経済産業省
Ministry of Economy, Trade and Industry
METI

Procedure for New Chemicals
under Chemical Substances Control Law (CSCL)

December 2015

Chemical Safety Office
Chemical Management Policy Division
Ministry of Economy, Trade and Industry (METI)

1. Outline of New Chemical Procedure under CSCL

Purpose and Scope of CSCL

Purpose

- To prevent environmental pollution caused by chemical substances that pose a risk of impairing human health and interfere with the inhabitation and growth of flora and fauna.

Scope

- Chemical substances

  Chemical compounds substance created through chemical reactions.
- Industrial chemicals

  Chemicals that are subject to other laws such as medicines and pesticides are outside the scope of CSCL

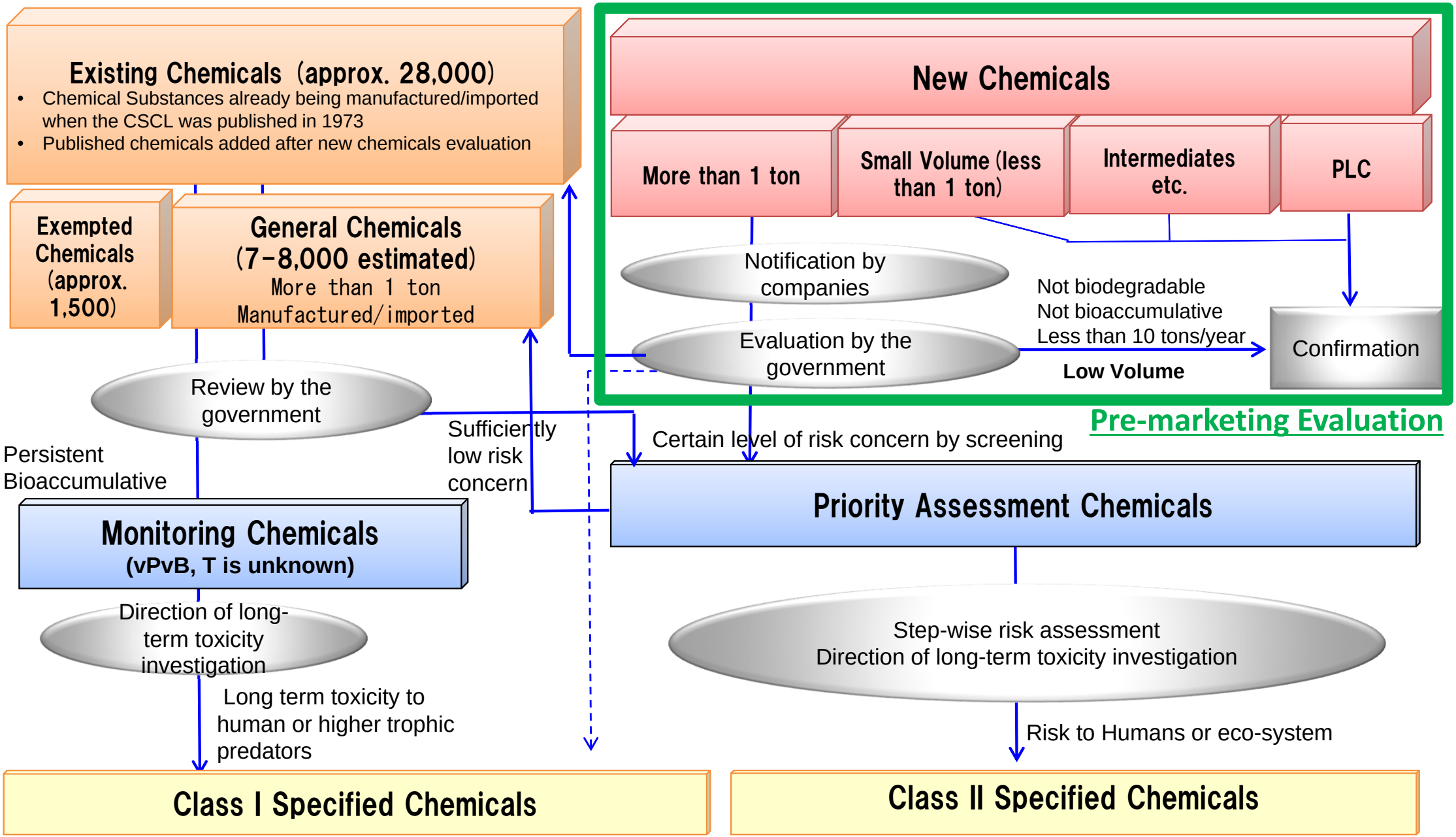
Outline

- New Chemicals

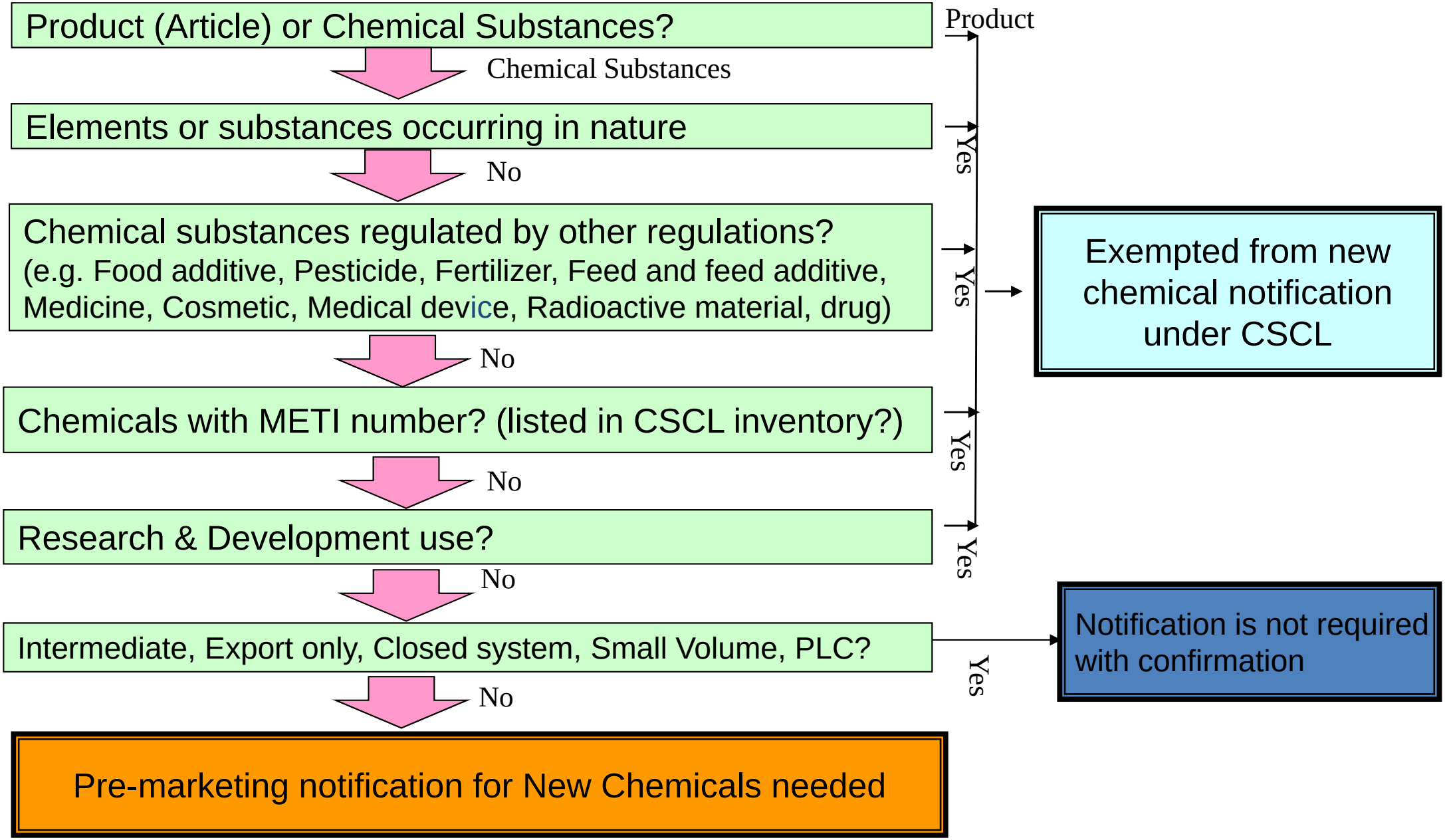
  Notification to and evaluation by the government are required before manufacture/import.
- Existing Chemicals

  Annual report of manufacture/import volume and usage is mandatory. The government conducts risk assessment based on this annual notification and may request additional toxicity information to the manufactures/importers if necessary.

