

## Guide to efficacy studies, especially for product type 18 and 19.

**Below is a brief presentation of the requirements that must be met in order for The Danish Environmental Protection Agency to consider efficacy of an insecticide or repellent (PT18 and 19). The guide contains general requirements that can inspire applicants within other product types.**

The text refers to "Appendix to chapter 7 in Technical notes for guidance on product evaluation – product type 18 and product type 19" (TNSG). This appendix describes in detail the requirements regarding efficacy studies and explains these requirements for the individual pest species or groups of species. TNSG is available from the ECHA homepage:

[http://echa.europa.eu/documents/10162/16960215/bpd\\_guid\\_tnsg-product-evaluation\\_en.pdf](http://echa.europa.eu/documents/10162/16960215/bpd_guid_tnsg-product-evaluation_en.pdf)

### Active substance or product?

Applicants have to be fully aware that it is the entire **finished product** and its **directions for use** that are considered for approval and not the active substance contained in the product. Usually the active substance itself is well known, and its effects on the relevant pests are known. What is to be assessed is the entire, formulated product in the packaging and with the directions for use under which it is to be made available on the market.

The product must apply to all points mentioned in the directions for use. Below some possible pitfalls are outlined:

#### Example 1

An applicant applies for approval of an ant bait station containing an effective bait; unfortunately, the ants do not like the station itself and will not enter it. Therefore, the entire formulated product does not fulfill the requirement concerning efficacy, even though the bait is attracting ants and the active substance considered effective.

#### Example 2

An applicant formulates an aerosol for flying insects for which the active sub-

stance is well known and effective, but a wrong type of nozzle or too low pressure or the wrong propellant is applied. This means that the tiny drops do not hang in the air as they must to be able to hit the flying flies; instead drops fall to the ground too quickly, and only very few flies are hit.

### Example 3

An applicant intends to launch a product for flies in stables, based on a sugar containing bait. However, a very large part of flies in stables may be stable flies, which do not eat sugar and therefore are not attracted by the bait. In this situation the claim must be more specific than “flies”. On the other hand, if the product in question is an aerosol, the term “flies” will be sufficiently precise because all flies flying about in the stables will be affected – irrespective of species.

## Directions for use

The direction for use provides the very basis of the efficacy assessment. What is described here determines the requirements regarding the necessary documentation. Therefore, there is a great deal of information, which both the user and those authorities, assessing the efficacy, must be able to obtain by reading the directions for use.

### **"Normal use" and "conditions for the approval"**

The directions for use are always assessed compared with what is considered normal use and in accordance with the conditions that may be imposed on the product.

Thus, the applicant must consider what “normal” use is as well as consider the “conditions for the approval” by answering the following 5 points in relation to the product in question:

1. Which type of formulation is it?
  - Spray, ULV (ultra low volume) product, bait, powder, aerosol, skin lotion, etc.
  
2. Method of application?
  - Surface treatment (applied with a brush, low-pressure spray equipment, etc.)
  - Treatment in cracks and crevices
  - Spraying directly on to the pests

- Room treatment (fogging)
- Treatment of specific, small areas
- Laying out as bait
- Powdering

### 3. Application rate

The applicant must indicate the dose or application rate of the product. This can sometimes be difficult, since treatments with products for use in household or industries are not always carried out uniformly. Nevertheless, an application rate must be provided. The application rate is a precondition for the consumer's use of the product and for the assessment of the submitted efficacy data.

Examples of application rates can be:

- Number of bait stations per m<sup>2</sup>
- Volume per m<sup>2</sup>
- Volume per m<sup>3</sup>
- Gram per m<sup>2</sup>
- Spray for "a number of" seconds per linear metre

### 4. Are several treatments required?

For some products repeated treatments are required for sufficient efficacy. In this case information on number and frequency of treatments must be available in the directions for use.

### 5. Additional subjects to consider

There might be preconditions, which should be met, such as:

- The surroundings needs to be cleaned prior to treatment
- The product is to be used together with another product
- The product is to be part of a broader control strategy
- Avoiding the use of hot water after treatment
- Avoiding treatment in places where domestic animals can access the product.

