Rationalizing the system of evaluating new chemical substances

7th March 2019

Safety Assessment Division

Chemical Management Center

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1. Introduction of OECD TG 301F

Background

・In principle, evaluation of degradability in the CSCL uses OECD TG 301C.

・However, there are few countries other than Japan that conduct OECD TG 301C degradability tests.

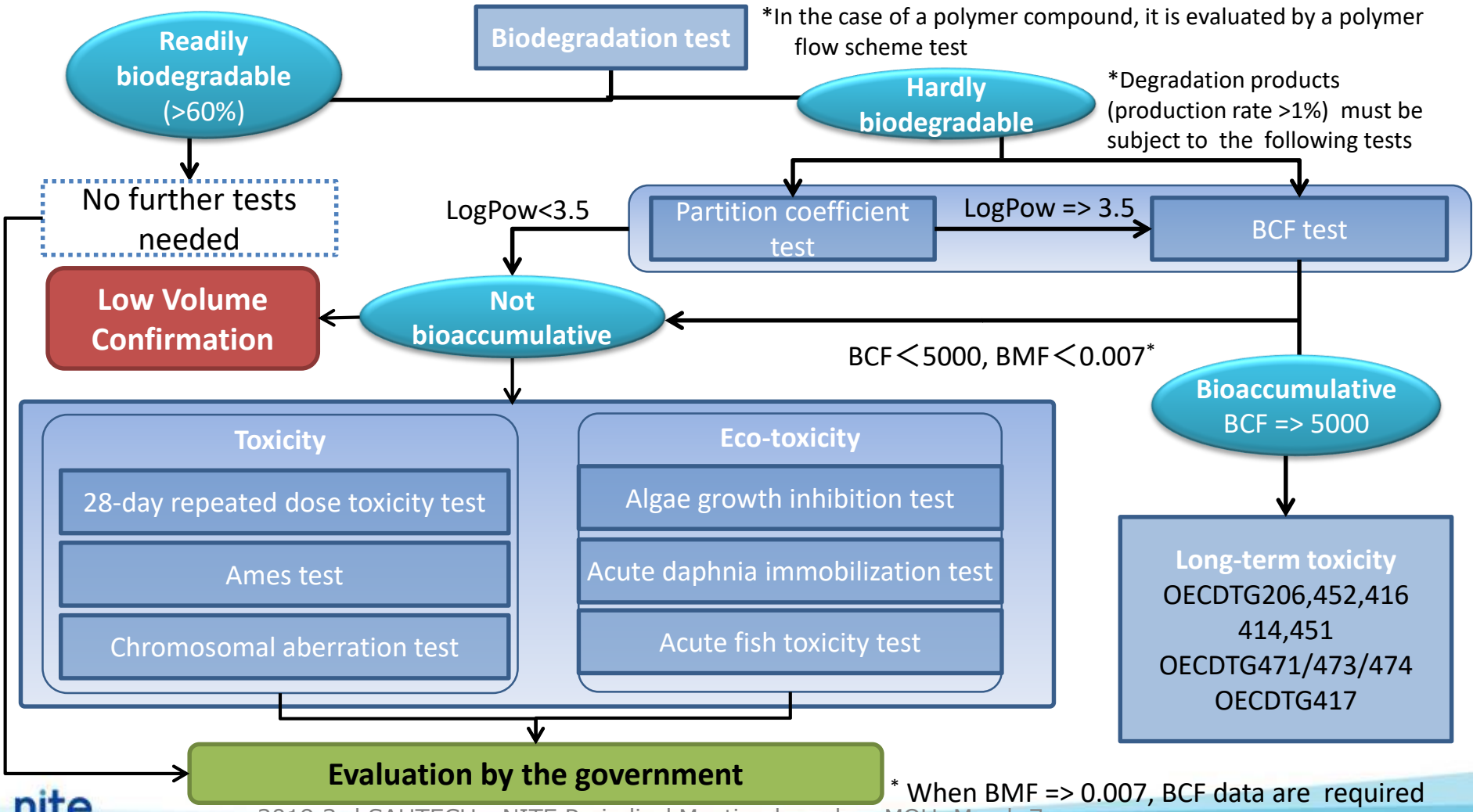
・Therefore, using OECD TG 301C is a problem in terms of international consistency.

→・OECD TG 301F has been conducted overseas.

・We introduced OECD TG 301F because we can promote reciprocal acceptance of test results in Japan and overseas.