Evaluation/Assessment Flow of CSCL

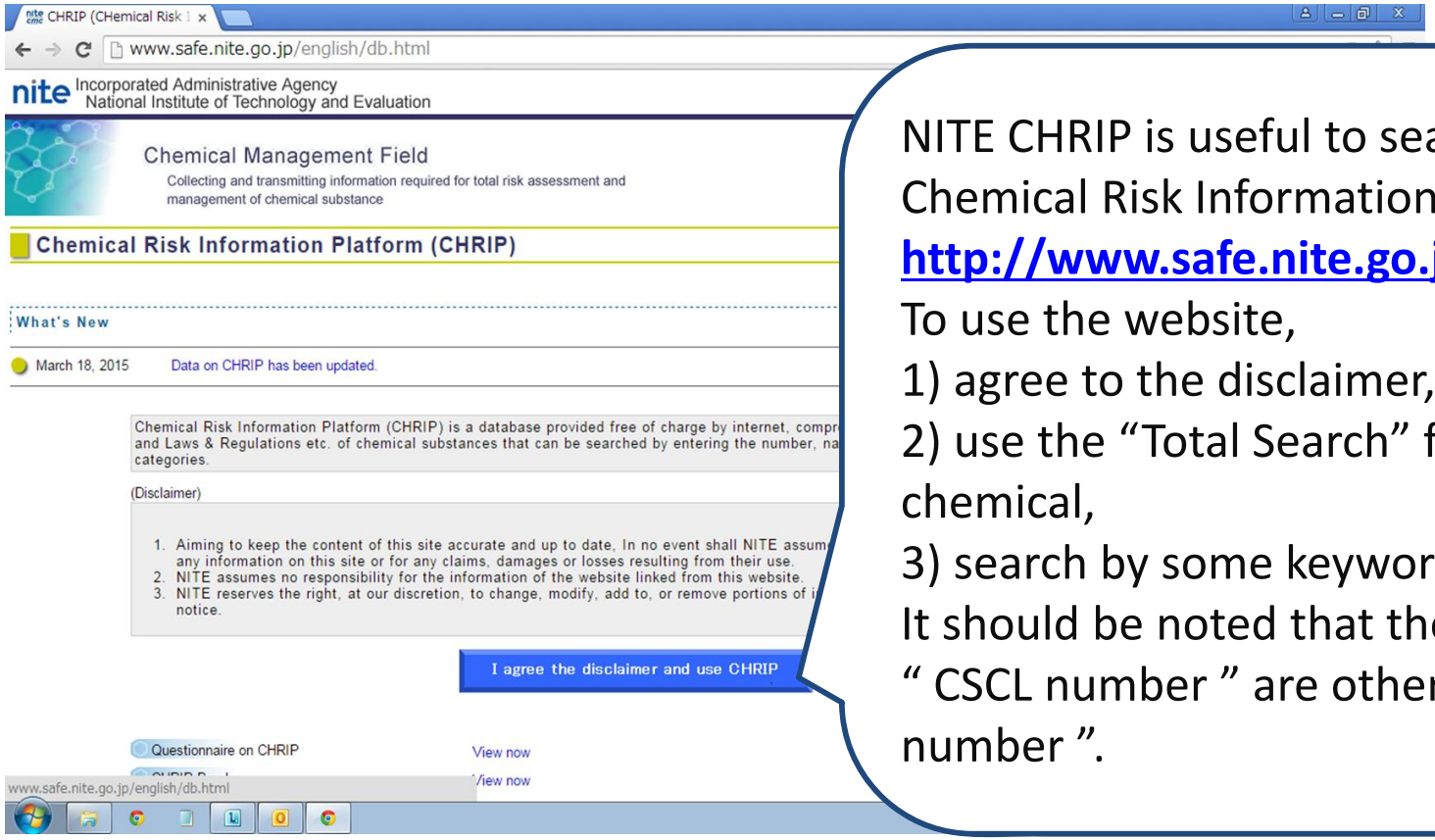


Whether Pre-marketing New Chemical Notification is necessary?



Search for CSCL number (METI number)

- If chemical substance has CSCL number (METI number), it is existing chemical under CSCL.
- Existing chemicals are not required to notify before manufacture and import.
- METI does not provide search service, but it is possible for companies to ask METI whether their understanding of CSCL numbers for some substances is right or not.



NITE CHRIP is useful to search for CSCL number.
Chemical Risk Information Platform (CHRIP):
http://www.safe.nite.go.jp/english/db.html
To use the website,
1) agree to the disclaimer,
2) use the “Total Search” function to search for the chemical,
3) search by some keywords or structure.
It should be noted that the “ MITI number ” and the “ CSCL number ” are other names for the “ METI number ”.

What is “Product”?

The “products”, which meet either of the following criteria, are not treated as chemical compounds under CSCL.

(i) Article

Products that possess specific shapes and do not change in their composition or shape when in use. (e.g. synthetic resin storage containers, plates, tubes, rods, and films)

Following changes are not treated as change in the composition or shape:

- Any change in the shape of a product that does not lead to any loss of its original function in use;
  (e.g. deformation in use or modification of a dimension that does not cause any modification of its functions)
- Any change in the shape of a product due to exercise of its original function;
  (e.g. wear on a rubber eraser)
- Any change that incidentally causes loss of its function as a commercial product.
  (e.g. damage in use)

(ii) Subdivided Mixtures

Mixtures in sufficiently subdivided states and in forms, with minimal modification such as label change, that will permit them to be sold over the counter. (e.g. synthetic resin paints containing pigments and household detergents.)

Research and Development Use

If new chemicals are manufactured or imported for “Research and Development Use”, such as testing and research as well as reagents, pre-marketing notification of them is not necessary.

Testing and Research

All of new chemicals must be used for testing, experiments, research, development, or inspection at schools, research institutes, laboratories or testing institutes regardless of whether these institutes are public or private.

For example, when the new chemical is manufactured in a so called “test plant” in order to verify the possibility of the practical application of the results of testing and research, premarketing notification of it is not necessary as long as it is manufactured for the purpose of testing, experiments, research, development, or inspection carried out by the manufacturer or the recipient of it.

