Methods for the Risk Assessment of Priority Assessment Chemical Substances

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I. Introduction

1. Background

On the basis of the international goal agreed upon in the World Summit on Sustainable Development in 2002, which is: “Aiming to achieve, by 2020, that chemicals are used and produced in ways that lead to the minimization of significant adverse effects on human health and the environment, using transparent science-based risk assessment procedures and science-based risk management procedures, taking into account the precautionary approach” (hereinafter referred to as the “2020 Goal”), the Act on the Evaluation of Chemical Substances and Regulation of Their Manufacture etc. (hereinafter “the Japanese Chemical Substances Control Act”) was amended in May 2009, and has fully come into force since April 2011.
The amended Japanese Chemical Substances Control Act aims to introduce an effective and efficient system; upon implementation of screening assessments on all General Chemical Substances including Existing Chemical Substances, and upon designation of applicable substances as Priority Assessment Chemical Substances, this system allows the government to implement the risk assessment through collecting information in a stepwise manner.

This document outlines the methods for risk assessments that are based on the basic concepts of the risk assessment on Priority Assessment Chemical Substances (described in the frames).

2. Objectives of the risk assessment

The Japanese Chemical Substances Control Act defines the risk assessment for Priority Assessment Chemical Substances as, “the assessment to determine whether there exists a risk of damage to human health or to the population and/or growth of animals and plants in the human living environment, due to environmental contamination attributable to chemical substances.”
This risk assessment aims to enable the Minister of Health, Labour and Welfare, the Minister of Economy, Trade and Industry and the Minister of the Environment (hereinafter, the “Three Ministers”) to determine the necessity for their exercise of regulatory authority such as the “Designation as Class II Specified Chemical Substances” and the “Rescission of Designation as Priority Assessment Chemical Substances” under the Japanese Chemical Substances Control Act.
In order to achieve the 2020 Goal, with international movements taken into consideration, the risk assessment shall, by the year 2020, be implemented to identify Priority Assessment Chemical Substances posing a considerable risk to human beings or animals and plants in the human living environment, to designate those chemical substances posing such risk as Class II Specified Chemical Substances, and to take necessary control measures, in accordance with the Japanese Chemical Substances Control Act.
Further, to lead international chemical management, Japan will, even after 2020, continue to conduct the risk assessment as required on those Priority Assessment Chemical Substances not posing a considerable risk on previous occasions, and to immediately designate those chemical substances as Class II Specified Chemical Substances where it is necessary to do so.
This requires the risk assessment for designation of Class II Specified Chemical Substances to be conducted as early as possible on substances in order of priority for this assessment, given that it takes considerable time to implement the long-term toxicity tests, etc., based on the instructions on hazard investigation.
From the advancement of the risk assessment by the government and at the same time the collection of information from business operators on chemical hazards and substance handling, Japan expects the further development of chemical management based on actions of the private and public sectors.

*The designation of substances as Class I Specified Chemical Substances, Monitoring Chemical Substances or Class II Specified Chemical Substances rescinds the designation as Priority Assessment Chemical Substances. However, the sole description of “rescission of designation as a Priority Assessment Chemical Substance” in this document indicates only the rescission of designation as a Priority Assessment Chemical Substance and indicates the reinstatement of the relevant substance as a General Chemical Substance.

Figure 1 illustrates the position of the risk assessment of Priority Assessment Chemical Substances under the Japanese Chemical Substances Control Act.

