Solubility **GM 1.2.1.0005.15**
Instead of SpH X
Instead of SpH X, p. 1, GM 42-0049-07

Definition of solubility in a pharmacopoeia analysis characterizes approximate solubility of pharmaceutical substances and additive substances (hereafter – substances) at a fixed temperature. Solubility test is performed at a 20 ± 2 °C, unless otherwise specified.

If the solubility is used as an indicator of substance purity, then the general monograph should indicate specific ratios of the substance and solvents.

It is recommended to use solvents with different polarity (usually – three): use of low-boiling and highly flammable (for example, diethyl ether) or highly toxic (for example, benzole, and methylene chloride) solvents is not recommended.

Solubility of a substance (calculated as 1 g) is expressed in terms provided in the table below.

Table – Designation of solubility of pharmaceutical substances and additive substances

Term	**Approximate amount of solvent (mL) required for dissolution of 1 g of substance**
Very easily soluble	up to 1 inclusive
Easily soluble	from 1 to 10 inclusive
Soluble	from 10 to 30 inclusive
Moderately soluble	from 30 to 100 inclusive
Slightly soluble	from 100 to 1,000 inclusive
Very slightly soluble	from 1,000 to 10,000 inclusive g
Practically insoluble	over 10,000

A substance is considered dissolved if no particles can be seen when examined against the light. The solution may contain trace components of physical impurities, such as fibers of filtering paper. A special indication must be made in the general monograph for substances that form opalescent solutions.

Term “is miscible with…” is used to characterise fluids miscible with the specified solvent in all proportions.

If it is indicated that a substance is soluble in fatty oils that means that it is soluble in any oil of the class ‘fatty oils’.

Method of determining solubility. Add a measured amount of solvent to an accurate weigh of finely ground substance and shake continuously for 10 min at a temperature of 20± 2 °C.

Slowly soluble substances requiring over 10 minutes for dissolution may be heated in a water bath to 30 °C. Observation is perfromed after the solution is cooled down to room temperature and after it was vigorously shaken for 1-2 minutes.

Dissolution conditions for slowly soluble substances are indicated in the general monograph.

For substances with unknown solubility the following analysis method should be used.

Add 1.0 mL of solvent to 1.0 g of finely ground substance and perform dissolution as described above. If the substance has fully dissolved than it is very easily soluble.

If the substance did not fully dissolve, add 1.0 mL of solvent to 100 g of the substance and perform dissolution as described above. If the substance has fully dissolved than it is easily soluble

If the substance did not fully dissolve, add 2.0 mL of solvent and continue dissolution. If the substance has fully dissolved than it is soluble.

If the substance did not fully dissolve, add 7.0 mL of solvent and continue dissolution. If the substance has fully dissolved than it is moderately soluble.

If the substance did not fully dissolve, add 10.0 mL of solvent to 10.0 g of finely ground substance and perform dissolution as described above. If the substance has fully dissolved than it is slightly soluble.

If the substance did not fully dissolve, add 100 mL of solvent to 10.0 g of finely ground substance and perform dissolution as described above. If the substance has fully dissolved than it is very slightly soluble.

And if the substance did not dissolve, then it is insoluble in this solvent.

For substances with known solubility, perform the analysis using the method described above, but only for extreme values for this term. For example, if a substance is soluble, then 100 g of this substance should not dissolve in 1.0 mL of solvent, but should fully dissolve in 3.0 mL.