Workshop on Repellents
Information about IR3535- and DEET-based products

Belgium input

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Before questions ...

SOME EXAMPLES
**Aerosol with 30% IR3535**

**Claims / Applicant**
- Repellent on skin; on clothes
- against mosquitoes, ticks, biting flies, wasps and bees
- in temperate and tropical areas
- 8 hours protection time

**Submitted data**

- Lab test with human volunteers with 0.00134 g product (30% IR3535)/cm² against *Ixodes scapularis* => 11 hours protection time
- Lab test with human volunteers, with 0.0018 g product (15% IR3535 pump spray)/cm² against *Ixodes ricinus* => 8 hours protection time
- Field tests (2 locations) with human volunteers with 0.000987 g product (30% IR3535)/cm² against mosquitoes. Exposure time = 1 min => 11 hours protection time

- Effective against ticks and mosquitoes
  - With 0.0018 g product /cm²
  - 8 hours protection time
  - In temperate conditions

- Effective only against mosquitoes
  - With 0.000987 g/cm²
  - 8 hours protection time
  - In temperate conditions
Spray with 20% IR3535

Claims / Applicant
- Repellent on skin
- against mosquitoes, ticks, biting flies (stable and sand flies), harvest mites, wasps and bees
- in temperate areas
- 8 hours protection time

Submitted data
- “Arm-in-cage” test with human volunteers, with 0.0018 g product (20% IR3535 spray)/cm² against mosquitoes (*Aedes sp* + *Culex sp*) or stable flies and against sand flies => 8 and 7 hours protection time respectively
- Choice-test with mice, with 0.0018 g product (20% IR3535 spray)/cm² against sheep ticks (*I. ricinus*) or against harvest mites (*Trombicula autumnalis*) => 6 and 5 hours protection time respectively
- Trap tests, with 0.0018 g product (20% IR3535 spray)/cm² against wasps or bees => 8 hours protection time

- Effective against mosquitoes, ticks, biting flies (stable and sand flies), harvest mites, wasps and bees
- With 0.0018 g product/cm²
- 5 hours protection time
- In temperate conditions
“Travel” Spray with 30% DEET

**Claims / Applicant**
- Repellent on skin
- against mosquitoes
- in temperate and tropical areas
- 8 hours protection time

**Submitted data**
- “Arm-in-cage” tests with human volunteers, with 0.0018 g product (30% DEET spray)/cm² against mosquitoes:
  - *Culex pipiens* => 8 hours protection time
  - *Aedes aegypti* => 8 hours protection time
  - *Aedes albopictus* => 7 hours protection time
  - *Anopheles gambiae* => 6 hours protection time

- Effective against mosquitoes
- With 0.0018 g product /cm²
- 6 hours protection time
- In temperate and tropical conditions
**Spray with 30% DEET**

**Claims / Applicant**
- Repellent on skin
- against mosquitoes
- in temperate areas
- 8 hours protection time

**Submitted data**
- Field test with human volunteers with 0.0018 g product (30% DEET spray)/cm² against mosquitoes. Exposure time = 3 min => 8 hours protection time
- “Arm-in-cage” tests with human volunteers, with 0.0018 g product (30% DEET spray)/cm² against mosquitoes:
  - *Culex pipiens* => 4 hours protection time
  - *Aedes aegypti* => 3-4 hours protection time

**Conclusion?**
- Effective against mosquitoes
- With 0.0018 g product/cm²
- 8h Protection time?
- In temperate and tropical conditions
Questions to WS-participants
Target organisms

- **Can we accept efficacy tests performed with *Ixodes scapularis* (deer tick)?**

NO / MS answers to NL e-consultation (July 2012)

⇒ BE eCA do not accept the tests with *Ixodes scapularis* (deer tick) according this e-consultation

According to the document TNsG-Eff_PT18&19, a product against ticks should normally be tested on the European sheep tick *Ixodes ricinus*.

American deer tick (*Ixodes scapularis*) is also a hard-bodied tick (family *Ixodidae*) but mainly found in America. *Ixodes scapularis* is also a vector for several diseases of animals, including humans.