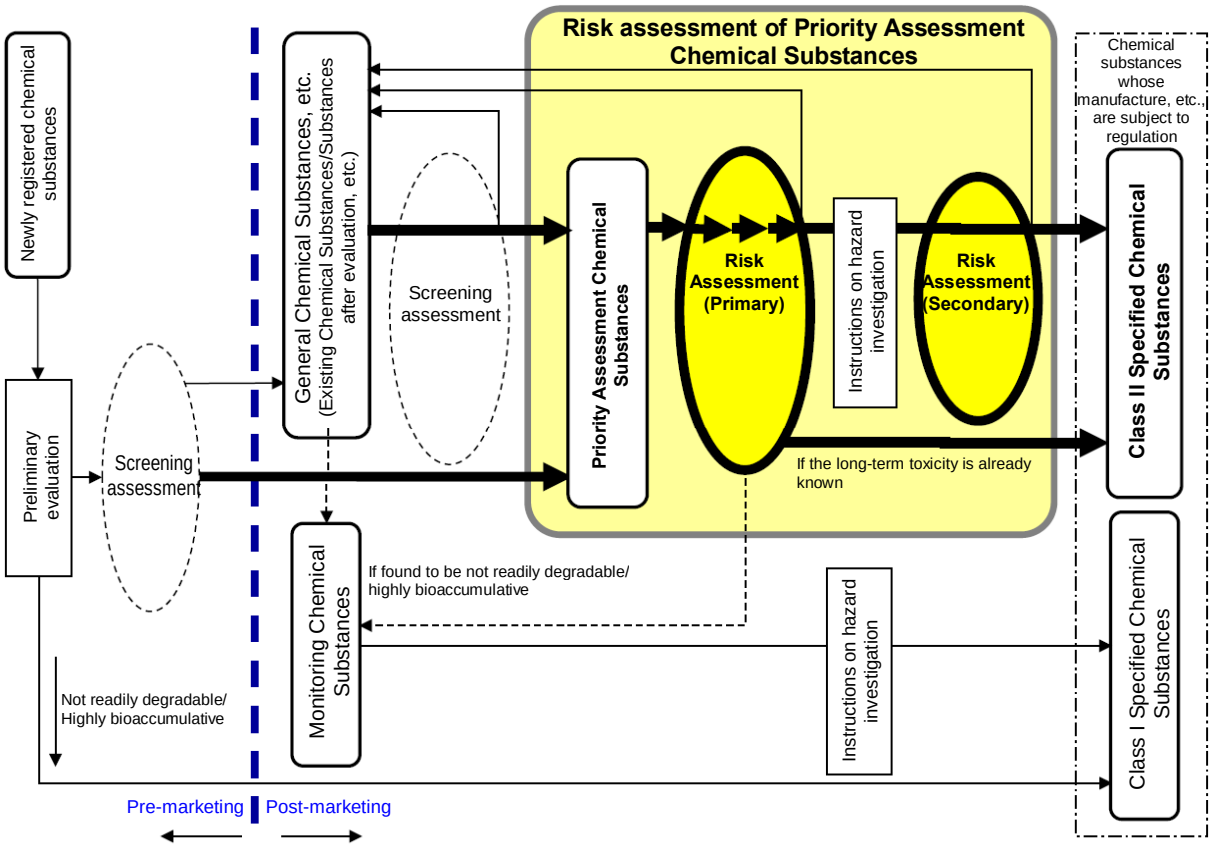


Figure 1 The Position of the Risk Assessment of Priority Assessment Chemical Substances in the Framework of the Japanese Chemical Substances Control Act

II. Basic premises and concepts of the risk assessment

3. Basic premises of the risk assessment

3.1 Scope of the risk assessment

In principle, the risk assessment under the Japanese Chemical Substances Control Act is conducted with the scope of the control of the Act taken into consideration. The chemical substances subject to the Act do not include elements, natural products, radioactive substances or those specified poisons under the Poisonous and Deleterious Substances Control Law. In relation to the scope of use subject to the Act, special attention should be paid to the following points in conducting the risk assessment: The use for food, etc., under the Food Sanitation Act, the use for agricultural chemicals under the Agricultural Chemicals Regulation Law, and the use for drugs, etc., under the Pharmaceutical Affairs Law are excluded from the scope.

Figure 2 illustrates the organization of the relations between the scope of the chemical substances subject to the Japanese Chemical Substances Control Act and the other applicable Acts and Laws, from the viewpoint of the target uses and regulating methods.

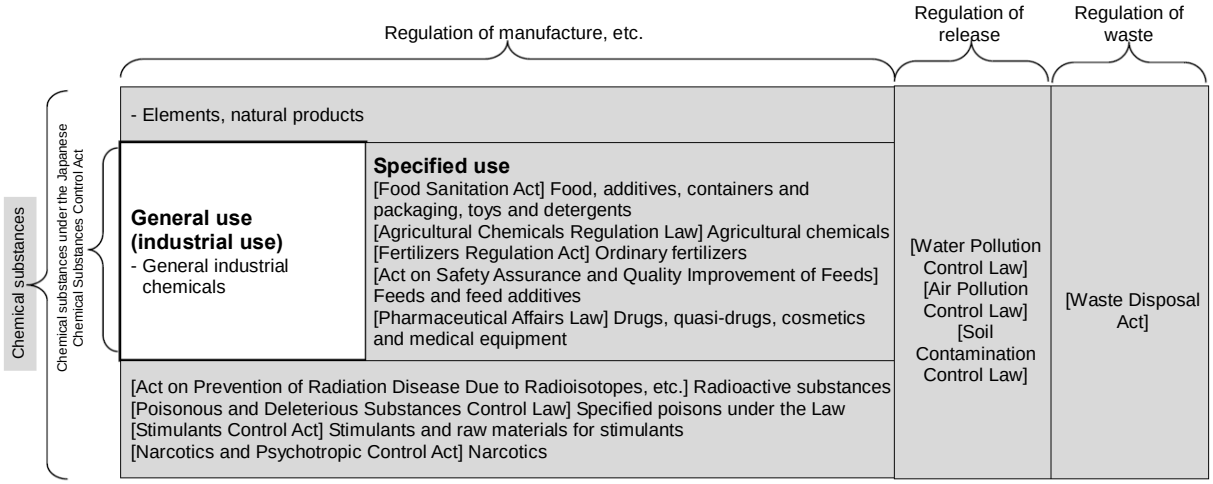


Figure 2 The Scope of the Chemical Substances Subject to the Control of the Japanese Chemical Substances Control Act (on the basis of a clause-by-clause interpretation)

