7.44 **MIXED FORMULATIONS OF CS AND SE (ZE)**

# Introduction

ZE is a mixed formulation of CS and SE and is a stable aqueous dispersion of microcapsules, solid fine particles and emulsion droplets, each of which contains one or more active ingredients. The formulation is intended for dilution into water prior to spray application. Formulating the active ingredients together eliminates the need for tank mixing, which can lead to incompatibility, and facilitates control of a wider range of pests with fewer applications. Like other aqueous liquid formulations, ZE formulations are easy to handle and measure, dust free, non-flammable and offer good miscibility with water.

One or more of the active ingredients is encapsulated for various purposes, such as to increase the residual biological activity, or to reduce the acute toxicity, or to obtain a physical or chemically stable water-based formulation. The purpose determines whether the “free” active ingredient and the “release rate” are relevant properties of a specific product.

Mixed formulations of CS and SE are not stable indefinitely and it is necessary to ensure that, after transportation and storage, the formulation remains suitable for use. Quantification of the following parameters, particularly after high and low temperature stability tests, serves this purpose.

 - Active ingredient, determined and expressed as “total”, “free” and “release rate”, as required.

 - Pourability.

 - Dispersion stability and wet sieve tests (to ensure the sprayability of the diluted ZE formulation).

Information about other properties may also be given, e.g. mass per millilitre (if relevant), but these parameters do not constitute essential parts of the specification.

 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 providing justification. From the “Notes” provided at the end of this guideline, incorporate only those which are applicable to the particular specification.

**[ISO common names] MIXED FORMULATION OF CS AND SE**

[CIPAC numbers]/ZE (month & year of publication)

7.44.1 **Description**

 The material shall consist of an emulsion of fine droplets of technical [ISO common name(s)] complying with the requirements of the FAO/WHO specification(s) […./TC (date)], in the form of [derivative, if appropriate]; and a suspension of fine particles of technical [ISO common name(s)] complying with the requirements of the FAO/WHO specification(s) […./TC (date)], in the form of [derivative, if appropriate]; combined with a suspension of microcapsules of technical [ISO common name(s)] complying with the requirements of FAO/WHO specification(s) […./TC (date)], in the form of [derivative, if appropriate], in an aqueous phase, together with suitable formulants. After gentle agitation the material shall appear homogeneous (Note 1) and be suitable for dilution in water.

7.44.2 **Active ingredients**

 7.44.2.1 **Identity tests** (Note 2)

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

 7.44.2.2 **[ISO common names] contents**

 7.44.2.2.1 **Total content** (Notes 2 & 3)

 The …[ISO common name] content shall be declared (g/kg or g/l at 20 ± 2 ºC, Note 4) and, when determined, the average contents measured shall not differ from those declared by more than the appropriate tolerances, given in the table of tolerances, Section 4.3.2.

 7.44.2.2.2 **Free, non-encapsulated content** (Notes 2 & 3), if required

 The free …[ISO common name] average content measured shall not exceed ….% of the determined total content.

 7.44.2.2.3 **Release rate** (Notes 2 & 3), if required

 The …[ISO common name] release rate measured shall comply with the following criteria: ……

7.44.3 **Relevant impurities**

 7.44.3.1 **By-products of manufacture or storage** (Notes 3 & 5), if required

 Maximum: …% of the total [ISO common name] content measured.

7.44.4 **Physical properties**

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

 Maximum acidity: …g/kg calculated as H2SO4.

 Maximum alkalinity: …g/kg calculated as NaOH.

 pH range: …to…

 7.44.4.2 **Particle size distribution** (MT 187), if required

 …% of particles shall be in the range … to … (Note 6)

 7.44.4.3 **Pourability** (MT 148.1)

 Maximum “residue”: …..%

 7.44.4.4 **Dispersion stability** (MT 180) (Note 7)

 The formulation, when diluted with CIPAC standard waters A and D, shall continue to comply with the following:

|  |  |  |
| --- | --- | --- |
|  | Time after allowing the dispersion to stand |  Limits of stability |
|  |  0 h |  initial dispersion complete |
|  |  0.5 h |  “cream”, maximum … ml free oil, maximum … ml sediment, maximum … ml |
|  |  24 h |  re-dispersion complete |
|  |  24.5 h |  “cream”, maximum … ml free oil, maximum … ml sediment, maximum … ml |

 7.44.4.5 **Wet sieve test** (MT 185) (Note 8)

 Maximum: ….% of the formulation shall be retained on a … µm test sieve.

 7.44.4.6 **Persistent foam** (MT 47.3) (Note 9)

 Maximum … ml after 1 min.