Reagents

Any chemical substance used for the detection or quantification of a substance by a chemical process, for experimental synthesis or a substance, or for measurements of the physical characteristics of a substance.

Points: There is no threshold of volume regardless whether or not compensation is received, but change of use is not allowable.

2. New Chemical Notification

- Normal
- Low Volume
- Small Volume
- Polymer Flow Scheme

Pre-marketing Notification and Evaluation

- There are two types of notification. (Normal, Low Volume)
- If companies choose Normal notification and evaluation procedure, they can manufacture or import the new chemical without volume limit.
- The name of the new chemical evaluated through Normal procedure will be published in five years and listed on the CSCL inventory.
- If companies choose Low Volume procedure, they can manufacture or import the new chemicals within the confirmed volume, less than 10 tons per year.
- The name of the new chemical evaluated through Low Volume will no be published.
- Required hazard information are different between two types.

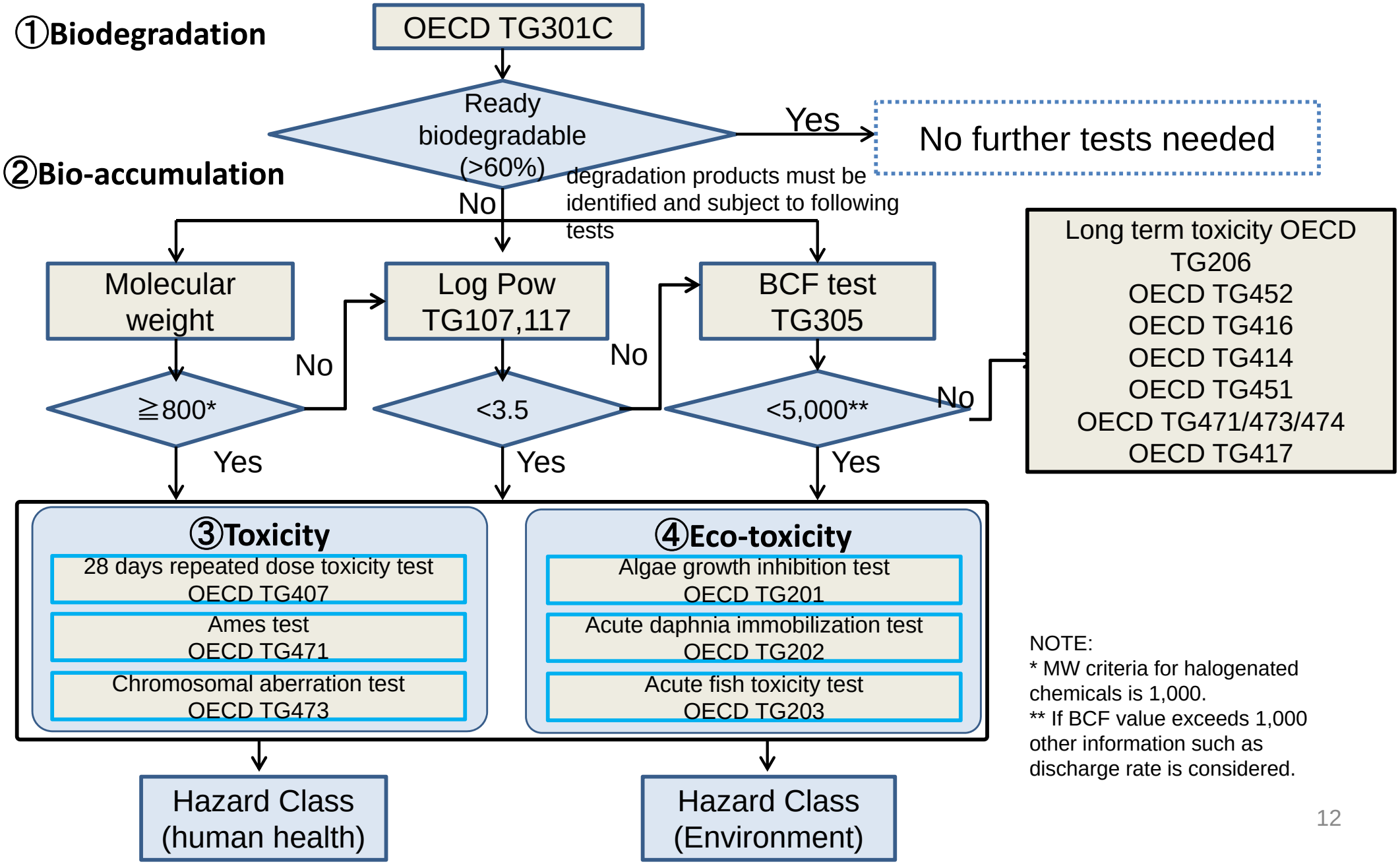
Types of procedure	Volume limit	Confirmation	Evaluation Points (Required Hazard Information)
Normal	No limit	No need	①Biodegradation, ②Bioaccumulation, ③Toxicity, ④Eco-toxicity
Low Volume	10 tons/year (in Japan)	Need (annually)	①Biodegradation, ②Bioaccumulation
Small Volume	1 ton/year (in Japan)	Need (annually)	No need

