7.23 **MICRO-EMULSIONS (ME)**

**Introduction**

A micro-emulsion is a mixture of water, water insoluble and water soluble components forming a visually homogeneous, transparent liquid. One or more active ingredients may be present in either the aqueous phase, the non-aqueous phase, or in both phases. A variety of micro-emulsion formulations may be prepared in which the aqueous phase can be considered the dispersed phase, the continuous phase or, alternatively, where the two phases are considered to be bicontinuous. In all cases micro-emulsions will disperse into water to form either conventional emulsions or dilute micro-emulsions.

One of the major benefits of micro-emulsions is that they, unlike other conventional dispersion formulations, are thermodynamically stable. In this respect they are somewhat similar to soluble concentrate (SL) formulations. However, micro-emulsions are often only stable within limited temperature ranges. For this reason particular attention should be given to the directions for formulation storage.

Given that they form emulsions or dilute micro-emulsions on dilution into water, micro-emulsions are treated in a similar fashion to emulsifiable concentrate (EC) formulations, with some additional modifications to take account potential use problems relating to storage and use at high and low temperatures.

Note for preparation of draft specifications. Do not omit clauses or insert additional clauses, nor insert limits that are more lax than those than given in the guidelines, without referring to section 4. From the “Notes” provided at the end of this guideline, incorporate only those which are applicable to the particular specification.

**...... [ISO common name] MICRO-EMULSION**

[CIPAC number]/ME (month & year of publication)

7.23.1 **Description**

 The material shall consist of technical ...... [ISO common name], complying with the requirements of FAO/WHO specification ....... , in the form of ....... (see Section 4.2), combined with water and other suitable formulants to give a stable, transparent liquid, free from visible suspended matter and sediment (Note 1).

7.23.2 **Active ingredient**

7.23.2.1 **Identity tests** (Note 2)

 The active ingredient shall comply with an identity test and, where the identity remains in doubt, shall comply with at least one additional test.

7.23.2.2 **...... [ISO common name] content** (Note 2)

 The ...... [ISO common name] content shall be declared (g/kg or g/l at 20 ± 2 ºC, Note 3) and, when determined, the average content measured shall not differ from that declared by more than the appropriate tolerance, given in the table of tolerances, Section 4.3.2.

7.23.3 **Relevant impurities**

7.23.3.1 **By-products of manufacture or storage** (Note 4), if required

 Maximum: ..….% of the …… [ISO common name] content found under 7.23.2.2.

7.23.4 **Physical properties**

 7.23.4.1 **Acidity** and/or **Alkalinity** (MT 191) or **pH range** (MT 75.3) (Note 5), if required

 Maximum acidity: ...... g/kg calculated as H2SO4.

 Maximum alkalinity: ...... g/kg calculated as NaOH.

 pH range: ...... to ......

7.23.4.2 **Persistent foam** (MT 47.3)

 Maximum ...... ml after 1 min (Note 6).

 7.23.4.3 **Emulsion stability and re-emulsification** (MT 36.3) (Note 7)

 The formulation, when diluted at 30 ± 2 °C with CIPAC Standard Waters A and D (Note 8), shall comply with the following:

|  |  |
| --- | --- |
| Time after dilution | Limits of stability, MT 36.3 |
|  0 h | initial emulsification complete |
|  0.5 h | “cream”, maximum: ...... ml |
|  2.0 h | “cream”, maximum: ...... ml“free oil”, maximum: ...... ml |
|  24 h | re-emulsification complete |
|  24.5 h | “cream”, maximum: ...... ml “free oil”, maximum: ...... ml |
| Note: tests after 24 h are required only where results at 2 h are in doubt. |

7.23.5 **Storage stability**

7.23.5.1 **Stability at 0 °C** (MT 39.3)

 After storage at 0 ± 2 °C for 7 days, the volume of solid and/or liquid which separates shall not be more than 0.3 ml. (Note 9).

7.23.5.2 **Stability at elevated temperature** (MT 46.3)

 After storage at 54 ± 2 °C for 14 days (Notes 9 and 10), the determined average active ingredient content must not be lower than ......% relative to the determined average content found before storage (Note 11) and the formulation shall continue to comply with the clauses for:

- by-products of manufacture or storage (7.23.3.1),

- acidity/alkalinity/pH range (7.23.4.1),

- emulsion stability and re-emulsification (7.23.4.3),

as required.

\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Note 1 Before sampling a commercial container to verify formulation quality, inspect it carefully to ensure that no phase separation has taken place. If the formulation has been subjected to a temperature extreme, the recovery to a transparent, visually homogeneous liquid may require some gentle agitation of the container before the sample is taken.

Note 2 Method(s) of analysis must be CIPAC, AOAC or equivalent. If the methods have not yet been published then full details, with appropriate method validation data, must be submitted to FAO/WHO by the proposer.

Note 3 In certain cases, micro-emulsion formulations may be quite viscous. In such a case, unless homogenization is carried out carefully, it is possible for the sample to become aerated. This can lead to errors in the determination of the active ingredient content in g/l. It is preferable, therefore, to determine the content in g/kg and, if necessary, to determine the mass per millilitre in g/ml, to calculate the active ingredient content in g/l.

Note 4 This clause should include only relevant impurities and the title should be changed to reflect the name of the relevant impurity. Method(s) of analysis must be peer validated.

Note 5 The method to be used shall be stated. If several methods are available, a referee method shall be selected. Treat ME as an emulsifiable concentrate.

Note 6 The mass of sample to be used in the test should correspond to the highest rate of use recommended by the supplier. The test is to be conducted in CIPAC standard water D.

Note 7 Unless another temperature is specified.

Note 8 As outlined in CIPAC MT 36.3, the test concentrations should be based on those in the recommended directions for use supplied with the product. Where several concentrations are recommended, the highest and lowest concentrations within the scope of the method should be used.

Note 9 In certain circumstances, phase separation may occur at high or low temperatures. The formulation shall be deemed to be acceptable if the recovery to a single phase is as rapid as the thermal equilibrium with ambient or use temperatures.

Note 10 Unless other temperatures and/or times are specified. Refer to Section 4.6.2 of this Manual for alternative storage conditions.

Note 11 Samples of the formulation taken before and after the storage stability test should be analyzed concurrently after the test in order to reduce the analytical error.