6.24 **WATER SOLUBLE TABLETS**

**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 be used.

Water soluble tablets (ST) are intended for use with conventional application equipment. The active ingredient of STs is soluble in water at use rate. However, water soluble tablets may contain insoluble inerts that disperse in the spray liquid. Soluble tablets are often not coated or highly compacted and possess lower mechanical strength. Such tablets 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 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] WATER SOLUBLE TABLETS**

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

6.24.1 **Description**

The material shall consist of a 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 dissolution in water. The formulation shall be of dry, of unbroken, free-flowing tablets and shall be free from extraneous matter.

6.24.2 **Active ingredient** (Note 1)

6.24.2.1 **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.

6.24.2.2 ...... **[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.

6.24.2.3 **Tablet dose uniformity** (Note 2), if required

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

6.24.3 **Relevant impurities** (Note 1)

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

Maximum: …… % of the …… [ISO common name] content found under 6.24.2.2.

6.24.3.2 **Water** (MT 30.6), if required (Note 4)

Maximum: ….. g/kg

6.24.4 **Physical properties**

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

 Maximum acidity: … g/kg calculated as H2SO4.

Maximum alkalinity: … g/kg calculated as NaOH.

pH range: … to …

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

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

Maximum: … % of residue after specified disintegration time.

6.24.4.3 **Solution properties of water soluble tablets** (MT 196) (Note 5)

Maximum: … % retained after 2 hours on a 75 μm test sieve.

6.24.4.4 **Persistent foam** (MT 47.3) (Notes 5 and 9)

Maximum: … ml after 1 minute

6.24.4.5 **Tablet integrity** (Note 10)

No broken, soft or sticky tablets should be present.

Fragments: yes/no

Soft/sticky: yes/no

6.24.4.6 **Attrition resistance of tablets** (MT 178.2) (Notes 11 & 12), if required

Minimum attrition: ......%.

6.24.5 **Storage stability**

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

After storage at 54 2C for 14 days (Note 13) without pressure (Note 14) the determined average active ingredient content must not be lower than … % relative to the determined average content found before storage (Note 15) and the formulation shall continue to comply with the clauses for:

- by-products of manufacture or storage (6.24.3.1),

- acidity/alkalinity/pH range (6.24.4.1),

- disintegration of tablets (6.24.4.2),

- solution properties of water soluble tablets (6.24.4.3),

- tablet integrity (6.24.4.5),

- attrition of tablets (6.24.4.6),

as required.

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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 be used. The following tests may require breaking tablets:

|  |  |  |  |
| --- | --- | --- | --- |
| Point | Property | CIPAC | Rate |
| 6.24.4.1 | Acidity or alkalinity | MT 191 | 10 g add 100 ml |
| pH range | MT 75.3 | 1 g make up 100 ml |
| 6.24.4.3 | Solution properties | MT 196 | Maximum recommended use-rate |
| 6.24.4.4 | 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, MT196 and MT 47.3.

Note 6 Before performing the CIPAC test covering the physical properties, 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 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 CIPAC standard water D into a 250 ml beaker. Add the powder to the beaker and stir gently with a spatulum 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 10 This requirement describes the physical state of the tablet for example whether it is broken or dusty with fragments or soft and 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 11 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 12 The scope of CIPAC MT 178.2 is to measure attrition resistance of water dispersible granules but the method is considered to be applicable to DT, WT and ST with a diameter of < 1 cm as well.

Note 13 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 14 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 15 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.