

Safety Evaluation Test Methods for Polymers (Flow Scheme for Polymers)  
(PROVISIONAL TRANSLATION)

1 Physicochemical stability and acid/alkali solubility tests

- (1) Particle size of the test substance Pulverize the test substance into grains as small as possible. 60-80 mesh is recommended.
- (2) pH range of the test liquid Adjust the pH to 4.0, 7.0, 9.0 and 1.2, as adopted in 111 "Hydrolysis as a Function of pH" in The OECD (Organization for Economic Co-operation and Development) Guidelines for the Testing of Chemicals (OECD Council Decision [C(81)30 Final Appendix 1]).
- (3) Testing temperature  $40\pm 2^{\circ}\text{C}$ .
- (4) Light Indoor light.
- (5) Air Stir the test liquid to facilitate its contact with air.
- (6) Testing period Two weeks, except for the testing period for pH 1.2, which is 24 hours, considering the retention time in digestive organs.
- (7) Test concentration of the test substance Set the concentration within the range of  $10^2$ - $10^4$  mg/l in accordance with the properties of the test substance (1,000 mg/l is recommended).
- (8) Number of repetitions  $n=2$
- (9) Analysis Analyze as many of the following parameters as possible at the beginning and end of the test to detect any chemical change.  
Dissolved oxygen concentration (DOC), weight, molecular weight, infrared absorption spectrum, etc.

2 Solubility in water and organic solvents

(1) Test solvents

- (i) As indices for lipophilicity n-octanol, n-heptane.
- (ii) As general solvents Toluene, 1,2-dichloroethane, Isopropyl alcohol, THF (Tetrahydrofuran), MIBK (Methyl isobutylketone), DMF (Dimethyl formamide).
- (iii) Water

(2) Testing conditions

- (i) Temperature Stir at  $35$ - $40^{\circ}\text{C}$  and subsequently cool to  $25\pm 2^{\circ}\text{C}$  to achieve equilibrium.
- (ii) Testing period Twenty-four hours.
- (iii) Test concentrations of the test substance Test at two concentrations, i.e., 200 mg/l and 2,000 mg/l.
- (iv) Particle size of the test substance Pulverize the test substance into grains as small as possible. 60-80 mesh is recommended.
- (v) Number of repetitions Two repetitions.
- (vi) Stirring Constantly stir or shake the test liquid to facilitate contact between the test substance and the solvent.

(vii) Analysis Perform a gravimetric analysis. For water, also perform a total organic carbon (TOC) analysis. Perform as many instrumental analyses as possible for other organic solvents depend on the properties of the test substance.

(3) Evaluation of solubility

As a general rule, confirm the insolubility of the test substance in nine solvents.

If the test substance has been confirmed to be soluble in one of the nine solvents, the remaining eight solvents do not necessarily need to be tested. However, it is recommended that solubility data on at least one solvent from each of the categories 2(1)(i) to (iii) are submitted.

3 Molecular Weight Distribution Measurement

As a general rule, if the test substance has been confirmed to be soluble in 2(3), perform molecular weight distribution measurement by gel permeation chromatography (GPC) paying attention to the following points:

(1) Molecular weight calculation method Choose from the following methods depend on the nature of the test substance.

- (i) Primary reference standard (Polyethylene glycol, polystyrene).
- (ii) Secondary reference standard (1-2 substances with known molecular weight or weight average molecular weight).
- (iii) Method based on extended-chain length.
- (iv) Method based on hydrodynamic volume.

(2) Stability The base line should be straight.

(3) Detector response sensitivity Preferably, the response sensitivity shows no dependence on molecular weight (correct the measurement if it shows dependence).

(4) Separation Preferably, the peak of the polymer does not overlap the peaks of other substances (additives, impurities in solvents, etc.).

(5) How to draw a baseline in the low-molecular-weight region Preferably, take the average of the two charts with stable baselines.