How to deal with extracts and oils of plant or animal origin?

This document was endorsed at the 23rd meeting of representatives of Members States Competent Authorities for the implementation of Directive 98/8/EC concerning the placing of biocidal products on the market (27-28 November 2006).

I. Introduction

Several oils and extracts of plant or animal origin have been notified according to the Commission Regulation (EC) No 1896/2000, predominantly for the product types 18 (insecticides, acaricides and products to control other arthropods) and 19 (repellents and attractants). In order to illustrate the potential number of substances addressed in this paper, Annex I lists the extracts / oils notified is provided to the TM.

Plant and animal oils and extracts differ from synthesized chemicals in their origin. Synthesized chemicals are based on chemical reactions whereas oils and extracts are manufactured by physically processing material of biological origin.

The significant difference between oils/extracts and synthetic chemicals is the composition or specification. Synthetic chemicals can be produced in standardized processes in resulting in repeatable purity range. The composition of an extract / oil, however depends on the material of biological origin, the manufacturing process(es) and may depend on further processing. Therefore extracts /oils have a larger variation in the qualitative and quantitative composition than synthetic chemicals.

The production of ingredients in the (living) biological origin depends on the climatic conditions, e.g. time of sunshine, rain, soil etc. and differs each year. Therefore the concentrations and kinds of the ingredients are varying naturally and affecting the quantitative and qualitative composition of the extract / oil produced from the biological material.

In addition, the way of processing the extract / oil has an impact on the composition of extracted material which varies depending on the technique applied, e.g. cold-pressing, water-steam-distillation, extraction with (organic) solvents or a combination of several steps but always resulting in a complex mixture of several constituents. As a result of this, an extract / oil of the same biological origin could have different compositions. Therefore certain physical parameters could be regarded as important for clarifying the identity of an extract / oil.

It has to be emphasized that single constituents isolated from an extract / oil cannot be regarded as being the extract / oil anymore. The single constituents would be active substances by themselves.

However (a) single constituent(s) might be selected as “marker” for analytical purposes as the extract / oil cannot be analyzed as a whole in the test matrix (soil, blood etc).

Taking all the considerations above into account the following questions arise:

1. What is regarded as the active substance in an extract / oil?
2. How precisely must an extract /oil be analyzed?
3. How to name the extract / oil comprising differences in the composition?
4. What shall be tested?
5. Criteria for read-across?
6. How to deal with studies which were conducted on single constituents of the extract / oil? Can they be used for evaluation?

1. What is regarded as the active substance in an extract / oil?

The whole mixture of all constituents comprising an extract / oil is regarded as the active substance as it is not possible to distinguish between individual modes of action assigned to each single constituent. There may be cases where there would be one main constituent in the extract / oil, but nevertheless if the application is for an extract / oil, the main constituent does not cover the substance identity.

2. How precisely must an extract /oil be analyzed?

The extract / oil should be analyzed as precisely as possible. Therefore 'all' detectable constituents should be identified. The main constituents (≥ 1.0 % (w/w)) have to be identified. However, constituents with a concentration ≤ 1.0 % (w/w) might be difficult to identify. If literature data indicate the occurrence of hazardous constituents than it is necessary to analyze the constituents down to 0.1 % as this information is needed for classification & labelling purposes.

As the whole extract / oil is regarded as the active substance, the purity of an extract / oil would always be regarded as 100%. This is also stated in the TNsG on data requirements (p 30; 2.7) "For substances of undefined or variable composition the purity is 100%...".

Example:

Constituents	**EC no: 297-385-2** Lavender, *Lavandula hybrida grosso*, ext.		**EC no: 297-384-7** Lavender, *Lavandula hybrida abrial*, ext.		**EC no: none** Lavender, *Lavandula hybrida super*, ext.	
	min % (w/w)	max % (w/w)	min % (w/w)	max % (w/w)	min % (w/w)	max % (w/w)
Linalool	24.0	35.0	26.0	38.0	25.0	37.0
Linalyl acetate	28.0	38.0	20.0	29.0	35.0	47.0
Camphor	6.0	8.0	7.0	11.0	3.5	6.5
Eucalyptol	4.0	7.0	6.0	11.0	3.0	7.0
Terpinen-4-ol*	1.5	5.0				
Lavandulyl acetate	1.5	3.0	1.0	2.0	0.6	2.2
Borneol	1.5	3.0	1.5	2.5	1.4	3.0
Limonene*	0.5	1.5	0.5	1.5		
cis beta Ocimene*	0.5	1.5	1.5	3.0		
alpha Terpineol*						
trans beta Ocimene*			3.0	7.0		
Lavandulol*						
Sum of the listed constituents	67.5	102.0	66.5	105.0	68.5	102.7
Purity	100	100	100	100	100	100

* These constituents do not appear in all Lavandula hybrida-extracts.