Even if *Ixodes scapularis* seems to be very similar to *Ixodes ricinus*, we have no information about the relative susceptibility of both *Ixodes* species to IR3535 or to DEET.
Test method and pass criteria (1)

- **Exposure time**: 1 min instead of 3 min acceptable in field conditions?

  Based on EPA guideline - Due to high biting pressure

- Can we accept that the Applicant provides only “Arm-in-Cage” tests with human volunteers to prove efficacy of products against mosquitoes?

  YES / MS answers to FR e-consultation: field tests not mandatory (mosquitoes) / available literature, reasons of standardization of testing and ethics.

- Can we accept that the Applicant provides only “Arm-in-Cage” tests with human volunteers to prove efficacy of products against sand flies?
Test method and pass criteria (2)

- Can we accept that the Applicant provides only “Arm-in-Cage” tests with human volunteers to prove efficacy of products against biting flies?

- Can we accept claims against mosquitoes based only on field tests i.e. without submission of “Arm-in-Cage” tests?

+ High discrepancy between test results:

“Arm-in-Cage” tests: 3-4h Protection Time / Field tests (8h Protection Time)

What is the more relevant protection time?
Test method and pass criteria (3)

- **Test method and pass criteria to prove efficacy of products against head lice?**

  Requirements and pass criteria for repellents used against lice are not currently mentioned in the TNsG on Product Evaluation-PT18&19!

  Lice are irritating, not highly dangerous but they might spread diseases and may be considered as a public health issue.

  ⇒ A repellent against lice might be considered to be sufficiently “effective” if:
  
  • ≥ 90% repellence can be achieved in lab conditions?
  • ≥ 80% repellence in field conditions?

  Comparative bio-clinical *in vivo* trials (done in a real-life setting) acceptable? Lab tests mandatory? From what we know, head lice cannot be bred in the laboratory and only have a very limited life span in the laboratory settings.
Test method and pass criteria (4)

- Test method and pass criteria to prove efficacy of products against harvest mites (*Trombicula autumnalis*)?

Tube choice test with mice (similar to the test used for ticks – “worse case” test §7.2.2.2 TNsG) acceptable (might spread diseases - ethics) ?

“Arm-in-Cage” tests more appropriate ?
All the efficacy tests have to be performed with the product (in its finale formulation) for which the authorization is sought !!!

- Can we consider efficacy tests performed on a pump spray to validate efficacy for an aerosol? Or efficacy tests performed on a lotion to validate efficacy for a spray?

Pump spray with 20% IR3535
/ The aerosol formulation with 20% IR3535 and a propellant which is lost after evaporation from the spray resulting in an higher applied concentration of IR3535 on skin (efficacy tests performed with the solution sprayed into a receptacle)
Application rate/Protection time

- Is it acceptable to set only one application rate/protection time for all the target organisms validated?

Considering that labels with multiple application rates/protection times for different target organisms is very confusing for consumers and may create some misunderstanding leading to misuses! Can consumers make the distinction between different mosquito species, biting flies, ... ? By taking into account the application rate/protection time identified for the most resistant target organism?

- How to mention the application rate on the label to be easy for consumers to observe?

Mentioning application rate such as 0.0018 g product/cm² is useless for the consumer! Number of pumps? Seconds of spraying? Amount of creamy product / volume of a walnut-nut-pea? Is a statement such as “sufficient wetness” acceptable?
Application rates for repellents: Efficacy & Risk assessment

**Basic principle**: Risk assessment should be performed according to the application rates validated from efficacy studies!

According to the default human factor values agreed in the HEEG Opinion 17, the following surface to body ratios should be used:

**Example for an adult (62.8 kg)**: 277 cm²/kg ⇔ 17396 cm²

Assuming that a short-sleeved shirt (i.e. T-shirt) and shorts are worn, 64% of the total body surface remains uncovered and is treated with repellent ⇔ 11133 cm²

- With 1g BP / 600 cm² ⇔ 1.8 mg BP / cm² ≈ 20 g BP per application
- With 0.987 mg BP / cm² ≈ 11 g BP per application

- *In the CAR for IR3535*: 3g BP per application as “safe” application rate
- *In the CAR for DEET*: 6g BP per application as “safe” application rate

=> Values to be used to perform the Risk Assessment?
Thank you very much for your attention!
The floor is yours.

what do you think?