Evaluation Points

Evaluation Points	Related test	OECD TG
①Biodegradation	Biodegradation test	TG301
②Bioaccumulation*	Partition coefficient test	TG107, TG117
	BCF test (if Log Pow>3.5)	TG305
③Toxicity	Ames test	TG471
	Chromosomal aberration test	TG473
	28days repeated dose toxicity test	TG407
③Eco-toxicity	Acute fish toxicity test	TG203
	Acute daphnia immobilization test	TG202
	Algae growth inhibition test	TG201

- QSAR and analogous are applicable for bioaccumulation evaluation. (Please check part 4 of this document.)
- Degradation products must be identified and evaluation of these products are required.

Flow of Evaluation Process



NOTE:
* MW criteria for halogenated chemicals is 1,000.
** If BCF value exceeds 1,000 other information such as discharge rate is considered.

Polymer Flow Scheme (PFS)

- If new chemicals are polymers, evaluation through Polymer Flow Scheme (PFS) may be possible.
- Polymer definition for the use of PFS is equivalent to OECD definition.
- The basic concept of PFS is that the following polymers can not pass through a biological membrane, which are deemed to be low concern for human health and environment.
  - Large molecular weight (MW)
  - Low rate of oligomer (MW<1,000)
  - Stable in neutral, acid, and alkaline water

OECD polymer definition;

"Polymer means a substance consisting of:

a. molecules characterized by the sequence of one or more types of monomer units;

b. a simple weight majority of molecules containing at least three monomer units that are covalently bonded to at least one other monomer unit or reactant;

c. less than a simple weight majority of molecules of the same molecular weight; and

d. molecules distributed over a range of molecular weights wherein differences in the molecular weights are primarily attributable to differences in the number of monomer units."

Criteria for Polymer Flow Scheme (PFS)

- If the new polymer meets meet following criteria, it is evaluated not to be hazardous under CSCL. (No additional evaluation, no additional data requirement)

<Criteria 1>

I. Number Average Molecular Weight (NAMW) >=1,000

II. Solubility
Soluble in water or solvents

III. Oligomer Content (Molecular Weight <1,000)
a) Oligomer Content =<1 weight %, or
b) Oligomer >1 weight % and no information to indicate bio-accumulation

IV. Stability
Chemical composition does not change in neutral, acid, and alkaline water. (e.g. less than 2 % weight change)

V. Chemical Structure
No Cationic polymer. No inclusion of heavy metal

<Criteria 2>

I. Number Average Molecular Weight (NAMW) >=1,000

II. Solubility
Not soluble in water and solvents

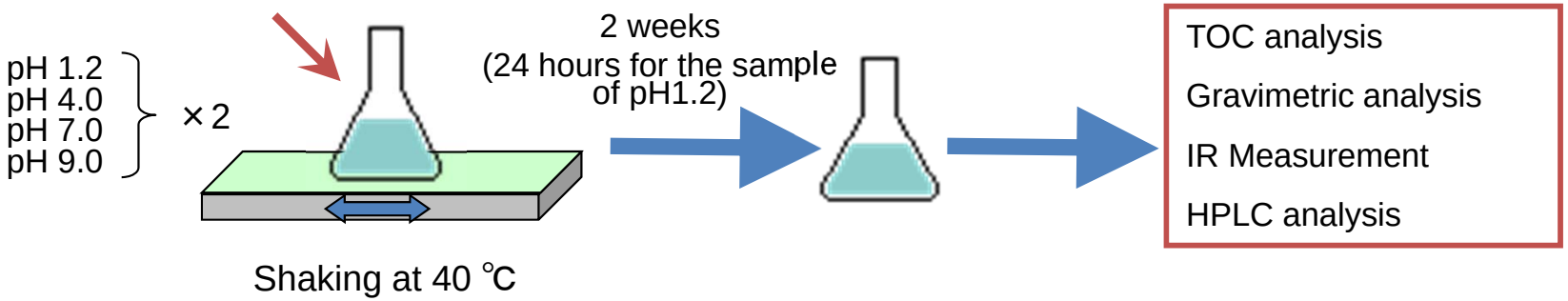
III. Stability
Chemical composition does not change in neutral, acid, and alkaline water. (e.g. less than 2 % weight change)