1. Introduction of OECD TG 301F

●Examination required for registration of the CSCL of new chemical substances



1. Introduction of OECD TG 301F

● **Examination required for registration of the CSCL of new chemical substances**

<table>
<tr><th colspan="2">Evaluation Points</th><th colspan="2">Related test (OECD TG)</th></tr>
<tr><td colspan="2" rowspan="2">Biodegradation (1. or 2.)</td><td colspan="2">1.Biodegradation test (OECD TG 301C)
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<tr><td colspan="2">Water stability test (in the case of inorganic compounds)</td></tr>
<tr><td colspan="2" rowspan="2">Bioaccumulation (1. or 2.)</td><td colspan="2">1.Partition coefficient test (OECD TG 107 or OECD TG 117)</td></tr>
<tr><td colspan="2">2.BCF test (OECD TG 305)</td></tr>
<tr><td rowspan="4">Toxicity</td><td>Screening for toxicity</td><td colspan="2">28-day repeated dose toxicity test (OECD TG 407)</td></tr>
<tr><td rowspan="3">Screening for carcinogenicity</td><td colspan="2">Ames test (OECD TG 471)</td></tr>
<tr><td rowspan="2">Chromosomal aberration test/Mutagenicity test (1. or 2.)</td><td>1.Chromosomal aberration test in cultured mammalian cells (OECD TG 473)</td></tr>
<tr><td>2.Mouse Lymphoma TK Assay (OECD TG 476)</td></tr>
<tr><td colspan="2" rowspan="3">Eco-toxicity</td><td colspan="2">Algae growth inhibition test (OECD TG 201)</td></tr>
<tr><td colspan="2">Acute daphnia immobilization test (OECD TG 202)</td></tr>
<tr><td colspan="2">Acute fish toxicity test (OECD TG 203)</td></tr>
<tr><td colspan="4">Polymer Flow Scheme</td></tr>
</table>

1. Introduction of OECD TG 301F

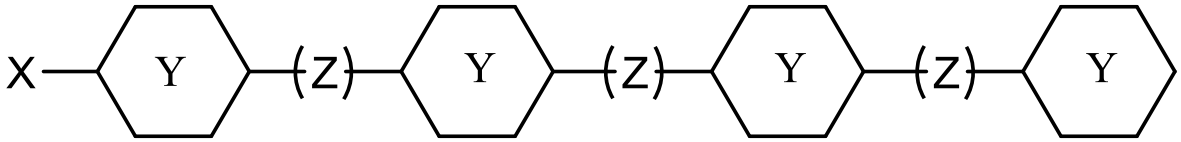
		Biodegradation test of CSCL (TG 301F)	Biodegradation test of CSCL (TG 301C)
Conditions of incubation	Concentration of test item	100 mg/L	
	Concentration of activated sludge	30 mg/L	
	Incubation temperature	22 ±1℃	25±1℃
	Incubation duration	28 days	
Inoculum		Activated sludge (Sludge in sewage treatment plants, mainly handling domestic wastewater)	Activated sludge (On-site sludge sampling was carried out at 10 locations)
Test solution	Abiotic control	Any number	1 point
	Test suspensions	2 points or more	3 points
	Inoculum blank	2 points	1 point
	Activity control	1 point (Aniline, Sodium benzoate, or Sodium acetate)	1 point (Aniline)
Other features	In the case of a test substance having inhibitory activity against microorganisms	Bottle with test substance concentration of 30 mg/L can be added	—
	When the test substance is a poorly water-soluble substance	Auxiliary substances may be used	—

2. Exemption from Biodegradation Test of Liquid Crystalline Substance

・From the findings of substances whose biodegradability was determined in the past (about 7,800 substances), liquid crystalline substances tended to be difficult to biodegrade in general.

→We analyzed past test data and extracted structures that can be said to be hardly biodegradable and no decomposition products.

→A substance group that can be evaluated as "hardly biodegradable and no decomposition products " was defined and it was made possible to make a decision without conducting a degradability test.



※The figure shows the case of 4 rings

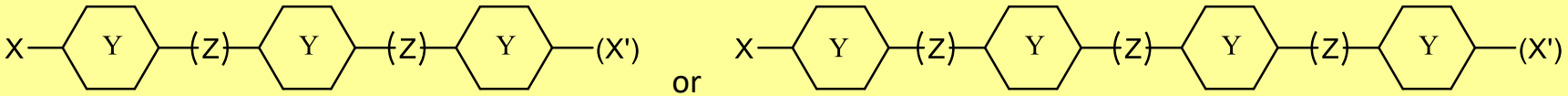
X: Chain portion

Y: Ring portion

Z: Portion connecting ring structures (Rings may be directly bonded to each other.)

2. Exemption from Biodegradation Test of Liquid Crystalline Substance

In the following cases, there is a possibility that it can be determined to be hardly biodegradable and no decomposition products.



