6.16 **WATER DISPERSIBLE TABLETS (WT)**

**Introduction**

Tablets are preformed solids of uniform shape and dimensions, usually circular, with either flat or convex faces. Their size and weight is determined by manufacturing and/or use requirements. For some physical tests the tablets must be broken and their fragments used in the testing.

Water dispersible tablets (WT) are intended for application using conventional application equipment after disintegration and dispersion in water.

Dispersible tablets are often not coated or highly compacted and possess lower mechanical strength. They require commercial packaging that minimizes or eliminates mechanical stress during normal handling and transport. Selection of physical tests methods must take into account the commercial packaging of tablets.

Certain clauses are not applicable to effervescent tablets. This type of tablets, according to Pharm Eur are "uncoated tablets generally containing acid substances and carbonates or hydrogen carbonates which react rapidly in the presence of water to release carbon dioxide”. The excess of acid and base will mask possible acidity or alkalinity that are conveyed by the active ingredient or coformulants in the tablet. For this reason, the clauses for acidity/alkalinity or pH range are not applicable to effervescent tablets.

*Note for preparation of draft specifications. Do not omit clauses or insert additional clauses, nor insert limits that are more lax than those 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] WATER DISPERSIBLE TABLETS**

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

6.16.1 **Description**

The material shall consist of an homogeneous mixture of technical ...... [ISO common name], complying with the requirements of FAO/WHO specification [ …], in the form of ....... (see Section 4.2), together with carriers and any other necessary formulants. It shall be in the form of tablets for application after disintegration and dispersion in water. The formulation shall be dry, of unbroken and free-flowing tablets, and shall be free from visible extraneous matter.

6.16.2 **Active ingredient** (Note 1)

6.16.2.1 **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.

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

The ...... [ISO common name] content shall be declared (g/kg) 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. [content of active ingredient]

6.16.2.3 **Tablet dose uniformity**, if required

The ...... [ISO common name] content, measured separately in ... tablets, shall have a relative standard deviation (RSD) of not more than …%.

6.16.3 **Relevant impurities** (Note 1)

6.16.3.1 **By-products of manufacture or storage** (Note 3), if required

Maximum: …… % of the …… [ISO common name] content found under 6.16.2.2.

6.16.3.2 **Water** (MT 30.6), if required

Maximum: ….. g/kg

6.16.4 **Physical properties**

6.16.4.1 **Acidity** and/or **alkalinity** (MT 191) or **pH range** (MT 75.3) (Notes 4, 5 & 6), if required (Note 7)

Maximum acidity: … g/kg calculated as H2SO4.

Maximum alkalinity: … g/kg calculated as NaOH.

pH range: … to …

6.16.4.2 **Disintegration of tablets** (MT 197) (Note 8)

For effervescent tablets (Note 7) or if required for non-effervescent tablets.

Maximum: … % of residue after specified disintegration time

6.16.4.3 **Wet sieve test** (MT 185.1) (Notes 5 & 9)

After complete disintegration of the tablet or a fragment of a tablet follow procedure (b) wet sieving of CIPAC MT 185.1.

Maximum: … % retained on a 75 μm test sieve.

6.16.4.4 **Suspensibility** (MT 184.1) (Notes 5, 10, 11 & 12)

A minimum of …% shall be in suspension after 30 min in CIPAC Standard water D at 25 ± 5°C.

6.16.4.5 **Persistent foam** (MT 47.3) (Notes 5 & 13)

Maximum: … ml after 1 minute.

6.16.4.6 **Tablet integrity** (Note 14)

No broken, soft or sticky tablets should be present

Fragments: yes/no

Soft/sticky: yes/no

6.16.4.7 **Attrition resistance of tablets** (MT 178.3) (Notes 15) if required

Minimum attrition resistance: ......%.

6.16.5 **Storage stability**

6.16.5.1 **Stability at elevated temperature** (MT 46.4)

After storage at 54 2C for 14 days (Note 16) without pressure (Note 17), the determined average active ingredient content must not be lower than … % relative to the determined average content found before storage (Note 18) and the formulation shall continue to comply with the clauses for:

- by-products of manufacture or storage (6.16.3.1),

- acidity/alkalinity/pH range (6.16.4.1),

- disintegration of tablets (6.16.4.2)

- wet sieve test (6.16.4.3),

- suspensibility (6.16.4.4)

- tablet integrity (6.16.4.6),

- attrition of tablets (6.16.4.7),

as required.

Note 1 Measuring the active ingredient content or relevant impurities requires a representative sample of the tablet. A representative sample is obtained by grinding one or several tablets and then sampling the homogeneous powder.

