Expert focus – How to bridge efficacy data from a few products to a biocidal product family

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A huge effort is required on the part of an applicant to conduct efficacy studies for all members of a biocidal product family. Stan de Groot, Triskelion expert in registration services and risk assessment, outlines how the task can be carried out more efficiently.

A fundamental component of the evaluation of biocidal products is the assessment of their efficacy. Under Article 19 (1) b of the biocidal products Regulation (BPR), authorisation will only be granted if a product is considered to be sufficiently effective. This in turn depends on whether the claims made for the activity of the product are in line with the efficacy demonstrated.

The registrant has to submit a set of efficacy studies to support this. For a biocidal product family, the amount of efficacy testing data required can, under appropriate conditions, be minimised.

Label claim

Each biocidal product must have a label claim, describing its purpose and how it should be used. The label should be based on the activity and benefits the applicant wishes to claim for the use of the product. It should be as specific as possible and must contain as a minimum the following information:

- the purpose of the claims (for example, disinfection of hard surfaces; controlling the growth and settlement of fouling organisms);
- the function or product type (insecticide, wood preservative, etc);
- the target organisms to be controlled (for example, bacteria, fungi, viruses, insects, etc);
- the desired effect on the target organisms (kill, control, repel, etc);
- in-use concentration; and
- conditions and area of use.

Label claims can (and in some cases must) be further specified. This might include how fast the effect occurs, its duration, and on what type of surface it should be applied.

The applicant must submit studies which demonstrate the efficacy of the biocidal product. It is crucial that the most suitable tests are performed under the right conditions to support the claim. Many different efficacy studies are usually needed to cover all conditions, strains, dilutions, etc of a product. Most product efficacy data come from laboratory-simulated use tests, usually in a two-step tiered approach (phase 2 tests). In some cases field studies performed under actual conditions of use are also required (phase 3 tests).

Biocidal product families and meta SPCs

To facilitate market access and minimise administrative expenses, applicants can submit a group of biocidal products under a single entry, described as a biocidal product family. As laid down in Article 3 (1) (s), the products within one family must have similar uses, the same active substance(s), a similar composition (with specified variations) and levels of risk and efficacy.

It would require a huge effort on the applicant's part to conduct efficacy studies for all members of a biocidal product family. It is therefore common practice to bridge the efficacy data from a few products. This, however, must be scientifically valid and fully justified.

As laid down in Article 19 (6) of the BPR: "The assessment of the biocidal product family, conducted according to the common principles set out in Annex VI, shall consider the maximum risks to human health, animal health and the environment and the minimum level of efficacy over the whole potential range of products within [it]." In other words, the least effective product combined with the highest risk is used for testing as a worst case for the whole family.

This 'worst-case' approach should cover the whole potential range of products. However, within a family, products can have different classifications, safety instructions, precautionary statements and risk management measures, relating to different risk and/or efficacy levels. To bring order to this, they can be categorised in sub-families; also known as 'meta SPCs' (summary of product characteristics). All products within a meta SPC have:

- a specified range in the compositions that is considered sufficiently similar;
- similar uses which are associated with a common set of risk management measures;
- the same hazard and precautionary statements; and
- a common set of first aid instructions, disposal, storage and shelf life.

It is therefore possible to do the assessment of the maximum risk and minimum level of efficacy at meta SPC level – instead of for the entire biocidal product family. In this way, authorities are able to evaluate whether all products comply with the legislation.

How to show efficacy for a full product family

As outlined in Chapter 5.2.2 of Echa's *Guidance on the BPR: Volume II Parts B+C,* the product containing the lowest concentration of the active substance(s) shall be the leading test material for the efficacy studies. These studies must be performed under the most stringent conditions. The lowest efficacious dose/concentration determined, may then also be applied for the other products within that meta SPC. Furthermore, the influence of the co-formulants on the efficacy should be taken into account.

If it is difficult to single out a worst-case product, a 'dummy' product may be used to cover all products in a meta SPC, containing the lowest combination of concentrations of actives and synergists/co-formulants. This product is solely used for testing purposes and is not intended to be put on the market. Alternatively, several products could be tested to cover the meta SPC as a whole. In some cases, efficacy studies performed for a product of one meta SPC, may also be valuable for a product in another, provided that variations in co-formulants like scents, colours, etc, have no influence on efficacy. Justification is needed for the acceptance of these forms of bridging.

Example of using a dummy product

To illustrate how the strategy using a dummy product can be approached, an example is presented below, based on a hypothetical disinfectant family.

	Family					**Dummy**
	***Meta* SPC 1**		***Meta* SPC 2**		***Meta* SPC 3**	
	Product 1	Product 2	Product 3	Product 4	Product 5	
Active 1	1%	2%	3%	2%	5%	1%
Active 2	5%	3%	5%	5%	5%	3%
PT	2	2,4	2,4	2,4	2,4	-
Target organisms	Yeast Bacteria	Yeast Bacteria	Yeast Bacteria Viruses	Yeast Bacteria Viruses	Yeast Bacteria Viruses	Yeast Bacteria
Use conditions	Clean conditions	Clean conditions	Clean conditions	Clean conditions	Dirty conditions	Clean conditions
Scent	1	2	1	2	1	Not relevant
Colour	1	1	2	2	3	Not relevant

In this example, the biocidal product family consists of five products, categorised provisionally under three different meta SPCs. Meta SPC division may be the result of the concentration range in active 1 and/or different hazard/precautionary statements. Keep in mind that different target organisms and/or different product types do not necessarily demand a separate meta SPC.

In the above example, there is no product that can be considered as an appropriate worst-case product for testing. Product 1 has the lowest concentration of active 1 and product 2 has the lowest of active 2. Therefore, it may be useful to formulate a dummy product, covering the lowest concentrations of both active substances. This would then contain 1% of active 1 and 3% of active 2.

Efficacy testing for yeast and bacteria under clean conditions should be done using this dummy product. The results would not only completely cover product 1 and 2 but can also be used for product 3 and 4. For these two products only, the virucidal efficacy still has to be tested. Furthermore, the dummy results can also reduce the number of tests performed for product 5. If you want to show the product is efficacious under dirty conditions, you are also required to do so under clean conditions. The dummy results can support this.

Regarding the virucidal claim for product 3 and 4, again a worst-case testing approach is applicable. No dummy is necessary as product 4 is the 'worst-case' product. Thus, efficacy testing for viruses under clean conditions can be done only for product 4. Again, these results may also be useful to support the claim for product 5, as described above.

This leaves the efficacy testing under dirty conditions for yeast, bacteria and viruses for product 5, using the product itself.

A well-grounded justification is necessary for the use of bridging test results. Furthermore, it is important that variations in co-formulants, scents, colours, etc, have no influence on the efficacy. A justification is also required for this aspect to allow bridging. Also, if the dummy product is not effective enough against the target organisms, the strategy should be adapted to include the actual products. In essence, great care must be taken when determining the most suitable approach. The example deals with the most important, but does not cover all, aspects of worst-case testing. For further guidance, see Echa's Guidance on the BPR: Volume II Parts B+C, and specifically Chapter 5.2.2.

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