X: alkyl group(-$(CH_2)_nCH_3$), Alkoxy group (-$O(CH_2)_nCH_3$)

※ Linear type, C≦5, The content of unsaturated bonds is acceptable.

X': alkyl group (-$(CH_2)_nCH_3$), Alkoxy group (-$O(CH_2)_nCH_3$), no replacement

※ Conditions of alkyl group or alkoxy group: Linear type, C≦5, The content of unsaturated bonds is acceptable.

Y: oxane-2,5-diyl, cyclohexane-1,4-diyl, naphthalene-2,6-diyl, 1,4-phenylene

※Only substitution with fluoro (-F), chloro (-Cl), bromo (-Br), and iodo (-I) is possible.

Z: ethylene (-CH 2 CH 2 -), oxy (difluoromethylene) (- OCF 2 -), oxymethylene (- OCH 2 -), rings may be directly bonded to each other.

*In order to exempt the biodegradability test, confirmation of expert advisors is also necessary.

3. Rationalization of Polymer Flow Scheme

The polymer flow scheme test is a test for simply evaluating the safety of polymers and consists of the following three test items.

- Physicochemical stability and acid/alkali solubility test
  Examine the test substance for a certain period under acid/alkali conditions and check the stability of the test substance by measuring the change in weight, dissolved organic carbon (DOC), IR spectrum, and molecular weight change.
- Solubility test in water and organic solvent
  Dissolve the test substance in water and organic solvent, and confirm the solubility in each solvent.
  If it is insoluble in all solvents, measurement of molecular weight distribution is not carried out.
- Molecular weight distribution measurement
  When dissolving in a solvent in the solubility test, measure the molecular weight distribution.

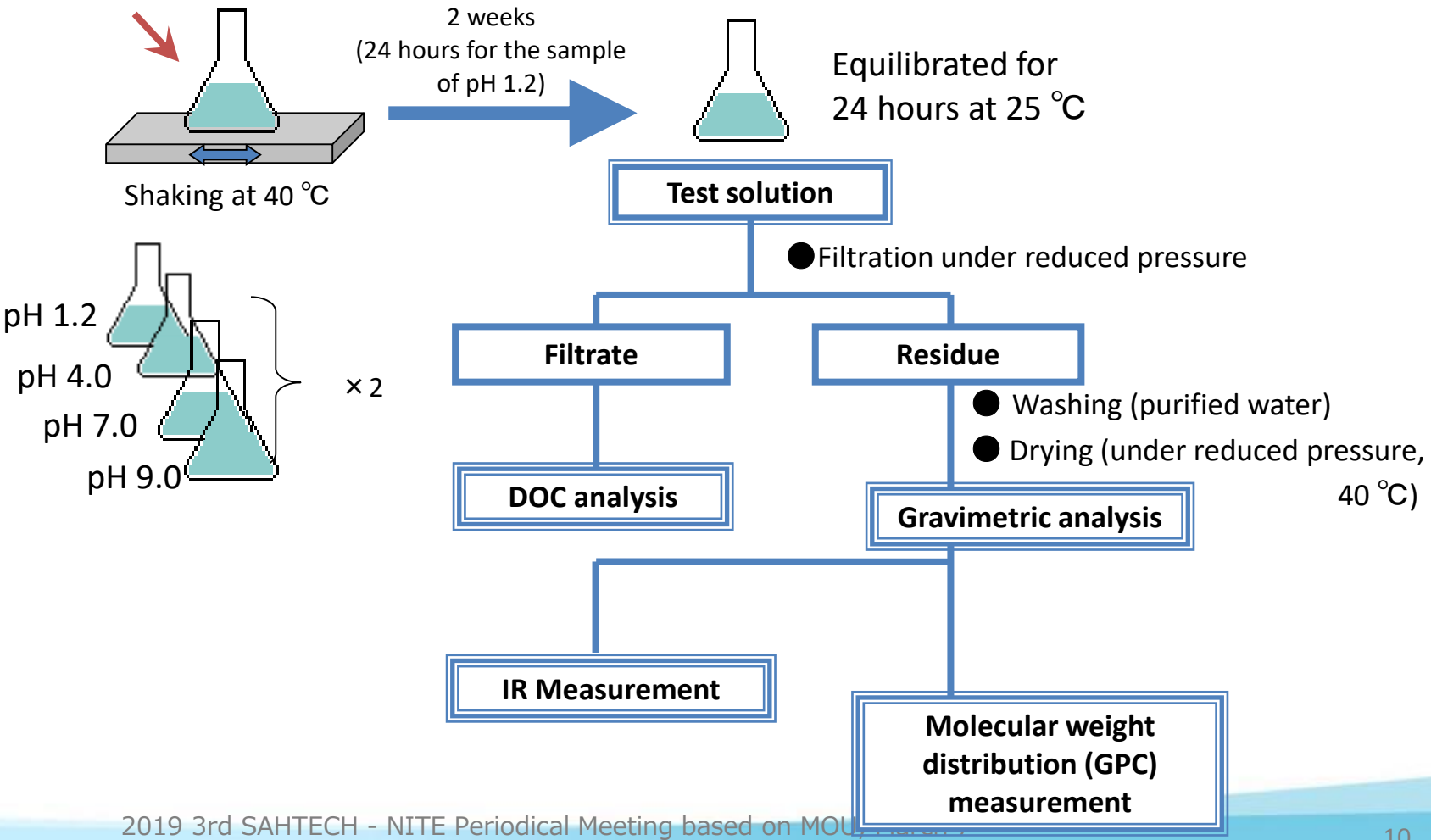
- From the test results of the above three items, biodegradation and bioaccumulation are judged.
- Toxicity and eco-toxicity are judged according to functional groups in the polymer compound.