3.2 Targets of the risk assessment (human health and the environmental effects)

Basically, implement the risk assessment on each of the Priority Assessment Chemical Substances and on those target substances which are, through the screening assessment, classified as having a “High” or “Mid” priority and required to be designated as Priority Assessment Chemical Substances (human health or the environmental effects). Accordingly, there are the following three types of Priority Assessment Chemical Substances. However, targets may vary depending on hazard information obtained after the designation of such targets as Priority Assessment Chemical Substances.

- The Priority Assessment Chemical Substances on which the risk assessment only in relation to human health is implemented
- The Priority Assessment Chemical Substances on which the risk assessment only in relation to the environmental effects is implemented
- The Priority Assessment Chemical Substances on which the risk assessment in relation to both human health and the environmental effects is implemented

3.3 Unit of substances for the risk assessment

In principle, the substance unit for the risk assessment is the unit used in designating a substance as a Priority Assessment Chemical Substance. However, the substance unit for the risk assessment should be

revised on the basis of information obtained through the processes of the risk assessment; for instance, a risk assessment may be implemented comprehensively on multiple chemical substances, where necessary.

The screening assessment for General Chemical Substances is generally conducted on the basis of the CAS as much as possible. However, in accord with obtained information such as information on the identification of chemical substances and hazard information, the assessment should be conducted, where necessary, in a unit of the reference numbers of the official gazette or in a unit of a group of those chemical substances for which common hazard information is available (for example, those chemical substances with isomeric mixtures or dissociation). The substance unit for the risk assessment is, in principle, determined during the screening assessment as mentioned above.
However, in the case where designation of Priority Assessment Chemical Substances takes place without information on hazardous properties obtained during the screening assessment, it is possible that the risk assessment may not be conducted appropriately in a unit of designated Priority Assessment Chemical Substances as shown by the examples below. Such cases are considered individually while the risk assessment is carried on.

Examples:
- In the case where, although a chemical substance has been designated as a Priority Assessment Chemical Substance, it becomes clear that it is more appropriate to assess it as a mixture; information obtained after the designation indicates that the substance is found in mixture properties.
- In the case where, although a group of multiple chemical substances including a mixture has been designated as Priority Assessment Chemical Substances, it becomes clear from information obtained after the designation with regard to some substances in the group that it is no longer appropriate to assess the group as a whole due to the properties of those substances.

Example cases of the assessment by group are those cases where common hazard information is available for the assessment, and further where the assessment in that unit is considered to be relevant; for instance, the existing knowledge of the hazard concerned (target substances of existing risk assessment reports and/or hazard assessment reports) has been assessed in a group.

4. Concepts of the risk assessment

4.1 Precautionary approach and transparent, science-based risk assessment

To achieve the 2020 Goal, it is necessary that the risk assessment uses “transparent science-based risk assessment procedures, taking into account the precautionary approach.”

(1) Precautionary approach

The “Precautionary Approach” means in the third environmental basic plan that “the lack of full scientific certainty shall not be used as a reason for postponing the implementation of measures, and actions shall be taken at the same time as improving scientific knowledge.”
The amendment to the Japanese Chemical Substances Control Act reflects the Precautionary Approach and designates chemical substances with a potential risk as Priority Assessment Chemical Substances. Even where full scientific certainty is not available, for instance when information from the government is limited, the risk assessment of Priority Assessment Chemical Substances should be set forward on the premise of safety, while scientific knowledge is enhanced through expanding the scope of gathering information about substances in order of the priority defined by the relative levels of their risk.
If necessary measures are determined while uncertainty still remains, such uncertainty needs to be made known. Further, if business operators, etc., offer information to reduce the uncertainty, its reliability needs to be confirmed before use of the information is considered.

(2) Transparent science-based risk assessment

Where designation of Class II Specified Chemical Substances or the instructions on hazard investigation into Priority Assessment Chemical Substances is to be determined as a result of a risk assessment, it is stipulated in the Japanese Chemical Substances Control Act that a council among the Three Ministers shall be held to deliberate the matter on the basis of scientific grounds. In that case, the council shall be held in public for the purpose of securing its transparency.
Further, the progress in the risk assessment for each substance requires to be disclosed. In addition, where designation as a Class II Specified Chemical Substance, the instructions on hazard investigation into a Priority Assessment Chemical Substance, or rescission of designation as a Priority Assessment Chemical Substance is to be determined, information on the relevant substance (the name and class reference number in the official gazette) and the outline of the risk assessment results shall be disclosed to the public with private information and copyright taken into consideration. Hazard information collected by the government is also disclosed with careful consideration of copyright, after the government has completed examination of the information.
Moreover, the methods for the risk assessment need to be established on the basis of scientific grounds and international movements, and to be disclosed as technical guidance for securing transparency.