3. How to name the extract / oil comprising differences in the composition?

1. The biological origin of the extract is most important, e.g. for plant the exact botanical name has to be given (TNsG on Data Requirements, p 30; 2.9). Where relevant, the part of the plant used should be mentioned.

2. The techniques of processing the extract / oil has to be stated in short and general terms, e.g. cold-pressing followed by extraction with ethanol (TNsG on Data Requirements, p 30; 2.6).

3. The main constituents (composition) have to be given in plausible ranges, covering the variation which could occur due to environmental (climate) influences.

Example:

Name of biological origin: Lavender, *Lavandula hybrida grosso*, Labiatae

Technique of processing: distillation with steam of freshly cut flowers

Composition in % (w/w):

Constituents	**lower limit**	**upper limit**
Linalool	24.0	35.0
Linalyl acetate	28.0	38.0
Camphor	6.0	8.0
Eucalyptol	4.0	7.0
Terpinen-4-ol	1.5	5.0
Lavandulyl acetate	1.5	3.0
Borneol	1.5	3.0
Limonene	0.5	1.5
cis beta Ocimene	0.5	1.5

4. What shall be tested?

The substance as placed on the market has to be tested. However, due to the natural variation, the test batch has to comprise a wider quantitative range of the constituents. The exact composition of the test batch has to be decided case-by-case depending on the (known) eco- / -toxicological profile of each single constituent. The following approach should be considered:

- Which constituents are present in the extract and what are the constituents with the most significant toxicological / eco-toxicological properties.
- Testing should be conducted on batch with a high level of the most toxic constituents.
- Basic toxicological, eco-toxicological and efficacy test should be done with a mid-range composition to ensure any synergistic effects are not overlooked even if sufficient data can be obtained from literature, single-constituent studies etc.

5. Criteria for read-across?

The same criteria have to be applied as the ones applied for synthesized chemicals. Therefore the applicant has to give scientific reasons for reading-across including the change of the biological source and the manufacture process. However read-across is a case-by-case-decision which has to be justified for each single endpoint.

Example:

The extract of *Lavandula hybrida super*, Labiatae (EC-number none; CAS-number not given) has been tested and the test result should also be used for the extract of *Lavandula hybrida grosso*, Labiatae (EC-number 297-385-2; CAS-number 93455-97-1). At a first step the data requirements for substance identification have to be given for both substances (manufacturing process(es); main constituents of the extract). As a second step based on this information it has to be decided by expert judgment whether or not the studies can be used for both extracts.

Technique of processing: distillation with steam of freshly cut flowers

Composition:

Constituents	**EC no: 297-385-2** Lavender, *Lavandula hybrida grosso*, ext.		**EC no: none** Lavender, *Lavandula hybrida super*, ext.	
	min % (w/w)	max % (w/w)	min % (w/w)	max % (w/w)
Linalool	24.0	35.0	25.0	37.0
Linalyl acetate	28.0	38.0	35.0	47.0
Camphor	6.0	8.0	3.5	6.5
Eucalyptol	4.0	7.0	3.0	7.0
Terpinen-4-ol	1.5	5.0		
Lavandulyl acetate	1.5	3.0	0.6	2.2
Borneol	1.5	3.0	1.4	3.0
Limonene	0.5	1.5		
cis beta Ocimene	0.5	1.5		
alpha Terpineol				
trans beta Ocimene				
Lavandulol				
Sum of the listed constituents	67.5	102.0	68.5	102.7
Purity	100	100	100	100

Both hybrida extracts differ in the quantitative and qualitative composition. The Lavender, *Lavandula hybrida grosso* extract contains additionally terpinen-4-ol, limonene and cis-ß-ocimene. These three constituents are classified as follows:

Terpinen-4-ol: X (harmful); R22 – Harmful if swallowed

Limonene: Xi (irritant); R10 – Flammable; R38 – Irritant to skin; R43 – May cause sensitization by skin contact and R50/53 – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment.

cis-ß-ociment: not known

Therefore it has to be decided whether additional information (literature data) on these three constituents has to be submitted or the full data set has also to be required for the Lavender, *Lavandula hybrida grosso* extract.