7.44.5 **Storage stability**

 7.44.5.1 **Freeze/thaw stability** (Note 10)

 After undergoing ... freeze/thaw cycles and following homogenization, the formulation shall continue to comply with the clauses for:

 - acidity/alkalinity/pH range (7.44.4.1),

 - pourability (7.44.4.3),

 - dispersion stability (7.44.4.4),

 - wet sieve test (7.44.4.5),

 as required.

 An increase in free …[ISO common name] content (7.44.2.2.2) shall be permitted, to a maximum of ...% of the total content determined under 7.44.2.2.1.

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

 After storage at 54 ± 2 ºC for 14 days (Note 11), the determined average total content of each active ingredient must not be lower than …%, relative to the determined average content found before storage (Note 12), and the formulation shall continue to comply with the clauses for:

 - by-products of manufacture or storage (7.44.3.1),

 - acidity/alkalinity/pH range (7.44.4.1),

 - pourability (7.44.4.3),

 - dispersion stability (7.44.4.4),

 - wet sieve test (7.44.4.5),

 as required.

 An increase in free …[ISO common name] content (7.44.2.2.2) shall be permitted, to a maximum of ..% of the total content determined under 7.44.2.2.1.

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Note 1 All physical and chemical tests listed in this specification are to be performed with a sample taken after the recommended homogenization procedure. Before sampling to verify formulation quality, inspect the commercial container carefully. On standing ZE formulations usually develop a concentration gradient from the top to the bottom of the container. This may result in the appearance of a clear liquid on the top and/or sediment on the bottom. Therefore before sampling, the formulation must be homogenized according to the instructions given by the manufacturer or, in the absence of such instructions, by gentle shaking of the commercial container (for example, by inverting the closed container several times). After this procedure the container shall not contain a sticky layer of non-dispersed matter at the bottom (if the ZE has flocculated it may not be possible to re-disperse this sticky layer). A suitable and simple method of checking for a non-dispersed sticky layer (“cake”) is by probing with a glass rod or similar device adapted to the size and shape of the container.

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 Separate tolerances for total content must be provided for each active ingredient, if their concentrations are not within a single range, as defined in Section 4.3.2. Separate clauses must be provided for each relevant impurity.

 Clauses for free active ingredient content and release rate of the active ingredient are required only for the encapsulated active ingredient(s) and only if appropriate to the intended properties of the capsules. A clause to control release rate is usually required for capsules intended to possess slow- or controlled-release properties. A clause to control free active ingredient is usually required where encapsulation is intended to control the release or stability of the active ingredient, or to decrease the risk to users from accidental exposure to the active ingredient. If more than one active ingredient is encapsulated, limits must be provided for each. Methods for determination of free active ingredient and release rate may be product-specific.

Note 4 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 mass per millilitre, and in calculation of the active ingredient content (in g/l), if methods other than OECD 109 or MT 3.3 are used. If the buyer requires both g/kg and g/l at 20 ºC, then in case of dispute the analytical results shall be calculated as g/kg.

Note 5 This clause should include only relevant impurities and should be omitted if there is none. Method(s) of analysis must be peer validated.

Note 6 Percentages may be specified in one or more ranges, as appropriate to the product. Laser diffraction is not always suitable to measure the particle size distribution of liquid formulations. This should be evaluated by 4.5.31 Wet sieve test and 4.5.43 Suspensibility or 4.5.44 Dispersion stability.

Note 7 This test will normally be carried out before and after the freeze/thaw stability (7.44.5.1) and the elevated temperature test (7.44.5.2), respectively.. The test should be carried out at 2% dilution or, alternatively, at the highest and lowest recommended rates of use.

Note 8 This test detects coarse particles (e.g. oversize capsules, crystals) or agglomerates (of capsules or from crust formation) or extraneous materials that could cause blockage of spray nozzles or filters in the spray tank.

Note 9 The mass of sample to be used in the test should correspond to the maximum application concentration recommended by the supplier.

Note 10 After manufacture and during shipping it is often impossible for buyer or seller to guarantee that the formulation has not been exposed to freezing temperatures. As freezing of a ZE formulation may result in undesirable, irreversible changes, including (but not limited to) capsule failure caused by crystallization of the active ingredient, the ability of the formulation to successfully withstand repeated freezing and thawing is an important property. Unless otherwise agreed, the freeze/thaw stability test shall cycle the formulation between room temperature (e.g. 20 ± 2 °C) and -10 ± 2 °C on 18-hour-freeze/6-hour-melt cycles for a total of 4 cycles.

Note 11 Unless other temperatures and/or times are specified. Refer to Section 4.6.2 for alternative storage conditions.

Note 12 Samples of the formulation taken before and after the storage stability test may be analyzed concurrently after the test in order to reduce the analytical error.