### **What does the product do and what is the advantage of using it?**

It must appear from the directions for use, which specific pest or group of pests you intend to control. Here you have three options:

1. Stating precisely which pest you intend to control with the product, for example German cockroaches. In this case, you must present efficacy data for the specific label claims.

2. Stating several specific species, which you intend to control, for example German cockroaches and bedbugs. In this case, you must present efficacy data for each species listed.

Pests may be mentioned in general terms, e.g. *crawling insects* or *flying insects*. In this situation the applicant must present documentation for specific representative species, as documentation for all crawling or flying insects is not feasible. The choice of representative species may vary according to what you wish to write in the directions for use. Generally, two cockroach species – German cockroach and one of the large species like Oriental cockroach or American cockroach – will be sufficient for an approval. Data for housefly, hornet and mosquitoes are sufficient for an approval for flying insects. However, studies of other relevant species may also be considered. One needs to be aware that if specific species are added to these otherwise general products, one must present documentation for the species mentioned. If, for example, one is to claim “- in warehouses” to “crawling insects”, one should also present studies of relevant store pests.

If, for example, you claim in the directions for use that the product “kills instantly” or “...has a certain long-term effect”, you must also provide documentation for these specific claims.

#### **At which level do you achieve an effect by using the product?**

1. Effect at individual level:

The product kills a few or a certain number of individuals of a pest species. This means that when you use the product directly on the insect, it will die, but you do not claim that the product controls all the insects at the site. For example: you spray directly on some cockroaches in a kitchen. It will kill them, but it will not kill all the cockroaches that are hiding.

2. Effect at population level:

The product is able to exterminate an entire population or to prevent a population from expanding.

#### For example:

A kitchen is treated with a barrier, which the cockroaches are forced to pass in order to get to water and food. After some time the entire cockroach population will be exterminated.

## The efficacy assessment

### Which documentation can be used for an efficacy assessment?

Studies included in the efficacy assessment must substantiate the effect that is described in the directions for use. Not many specific guidelines cover the pests and uses included in the notes for guidance on efficacy assessments (product type 18 and product type 19). The use of specific guidelines is therefore not a precondition for a study to be considered acceptable and for it to be included in the evaluation. All studies, published or non-published, will be assessed on the basis of their content. However, one precondition is that methods and results are described in such detail that the study can be repeated on the basis of this description.

Documentation in the form of descriptions of what one or more persons have experienced when using the product cannot be used in connection with an efficacy assessment. Thus, studies based on health claims from private persons, companies or “experts” and not followed up by concrete, well-documented data material will not be included in the efficacy assessment.

### Which types of studies must be provided?

You must provide:

1. laboratory studies
2. studies simulating the end use of the product and
3. field studies.

Please note that all three types of studies must be present in the documentation material. Simulated tests may be excluded if several good field studies are available. All tests must be carried out with the pest insects that you claim the product is effective against. The requirements regarding field studies can deviate a little in very special cases. In these cases, the field studies can be replaced by so-called “semi-field trials”, which means that you create a situation under monitored conditions that resembles the way in which the product is to be used and then carry out the study under these conditions. When this is relevant and for which types of products can be seen from the detailed exposition in TNSG.

“Field studies” means studies carried out in places where the product is to be used, such as private dwellings, industrial kitchens, piggeries, cowhouses, stables, grain stores, etc.

## Requirements regarding the quality of efficacy data

The documentation for the efficacy of a product must comply with the general requirements to be met by scientific studies regarding data collection, statistical treatment as well as reporting.

The list below states, which information must be available in a report, no matter the experiment you intend to report.