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

Note 3 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 4 The method to be used shall be stated. If several methods are available, a referee method shall be selected.

Note 5 If tests need to be conducted at use rate a tablet may be broken and fragments used. The following tests may require breaking tablets:

|  |  |  |  |
| --- | --- | --- | --- |
| Point | Property | CIPAC | Rate |
| 6.16.4.1 | Acidity or alkalinity | MT 191 | 10 g add 100 ml  |
| pH range | MT 75.3 | 1 g make up 100 ml |
| 6.16.4.3 | Wet sieve test | MT 185.1 | Maximum recommended use rate |
| 6.16.4.4 | Suspensibility | MT 184 |
| 6.16.4.5 | Persistent foam | MT 47.3 |

Tablets or fragments of tablets must be completely disintegrated for the purposes of
CIPAC methods MT 191, MT 75.3, MT 185.1, MT 184 and MT 47.3.

Note 6 Before performing the CIPAC test, it is necessary to let the tablet(s) or fragments of a tablet disintegrate completely in a 250 ml beaker containing 50 ml of the water required by the method. A gentle stirring may be needed.

Note 7 This clause is not applicable to effervescent tablets, as they incorporate an effervescent system.

Note 8 The determination of an end-point of disintegration for tablets is difficult and subjective as tablets or fragments of tablets are not visible in bubbling and opaque suspensions. Instead of an endpoint of dissolution this method measures a residue after a fixed disintegration time.

Note 9 Weigh out the appropriate amount of the tablet(s) to prepare 100 to 250 ml of a dispersion of the maximum recommended use rate. Break or cut the tablet if necessary, do not grind.Then add the required tablet(s) or fragment(s) to 100 - 250 ml of CIPAC standard water D at 25 ± 5°C and stir gently at 200 rpm for the time specified by the manufacturer. If the stirring time is not specified by the manufacturer of the tablet, then stir for 10 minutes. After complete disintegration of the tablet or a fragment of a tablet follow procedure (b) wet sieving of CIPACT MT 185.1.

Note 10 Before performing the suspensibility test, it is necessary to let the tablet(s) or fragment(s) of a tablet disintegrate completely in a 250 ml beaker containing 50 ml of the water required by the method. Therefore, weigh out an appropriate amount of the tablet(s) or fragment(s) required to make 250 ml of a suspension in water. Break or cut the tablet if necessary, do not grind. Add the weighed sample to a 250 ml beaker containing 50 ml CIPAC standard water D at 25 ± 5°C and stir gently with a spatula until the sample is fully dispersed. Fill the suspension carefully in the 250 ml measuring cylinder and rinse the beaker with CIPAC standard water D to get a final volume of 250 ml. Stopper the cylinder and proceed with the method as per (b) Determination of sedimentation.

Note 11 The formulation should be tested at the maximum use rate recommended by the supplier. If the dimensions of the fragments do not allow exact weighing of the required amount an excess of up to 120 % of the recommended use rate is allowed.

Note 12 Chemical assay is the only fully reliable method to measure the mass of active ingredient still in suspension. However, the simpler gravimetric method may be used on a routine basis provided that it has been shown to give equal results to those of chemical assay. In case of dispute, chemical assay shall be the referee method.

Note 13 Grind the tablet or fragments of it with a mortar and pestle to a fine powder. Weigh out an appropriate amount of powder required for 200 ml of water. Fill 150 – 180 ml of Standard water D into a 250 ml beaker. Add the powder to the beaker and stir gently with a spatula until the tablet/fragments is fully dissolved. Fill the solution carefully in the 250 ml measuring cylinder and rinse the beaker with CIPAC standard water D to get a final volume of 200 ml. Stopper the cylinder and follow the method.

Note 14 This requirement method describes the physical state of the tablet for example whether it is broken or dusty with fragments or is soft and/or sticky. Visual observation only. Unless otherwise indicated, at least one pack/package containing multiple tablets should be inspected for color, texture, fragments and dust.

Note 15 An attrition test is only required for bulk packaged tablets with a diameter < 1 cm that may exhibit surface wear during transport and handling.

Note 16 Unless other temperatures and/or times are specified. Refer to Section 4.6.2 of this manual for alternative storage conditions. Whole tablets must be stored. After storage tablets may be broken for tests as specified in Note 5.

Note 17 Without pressure means that the test is performed as specified by CIPAC MT 46.4, but no pressure is applied to the sample during aging.

Note 18 Samples of the formulation taken before and after the accelerated storage stability test may be analysed concurrently after the test in order to reduce the analytical error.