The methods for the risk assessment of Priority Assessment Chemical Substances are the systemization of various, individual methods such as mathematical models. Individual methods have been selected from existing ones, and improved for the application of them under the Japanese Chemical Substances Control Act.
In the selection of the methods from existing ones, the methods' validity and consistency with the methods used internatinally are taken into consideration. Specifically, the conditions in the selection are that candidate methods have been applied to a chemical management system or the like in Japan or other countries, and that their grounds for being scientific methods are traceable. This selection is based on the concept that the selection of risk assessment methods from those with recognized validity secures the transparency and reliability of the methods for the risk assessment so that authorities can base their decisions on the assessment.
Moreover, the risk assessment methods are compiled as the technical guidance for standard methods and disclosed to the public in line with the following two concepts:

- To secure the impartiality and consistency among substances in relation to the risk assessment that serves as the ground for exercising a regulatory measure under the Japanese Chemical Substances Control Act; and
- To secure the transparency of the concepts and technical methods of the risk assessment.

From these aspects, in addition to the concept and procedures of the risk assessment, the technical guidance includes actual formulae and parameters, the circumstances and grounds for the selection and setting of such formulae and parameters, and results of the verification and sensitivity analysis of the methods.

4.2 Stepwise procedures of the risk assessment

Aiming to advance the risk assessment promptly and thereby aiming to reach the 2020 Goal, Japan aims, in accordance with the Japanese Chemical Substances Control Act, to implement the risk assessment of substances in order of priority through instructing business operators to conduct a hazard investigation, etc., and collecting the necessary information from them in a stepwise manner. The required information includes notification of their manufacturing/import quantities, etc., hazard information and reports on their substance handling.
The stages of the risk assessment are basically divided into two parts from the aspect of hazard information: "Risk Assessment (Primary)" at the stage in which data on long-term toxicity have not been obtained; and "Risk Assessment (Secondary)" in which such data have been obtained from the instructions on hazard investigation and are available. Further, the implementation of the "Risk Assessment (Primary)" is divided into three stages: "Assessment I" which is to set an order of priority for the implementation of the risk assessment by only using information notified, such as manufacturing/import quantities, as exposure information; "Assessment II" in which existing PRTR data and monitoring data are utilized to determine which use requires a report on substance handling; and "Assessment III" in which information on substance

handling and additional monitoring data are utilized to determine whether to give the instructions on hazard investigation.

The introduction of the stepwise risk assessment procedures as above was based on the following reasons.

- Because of the large number of Priority Assessment Chemical Substances, it is not realistic from the beginning to conduct detailed risk assessment on all substances as it requires a great amount of information, time and human resources.
- In addition to the fact that the Japanese Chemical Substances Control Act obliges business operators to notify the authorities of their manufacturing quantities, etc., the government may require business operators to report on hazard information or on substance handling where necessary, and may instruct them to conduct a hazard investigation, for the purpose of implementing the risk assessment of Priority Assessment Chemical Substances. Accordingly, the risk assessment procedures are required to be coordinated with the stepwise system for collecting information.

4.3 Continuous implementation of the risk assessment

Under the Japanese Chemical Substances Control Act, business operators are required each year to notify the authorities of their manufacturing/import quantities, etc., of Priority Assessment Chemical Substances. This notification system enables re-assessments where there is a change in their manufacturing/import quantities of those Priority Assessment Chemical Substances on which the risk assessment has already been conducted.
For this reason, in Assessment I, which is implemented only with notified information such as manufacturing/import quantities, etc., the assessment is repeated every year to review the order of priority. In relation to Assessment II or a subsequent assessment, re-assessments are conducted as required.
Similarly, it is possible that those substances, which are General Chemical Substances as their designation as Priority Assessment Chemical Substances has been rescinded, may be re-designated as Priority Assessment Chemical Substances, as the screening assessment is repeated every year. However, the screening assessment of such substances takes account of results of risk assessments.

4.4 Concepts of the hazard assessment

Basically, the hazard information used for classifying substances into hazard classes in the screening assessment and hazard information subsequently collected are used for the hazard assessment. In principle, the same uncertainty factors as those used in the screening assessment are used for deriving the hazard assessment values or PNECs. In so doing, examine, as required, the hazard information of those substances that have not undergone individual decisions by the experts in the screening assessment. Depending on the progress in the assessment, review the application of uncertainty factors with relevant international consistency taken into consideration. Further, where new hazard information is obtained, use all available information in the risk assessment as such information becomes available, in accordance with the data reliability criteria stipulated by the government.