- Name and concentration of the active substances included in the study.
- The identity of the tested products in relation to the product applied should be transparent. If composition of the product tested differs from the product applied for, the composition of the tested product must be available for assessment of similarity of the products to evaluate if efficacy data can be applied for product authorisation.
- Aim of the study must be clearly presented as well as what will be determined in the study.
- A detailed description of the experimental conditions – temperature, relative humidity, light conditions, research animals' access to feed, their access to water, the layout of the trial site (this may for example be a cage or an entire stable), the geographical location of the site and other relevant conditions.
- A detailed description of the method used to collect data.
- Description on the test animals used.
  - Was animals acclimatized before the trial and how?
  - How many test animals are involved in the trial?
  - Are the test animals adults? Are both sexes represented? Are they larvae or nymphs? How old are they? Are they fasting or have they been fed? Where do the test animals come from, and what is their history (caught in the wild or reared in a laboratory)? etc.
  - What is the resistance status of the test animals seen in relation to the active substance – are you testing a particularly susceptible strain or a resistant strain collected in the field?
- Replications (replicates).
  - How many replications are used in the experiment?
  - How many individuals are included in a replication?
  - What considerations are behind the choice of the number of animals and replications, and which precision can you therefore expect from the study?

- To what extent are the replications independent of each other, and how will a lack of independence between the replications, if any, affect the result?
- In field trials, replicates are rarely real replicates. Instead, you have to carry out your experiments at a number of sites, which resemble each other as much as possible. In such a situation you must report the size of the pest population before and after the treatment. Furthermore is a very detailed description of the experimental conditions generally required when field studies are reported.
- Untreated control experiments (negative control).
  - Control experiments without any active substance but with exactly the same set-up and the same extent must always be presented. In some situations a positive control is also used in which the product applied for is measured against a comparable, but well-described product. Such studies cannot replace negative control experiments.
- When bait is tested, the following questions must be discussed:
  - Is alternative food available during the experiment? Can the test animals for example find their normal food in the surroundings, are they offered a non-toxic alternative, or are they offered a competing product?
  - If you measure the amount of food intake, a covered reference bait must also be included in the trial in order to correct for absorption of moisture.
- Raw data must always be enclosed.
  - Data are presented in the actual report with relevant calculations and tables, but data in their raw form must also be available – preferably in an appendix
  - Raw data is the data collected during the experiment before calculation.
  - All data must be presented in the report, both the data of the product applied for and of the untreated control.
- If the report contains references to guidelines, then these guidelines must be enclosed in full.
- The statistical methods used must be reported.

### **“The worst pitfalls”**

- The results are reported in the form of percentages without the raw data being enclosed.
- Experiments are carried out with species not representative of the use of the product that is stated on the label.

- Not the same number of untreated control experiments are carried out as the number of experiments with the product.
- A number of national guidelines are being referred to without these being enclosed and without information about how the current experiment differs from those guidelines.
- Letters, popular articles and other material from highly satisfied customers are enclosed as documentation – this cannot form part of the documentation for the product.
- Papers from internationally recognized scientific journals are enclosed, documenting that the active substance is effective or that a number of named products are effective. This can only be used as documentation if the product applied for – that is the precise formulation applied for – was studied in the papers in question.
- In recent years, directions for use have appeared to have been translated by online translation services. These are often almost unintelligible and translates to species that do not exist in Danish. Such text cannot form the basis of an efficacy assessment and will obviously pose a risk of stopping the entire evaluation process.
- The use of local names for pests may be necessary and acceptable; however, it cannot be used if there is a risk that it will result in misunderstandings, for example “Wasp killer”. Wasps are a very large group with plenty of harmless species, but every Dane knows that by wasps you think of the stinging ones with yellow cross stripes, which are actually called hornets. Therefore, it is acceptable to write “wasps” on the label. By contrast, the term “botflies” is often understood as the flies that settle on horses, bite a hole and suck blood, but these are actually horseflies. Botflies are flies that – during flight – lay their eggs on the front legs of the horse; from here, the horse licks them up, and they then go on to live in the horse as parasites. If a product claims to be able to deter botflies, then this is the fly for which an effect needs to be documented. However, if you mean horseflies, you have to write that, and then it is accepted that you write an explanatory text, which makes it intelligible to the reader what you mean.