (Diptera: *Psychodidae*). *Parasitol Res* (2002) 88:712-713. DOI 10.1007/s00436-002-0635-2.
- [8] Pesson, B. and Perrotey, S. (2005) Study of the Repellent Efficacy of BAYREPEL® on *Phlebotomine* Sandflies: testing of new AUTAN® products on laboratory-bred *Phlebotomine* Sandflies. Unpublished LANXESS report.

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