4.5 Concepts of the exposure assessment

Although the exposure assessment is basically conducted with the use of information obtained pursuant to the Japanese Chemical Substances Control Act, the following information should be actively utilized to ensure a more sophisticated risk assessment, depending on the stage of the assessment: PRTR data on Class I Designated Chemical Substances (PRTR target substances) under the Act on Confirmation, etc. of Release Amounts of Specific Chemical Substances in the Environment and Promotion of Improvements to the Management Thereof (the Act for PRTR and Promotion of Chemical Management); obtainable environmental monitoring data; and other information voluntarily provided from business operators. Furthermore, the government is to treat as many substances of high priority as possible as targets of environmental monitoring. From the information above, estimate the environmental concentration, human intake, the exposure concentration of aquatic organisms, etc., on the basis of a certain hypothesis in the exposure assessment. In particular, when a regulatory decision is to be made on whether a substance is a Class II Specified Chemical Substance, make the decision on the basis of a comprehensive consideration with other detailed information taken account of.
Regarding various data and mathematical models for the exposure assessment, refer to the concepts of the exposure assessment organized by international organizations, consult with experts as required, and use such data and models with due consideration of their reliability and application scopes.

Basically, mathematical models should be used for estimating the environmental concentration, amounts of human intake, the exposure concentration of aquatic organisms, etc. In Assessment I, use mathematical models for which information obtainable under the Japanese Chemical Substances Control Act can be used for estimations. In addition to this, PRTRs can also be used in Assessment II and a subsequent assessment; utilize appropriate information depending on the properties, use, etc., of the target substance.

4.6 Concepts of the risk assessment

Regarding the view of one of the requirements of Class II Specified Chemical Substances, “concern over risk in a considerably wide area,” results of the risk assessment are basically shown in terms of the nationwide distribution of the areas of risk concern. In so doing, make a comprehensive decision on the basis of results obtained from detailed information as well as results of the risk assessment on each of the release sources.

III. Overview of risk assessment methods

As shown in 4.2, the risk assessment under the Japanese Chemical Substances Control Act is put forward in a stepwise manner. The overview of the stages is provided in Table 3. In this section, the methods are organized according to the stages.

Table 3 Overview of the Risk Assessment Stages

Risk Assessment (Primary)		**Assessment Implemented on All Priority Assessment Chemical Substances as Targets**
Preparation for assessment		Information organization and degradability/accumulation assessment for the extraction and Assessment I of Priority Assessment Chemical Substances according to manufacturing quantities, etc.
	Information Organization	Organize notified information such as manufacturing quantities and information on properties (degradability, accumulation, hazardous properties, physicochemical properties)
	Extraction of Priority Assessment Chemical Substances	Organize and aggregate notified information such as manufacturing quantities. Monitor the manufacturing/import quantities for the time being where the total manufacturing/import quantity in the assessed year is 10 tons or less.
	Identification of assessment target substances	Identify assessment target substances from the following aspects: - Substances after assessment/determination: identification and selection of assessment target substances by checking the presence/absence of degradation products in a degradation test (whether they are parent compounds or degradation products, etc.) - Substances before assessment/determination: checking the appropriateness of the correspondence relation between the unit of Priority Assessment Chemical Substance designation and hazard information
	Data selection	For each of the assessment target substances, select data on degradability, accumulation and physicochemical properties on the basis of the reliability ranks.
	Assessment of degradability and accumulation	- Extract substances suspected of being not readily degradable/highly accumulative - Assessment of degradability and accumulation (predictions from the structure, overall assessment by analogy, etc.)
Assessment I		Setting an order of priority for the subsequent stage on the basis of minimal information
	Hazard Assessment I	- Human health: derive hazard assessment values for general toxicity/reproductive and developmental toxicity, and extract mutagenic or carcinogenic substances - The environmental effects: derive PNECs of aquatic organisms
	Exposure Assessment I	- Estimate the released quantity of each hypothetical release source from notified information such as manufacturing quantities, etc. - Estimate the model exposure amount for each hypothetical release source from the estimated released quantity Human health: estimate the inhalation exposure amount (atmospheric inhalation) and the oral exposure quantity (intake of drinking water, agricultural crops, animal products and fish and shellfish) The environmental effects: estimate the exposure concentration of aquatic organisms (riverine water concentration)
	Risk Estimation I	- Compare the exposure quantity of each hypothetical release source with the hazard assessment values (for aquatic organism, PNECs), and if the hazard assessment values $\leq$ the exposure quantity, determine it as a risk concern. - Human health: calculate the number of nationwide, hypothetical release sources of the risk concern, and calculate the effect areas of the risk concern - The environmental effects: aggregate the number of nationwide, hypothetical release sources of the risk concern
	Setting priorities	- In the case where the total of the estimated release quantities is one ton or less, monitor the manufacturing/import quantities for the time being - Regarding the substances on which Risk Estimation I has been conducted, set priorities on them for Assessment II on the basis of the results of Risk Estimation I - Regarding mutagenic or carcinogenic substances, set priorities on them for Assessment II on the basis of their released quantities, etc. - Regarding substances without hazard information, set priorities on them for hazard information collection from their released quantities
Assessment II		Multi-layered assessment of substances/hazard items subject to Assessment II with the use of existing information
	Hazard Assessment II	- Investigate existing assessment reports as well as the information from Hazard Assessment I, add hazard information and select key studies - Human health: derive hazard assessment values (general toxicity, reproductive and developmental toxicity and carcinogenicity) - The environmental effects: derive PNECs (aquatic organisms, and if necessary, sediment organisms)
	Exposure Assessment II	Prepare model estimates of the exposure quantities on the basis of notified information such as manufacturing quantities, and conduct a multi-layered and multidimensional analysis and assessment - Collect existing information on exposure, and examine data on degradability and physicochemical properties - Prepare model estimates of the exposure quantities on the basis of notified PRTR information (in the case of PRTR target substances) - Use environmental monitoring information (in the case of environmental monitoring target substances) - Add exposure scenarios and model estimating methods in accordance with the use, etc.
	Risk Estimation II	- Indicate this in, for instance, the nationwide distribution of the areas of the risk concern
	Summarization	Summarize information obtained in the processes of the risk assessment and assessment results in a risk assessment report, etc., so that such information and results can be utilized for determining measures such as the instructions on hazard investigation
Assessment III		Re-assessment that reflects newly obtained exposure information and is implemented on those substances whose assessment results are insufficient to be used as grounds for determination in Assessment II
		- Information obtained from the industry includes the release situation at the release sources of the risk concern considered in Assessment II - Implement a re-assessment with newly obtained exposure information and hazard information taken into consideration
Risk Assessment (Secondary)		**Assessment of target Priority Assessment Chemical Substances to which the instructions on hazard investigation were made**
		- Re-assessment for confirming the applicability of exposure requirements by using newly obtained long-term toxicity information