NITE analyzed past results of polymer flow test, thereby reducing test items.

3. Rationalization of Polymer Flow Scheme

- Physicochemical stability and acid/alkali solubility test (before)

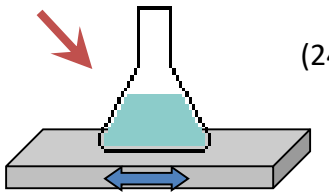
Test concentration: 1,000 mg/L



3. Rationalization of Polymer Flow Scheme

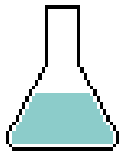
● Physicochemical stability and acid/alkali solubility test **(Now)**

Test concentration: 1,000 mg/L



Shaking at 40 ℃

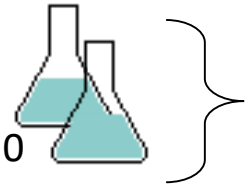
2 weeks
(24 hours for the sample of pH 1.2)



Equilibrated for 24 hours at 25 ℃

Test solution

● Filtration under reduced pressure



pH 4.0
pH 9.0

× 2

Omitted pH 1.2 and 7.0

Filtrate

DOC analysis

Residue

● Washing (purified water)

● Drying (under reduced pressure, 40 ℃)

Omitted gravimetric analysis

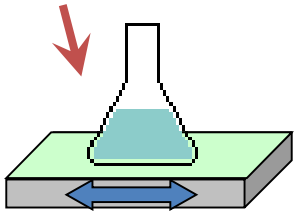
IR Measurement

Molecular weight distribution (GPC) measurement

3. Rationalization of Polymer Flow Scheme

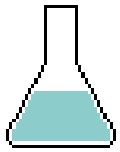
● Solubility test in water and organic solvent (before)

Test concentration: 2,000 mg/L



Shaking at 35-40 ℃

1 hour

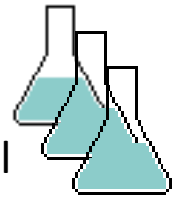


Equilibrated for
24 hours at 25 ℃

Water

Heptane/octanol

THF/DMF



× 2

Test solution

● Filtration under reduced pressure

Filtrate

Residue

● Drying (under reduced pressure, 40 ℃)

DOC analysis

※Water

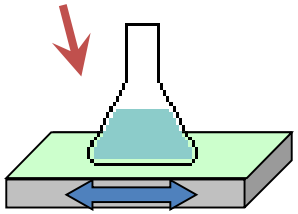
Gravimetric analysis

※Water
Heptane/octanol
THF/DMF

3. Rationalization of Polymer Flow Scheme

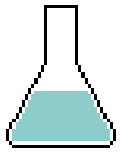
● Solubility test in water and organic solvent **(Now)**

Test concentration: 2,000 mg/L



Shaking at 35-40 ℃

1 hour



Equilibrated for
24 hours at 25 ℃

Water

THF/DMF

× 2

Omitted heptane/octanol

Test solution

● Filtration under reduced pressure

Filtrate

Residue

● Drying (under reduced pressure, 40 ℃)

DOC analysis

Gravimetric analysis

※Water

※THF/DMF

Reduction of the examination expense burden on the reporting person due to a decrease in testing man-hours

Omitted gravimetric analysis of water

Summary

- ✓ In this amendment, we have reduced the testing expense burden on businesses by introducing OECD TG 301F, allowing an exemption from the biodegradation test of liquid crystalline substances, and rationalizing the polymer flow scheme test.
- ✓ We plan to review the contents of the test in the future by conducting hearings with business operators.

Thank you for your attention.