IV. Chemical Structure
No Cationic polymer. No inclusion of heavy metal

Test method for PFS

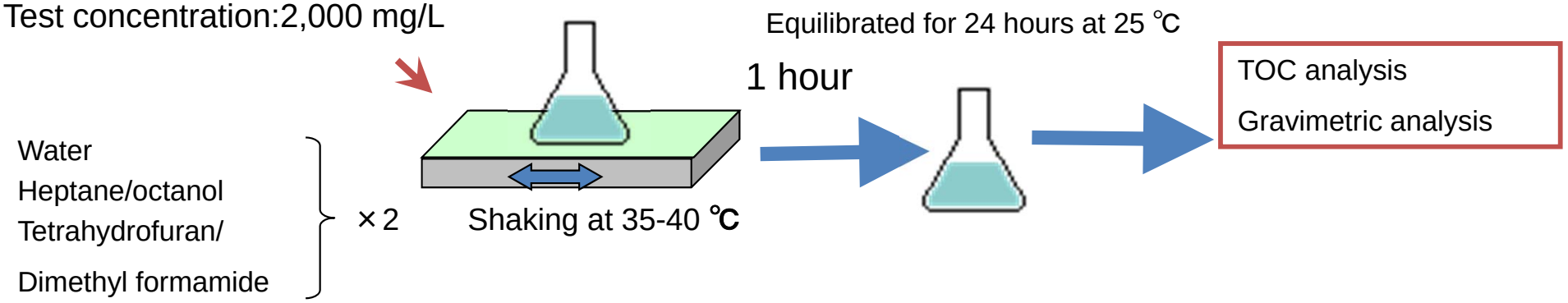
Stability test

Test concentration:1,000 mg/L



Solubility test

Test concentration:2,000 mg/L



3. New Chemical Confirmation

- Intermediates
- Small Volume Intermediates
- Polymers of Low Concern (PLC)

Intermediate, Closed system, Export only

- If companies get either of following confirmations for the new chemicals from the government, they can manufacture or import the new chemicals.
- They do not have to get this confirmation annually, but the government may check whether companies follow the conditions of confirmation.

Intermediate (Normal)

- Companies will manufacture or import a new chemical as the intermediate to another chemical.
- Companies will take the necessary measures to prevent environmental pollution from the new chemical during the period until the new chemical is transformed intro the other chemical.

Closed system

- Companies will manufacture or import a new chemical for use in such a way as to prevent any emission outside the facility or equipment.
- Companies will take the necessary measures to prevent environmental pollution from the new chemical during the period during until the new chemical is disposed of.

Export only

- Companies will manufacture or import a new chemical for the purpose of export.
- Companies will take the necessary measures to prevent environmental pollution from the new chemical during the period until the new chemical is exported.

A New Rule for Small Volume Intermediate/Export only

- A new confirmation scheme for new chemicals, “Small Volume Intermediates/Export Only” started in October 2014.
- This is a new rule for small volume and intermediate chemicals to be exempted from normal new chemical assessment procedures under CSCL.

Small Volume Intermediate/Export only

- A company that intends to manufacture/import a new chemical substance for intermediates, of less than or equal to 1 ton/year can get confirmation from the government.
- A company with this approval can manufacture/import this new chemical substance for intermediates, of less than or equal to 1 ton/year without undergoing normal assessment (evaluation) procedures by the government.

Characteristic:

- There is already “Intermediate” rule for exemption. But it may take time to get confirmation (approval) as many application documents are required.
- Getting confirmation of “Small Volume Intermediates” is much easier and faster than getting confirmation of “Intermediates.”

Confirmation of Polymers of Low Concern (PLC)

- If companies get confirmation that the new chemical meets following PLC criteria, they can get PLC confirmation and manufacture or import the new chemicals.

Criteria 1. Polymers that meet following criteria

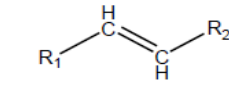
- Meet I, II and III of Criteria 2 for PFS (Please see page 14 of this document).
- Do not contain metals other than Na, Mg, K, Ca.
- Do not show cationic characteristics when solved in acid and/or alkaline.

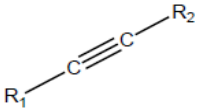
Criteria 2. Polymers that meet following criteria.

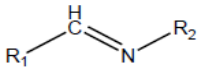
- Meet I, II and IV of Criteria 1 for PFS (Please see page 14 of this document).
- Oligomer content (MW<1000) =< 1%, and no information suggests they are highly bioaccumulative
- Do not contain As, Se.
- Do not contain metals other than Na, Mg, K, Ca.
- Do not show cationic characteristics when dissolved in acid and/or alkaline.
- Meet either criteria A or B.

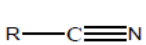
A: Mw >= 10,000

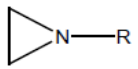
B: 1,000 <Mw<10,000,
all monomers are existing chemicals etc, and
do not contain any functional groups below:

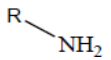

C-C double bond

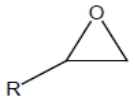

C-C triple bond

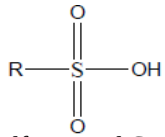

C-N double bond

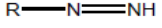

C-N triple bond

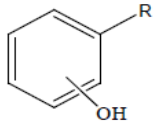

Aziridyl Group


Amino Group

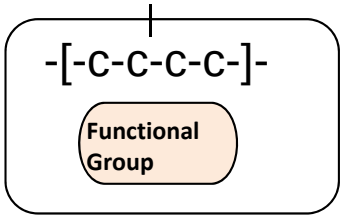

Epoxy Group


Sulfonic acid Group


Hydrazino Group


Phenolic hydroxyl Group


Fluorine



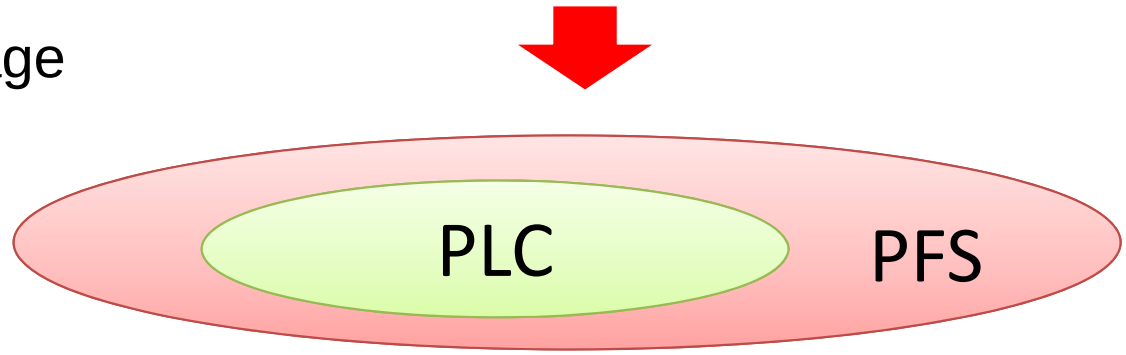
Difference between PFS and PLC

- PLC criteria is similar to PFS criteria.
- Polymers that meet PFS criteria is more than polymers that meet PLC criteria because the treatment for them is different under CSCL.

Difference between PFS and PLC

	Polymers that pass PFS	Polymers meeting PLC
Assessment by experts (in the Chemical Councils)	Yes	No
Time of gov. procedure	Long (approx. 2-3 months)	Short (about one month)
Listed in the Inventory	Listed	Not listed

Coverage



4. Recent Topics
(New Guidance for Bioaccumulation Assessment)

- QSAR and analogous (in 2013)
- Log D (for Ionic Substance) (in 2014)

Bioaccumulation Assessment by using QSAR

- In response to the request to reduce testing cost and time and the international demand to reduce animal tests, Japan made a new guidance on bioaccumulation assessment by using analogous and QSAR.

1. Bioaccumulation Assessment by using QSAR and Read-across

If chemical A meets following criteria, chemical A can be assessed to be not highly bioaccumlative:

(1) Chemical A is similar in structure to Chemical B (specifically as follows):

i. Chemical A has the same basic skeleton as Chemical B and chemical A's structure is partially changed from compound B, or

ii. Chemical A is an isomer of Chemical B.

(2) Measured BCF (bio-concentration factor) of chemical B < 500.

(3) Bioaccumulation of chemical A is estimated in a rational way to be almost the same as or lower than chemical B based on their chemical structure. (specifically as follows)

i. Calculated BCF by using QSAR of chemical A is almost the same as or lower than measured and calculated BCF of chemical B.

ii. Two or more similar chemical B have measured BCF <100.

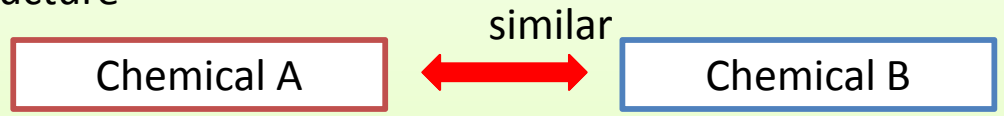
※ Recommended QSAR model is either BCFBAF (EPI SUITE) or BCF base-line model (OASIS Catalogic).

※ Japan added the published measured BCF data on the website in Sep. this year in order to facilitate the above approach. NITE website is useful to search measured BCF data because it includes how to use it by OECD QSAR toolbox. (both in Japanese…)

Example (1)