5. Preparation for the risk assessment

This stage is to identify target substances for the risk assessment and to organize information for the assessment. There are four steps in the preparation for the assessment: “information organization,” “extraction of Priority Assessment Chemical Substances,” “identification of assessment target substances” and “selection of data on properties.”
Where the nationwide total of the manufacturing/import quantities of a Priority Assessment Chemical Substance is 10 tons or less, monitor the manufacturing/import quantities for the time being. When the nationwide total exceeds 10 tons during the period of this monitoring, the substance shall be subject to Assessment I.

(1) Purpose of the preparation for assessment

The purpose of the preparation for assessments is to identify target substances for the risk assessment, and organize information to be used for Assessment I.
There are four steps in the preparation for the assessment: “information organization,” “extraction of Priority Assessment Chemical Substances,” “identification of assessment target substances” and “selection of data on properties.” At this stage, the “assessment of degradability and accumulation” is also conducted separately from the risk assessment.

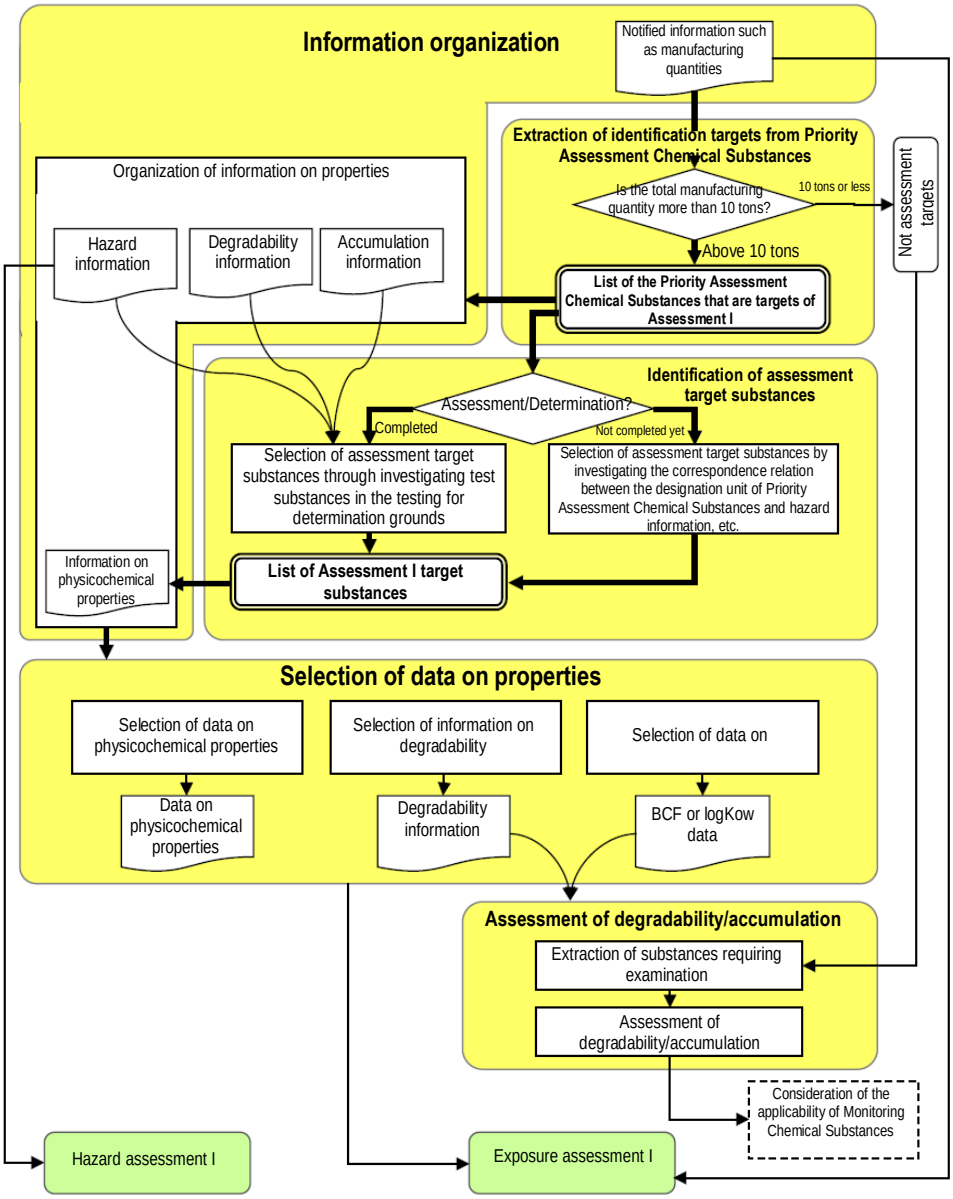


Figure 4 Steps of the Preparation for the Assessment

(2) Information organization

On the basis of the list of Priority Assessment Chemical Substances of the assessment year, organize the information described in Table 5.

Table 5 Information to Be Organized and Use Purposes

Information to be organized		Use purposes
Notified information such as manufacturing quantities of Priority Assessment Chemical Substances		- Estimation of the released quantity in the exposure assessment
Information on properties	Degradability	- Assessment of degradability - Estimation of the released quantity from sewage treatment plants in the exposure assessment
	Accumulation	- Assessment of accumulation - Estimation of the environmental concentration (in fish and shellfish) in the exposure assessment
	Physicochemical properties	In the exposure assessment: - Estimation of the released quantity (the selection criteria for emission factors) - Estimation of the environmental concentration (parameters for mathematical models)
	Hazard	- Derivation, etc., of hazard assessment values and PNECs in the hazard assessment.

(3) Extraction of Priority Assessment Chemical Substances

Before the risk assessment of Priority Assessment Chemical Substances, extract the Priority Assessment Chemical Substances, which are to be identification targets, by using the notified manufacturing quantities, etc., for the assessment year[1]. Aggregate the manufacturing and import quantity of each of the Priority Assessment Chemical Substances from information provided by each of the manufacturers and importers, and extract those substances with the respective total quantities of more than 10 tons as assessment target substances of the assessment year.