6. How to deal with studies which were conducted on single constituents of the extract / oil? Can they be used for evaluation?

In general, extracts / oils are complex mixtures comprising a number of constituents therefore the whole extract is regarded as the active substance. However, there might be constituents with different toxicological and eco-toxicological properties.

Therefore studies conducted with single active constituents can be used for supporting the evaluation to predict how an extract / oil might behave but they can normally not replace studies which were conducted on the full extract / oil. Some testing should be done on the extract / oil to ensure synergistic effects are not overlooked, and scientific reasons have to be given that read-across is possible.

All three Lavender, *Lavandula hybrida* extracts contain “linalool” (EC no 201-134-4; CAS no 78-70-6) as constituent. Experimental data on linalool do not cover the extracts but can be used to support the data established for the extracts.

Annex I
Listing of notified oils / extracts

EC-name of extract / oil	EC-description	EC-no	CAS-no	Supported PT	RMS
Bone oil / Animal oil	Substances obtained by destructive distillation of bones. Contains pyrrole, aniline, stearonitrile, valeronitrile, pyridine, methylamine and other nitrogenous compounds.	232-294-3	8001-85-2	19	DE
Rape oil	Extractives and their physically modified derivates. It consists primarily of the glycerides of the fatty acids eruic, linoleic and oleic. (*Brassica napus, Cruciferae*)	232-299-0	8002-13-9	18	DE
Garlic ext.	Extractives and their physically modified derivates such as tinctures, concretes, absolutes, essential oils, oleoresins, terpenes, terpene-free fractions, distillates, residues, etc., obtained from *Allium sativum, Liliaceae*.	232-371-1	8008-99-9	03;04; 05; 18;19;	PL
Margosa ext.	Extractives and their physically modified derivates such as tinctures, concretes, absolutes, essential oils, oleoresins, terpenes, terpene-free fractions, distillates, residues, etc., obtained from *Azadirachta indica, Meliaceae*.	283-644-7	84696-25-3	01; 03; 08; 09; 18; 19	DE
Melaleuca alternifolia, ext. / Australian tea tree oil	Extractives and their physically modified derivates such as tinctures, concretes, absolutes, essential oils, oleoresins, terpenes, terpene-free fractions, distillates, residues, etc., obtained from *Melaleuca alternifolia, Myrtaceae*.	285-377-1	85085-48-9	01; 02; 03; 19	ES
Chrysanthemum cinerariaefolium, ext.	Extractives and their physically modified derivates such as tinctures, concretes, absolutes, essential oils, oleoresins, terpenes, terpene-free fractions, distillates, residues, etc., obtained from *Chrysanthemum cinerariaefolium, Compositae*.	289-699-3	89997-63-7	18; 19	ES
Juniper, Juniperus mexicana, ext	Extractives and their physically modified derivates such as tinctures, concretes, absolutes, essential oils, oleoresins, terpenes, terpene-free fractions, distillates, residues, etc., obtained from *Juniperus mexicana, Cupressaceae*.	294-461-7	91722-61-1	19	FR
Lavender, Lavandula hybrida, ext. / Lavandin oil	Extractives and their physically modified derivates such as tinctures, concretes, absolutes, essential oils, oleoresins, terpenes, terpene-free fractions, distillates, residues, etc., obtained from *Lavandula hybrida, Labiatae*.	294-470-6	91722-69-9	18; 19	PT
Pine ext.	Extractives and their physically modified derivates such as tinctures, concretes, absolutes, essential oils, oleoresins, terpenes, terpene-free fractions, distillates, residues, etc., obtained from *Pinus, Pinaceae*.	304-455-9	94266-48-5	10	LV