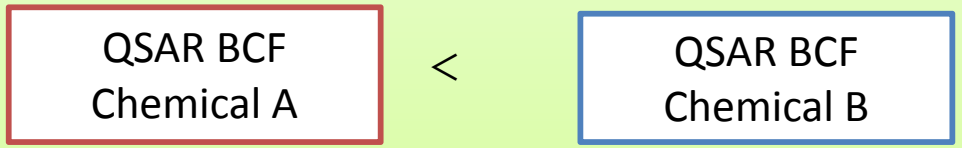
Case 1

(1) Chemical Structure



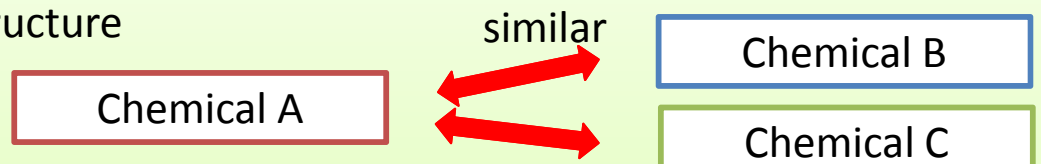
(2) Measured BCF

(3) Calculated BCF by using QSAR

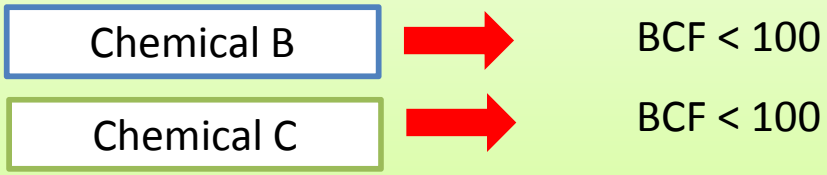


Case 2

(1) Chemical Structure



(2) Measured BCF



Chemical A is not highly bioaccumulative in both cases.

Bioaccumulation Assessment by using Analogous

- In response to the request to reduce testing cost and time and the international demand to reduce animal tests, Japan made a new guidance on bioaccumulation assessment by using analogous and QSAR.

2. Bioaccumulation Assessment Based on the Comparison of Hydrophilicity (Polarity) by HPLC

If chemical A meets the following criteria, chemical A can be assessed to be not highly bioaccumulative:

(1) Chemical A is similar in structure to chemical B. (specifically as follows):

i. Chemical A has the same basic skeleton as Chemical B and chemical A's structure is partially changed from compound B, or

ii. Chemical A is an isomer of Chemical B.

(2) Measured BCF of chemical B is < 500.

(3) It is observed that chemical A is more hydrophilic (polar) than chemical B by reversed-phase HPLC.

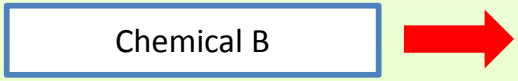
※ This analogous method does not apply to surfactants, organic metallic compounds, low purity compound and inorganic compound.

Example (2)

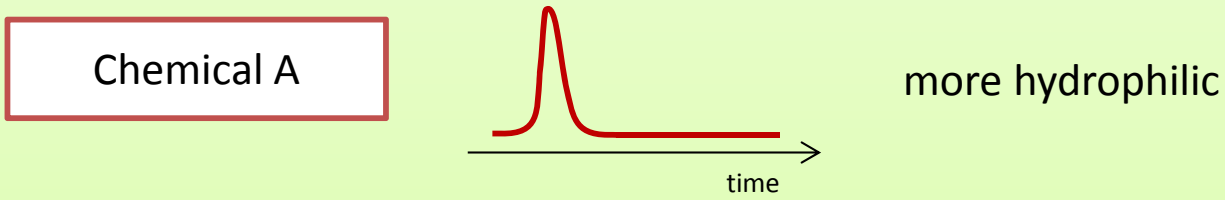
Case 3

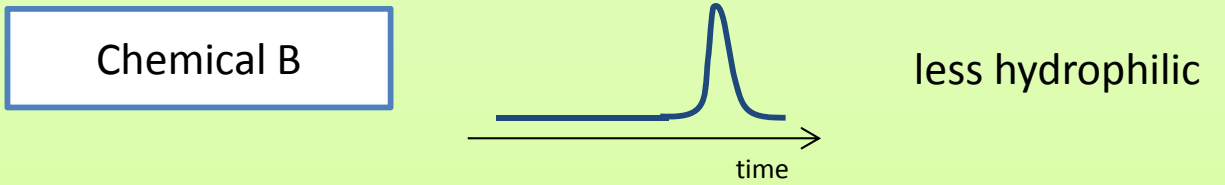
(1) Chemical Structure

(2) Measured BCF



(3) Comparison of Hydrophilicity (Polarity) by reversed-phase HPLC





Chemical A is not highly bioaccumulative.

Bioaccumulation Assessment of Ionic Substances

- If log Pow is <3.5, that substance is assessed to be not highly bioaccumlative.
- However, measuring log Pow of ionic substances in undissociated state is difficult.
- In order to simplify bioaccumulation assessment of ionic substances, Japan made a new guidance to use log Dow (the partition coefficient determined around a pH of 7).

◆ If log Dow of an ionic compound (e.g. sulfonic acids, carbonic acids, zwitterionic substances, quaternary amines, etc.) which is difficult to measure log Pow in undissociated state is < 2.5, that chemical substance can be assessed to be not highly bioaccumulative.

◆ This method can not apply to any compounds which partialy includes trifluoromethyl (CF3-) or tetrafluoroethylene (-CF2-CF2-) in their structure.

※Under OECD TG107 (Shake-Flask method) and TG117 (HPLC method), log Pow should be measured in undissociated state.
※Under this method, “an ionic compound which is difficult to measure log Pow in undissociated state” means, in principle, a compound whose pKa is less than 3 for acids and more than 11 for base.
※This method does not apply to surfactants, mixture which has distribution of molecular weight, organic metallic compound, low purity compound (except for HPLC method) and inorganic compound.
※Please consult with METI for using this method.
※Both Shake-Flask method and HPLC method are applicable to measure log Dow.