(4) Identification of assessment target substances

Apart from the identification of target substances for the risk assessment from their structural formulae, etc., the identification of assessment target substances in the methods concerned herein is implemented through checking substances from the following two aspects: (a) checking the presence/absence of degradation products that are to be subject to the risk assessment; and (b) checking the necessity for reviewing assessment units, as mentioned in 3.3.

(a) Checking whether assessment target substances contain degradation products
(b) Checking whether the units of those chemical substances designated as Priority Assessment Chemical Substances and the units of chemical substances used in information on properties, such as hazard information, correspond to each other appropriately.

(5) Selection of data on degradability, accumulation and physicochemical properties

For each of the parent compounds designated as Priority Assessment Chemical Substances and for each of the target substances of the risk assessment that are identified in the previous step (4), select and prepare a set of data on properties necessary for Assessment I.

[1] According to the notification system for manufacturing quantity, etc., manufacturers and importers of Priority Assessment Chemical Substances must report to the Minister of Economy, Trade and Industry on their actual quantities of the fiscal year during the period between April and June in the following fiscal year. Assessment I is supposed to take place within the fiscal year (or in the following year) with the information provided before June in the year.

The items to be selected are degradability (the classification of "not readily degradable" or "readily degradable"), accumulation (octanol-water partition coefficient for estimating a bioconcentration factor or bioconcentration) and physicochemical properties (molecular weight, boiling point, melting point, vapor pressure, water solubility, octanol-water partition coefficient, Henry constant, soil adsorption coefficient based on organic carbon content, and dissociation constant)[1]. Where actual values cannot be obtained, accumulation and physicochemical properties are complemented with estimated values.
Provide a reliability rank to each piece of data collected, and sort out usable data from such data. The reliability rank is a rank based on the concept of the Klimisch Code[2], which is internationally utilized for reliability assessment of testing data[3]. Where multiple pieces of data that can be used for one item (boiling point, vapor pressure, etc.) are obtained, select the appropriate data in accordance with the selection rules for each of the items.

Apart from the four steps of (2) to (5), among the Priority Assessment Chemical Substances that have not undergone audit/judgement, there are those substances whose degradability and accumulation are not known. If, for instance, a chemical substance is not readily degradable but highly accumulative, the Japanese Chemical Substances Control Act provides that the substance shall be managed as a Monitoring Chemical Substance (a former Type I Monitoring Chemical Substance) within a different framework from the one for Priority Assessment Chemical Substances (see Figure 1). For this reason, substances suspected of being not readily degradable and highly accumulative are required to be extracted and to go through an examination on their degradability and accumulation. From this, the applicability of Monitoring Chemical Substances can be considered when necessary[4]. Here, those Priority Assessment Chemical Substances whose manufacturing/import quantities are below a certain level in "(3) Extraction of Priority Assessment Chemical Substances" are also subject to such extraction. General Chemical Substances are also subject to the examination of degradability and accumulation, and extraction of these substances is carried out as necessary.

6. Assessment I of the Risk Assessment (Primary)

In this stage, implement the risk assessment on all target Priority Assessment Chemical Substances, basically with the use of notified information (manufacturing and import quantities, use, etc.) under paragraph 1, Article 9 of the Japanese Chemical Substances Control Act and hazard information used in the screening assessment.
The hazard assessment of Assessment I is generally conducted through deriving hazard assessment values by using the same uncertainty factors as the ones used in the screening assessment, in relation to the endpoints, which are targets in the screening assessment. The exposure assessment involves proposing, on the basis of manufacturing/import quantities notified by business operators, hypothetical release sources according to the prefectures, life-cycle stages and use in line with a series of hypotheses with regard to substance release (emission scenario). Subsequently, it involves estimating the released quantity by multiplying the emission factor for each of the applicable, specific use classifications, and further estimating the environmental concentration and amounts of human intake in line with a series of hypotheses with regard to exposure (exposure scenario). The risk is assessed through comparing the result of the hazard assessment and that of the exposure assessment. The result of this comparison shows, as an indicator, the number of nationwide release sources posing the relevant risk concern (the number of locations of the risk concern) and the nationwide total area of regions of the risk concern (the effect area of the risk concern) in the case of human health. It also shows the number of locations posing the risk concern as an indicator, in the case where ecological effects are concerned.

[1] The selection of hazard data is later explained in "6.1 Hazard assessment."
[2] Klimisch, H.-J. et al. (1997) A systematic approach for evaluating the quality of experimental toxicological and ecotoxicological data. Regulatory Toxicology and Pharmacology 25, 1-5.
The Manual for Investigation of HPV Chemicals Program prepared by OECD introduces the reliability ranking proposed by Klimisch et al. as an initial method to determine the reliability of existing data. Although its applicability to toxicity testing data is proposed, it is also considered that the ranking can be utilized for testing data for the items of physicochemical properties and environmental fate.
The Manual for HPV Investigation: OECD (2007) Manual for Investigation of HPV Chemicals.
[3] Check the reliability of data on human health hazard and on ecotoxicity in the same manner as above, and rank such data.
[4] Incompletion of this part of the assessment does not mean that Assessment I cannot take place; the part should be carried out along with Assessment I.

On this basis, the purpose of Assessment I is to set priorities on those Priority Assessment Chemical Substances that proceed to Assessment II. Where hazard information on mutagenicity or carcinogenicity is available, rank such information according to estimated released quantities. Regarding Priority Assessment Chemical Substances for which no hazard information is available, use estimated released quantities in setting priorities on them for the request for hazard information reports.
In the case where the nationwide, estimated released quantity of a Priority Assessment Chemical Substance is one ton or less, generally the substance does not proceed to Assessment II; its manufacturing/import quantity to be notified in the subsequent years is to be monitored.

6.1 Hazard Assessment I

(1) Purpose of Hazard Assessment I

The purposes of Hazard Assessment I are the following two points:

(a) Derive hazard assessment values[1] (PNECs for the environmental effects) for use in Risk Estimation I; and
(b) Identify investigation items where a submission of hazard information is to be requested.

The details of (a) are provided in (2) and (3) below. In relation to (b), among the items stipulated in the Ministerial Ordinances concerning the Request for Hazard Information Submission, identify individually which request is to be made according to the presence/absence of hazard information on Priority Assessment Chemical Substances. Further, confirm the availability of existing knowledge before making a request for hazard information submission.

(2) Hazard assessment for human health

[1] Premises and Basic Concepts

(i) Hazard information to be used

The information for the hazard assessment is one of the following:

- The information used in the screening assessment;
- The information reported from business operators after the designation of the relevant substance as a Priority Assessment Chemical Substance; or
- The information collected by the government after the designation of the relevant substance as a Priority Assessment Chemical Substance.

[1] These indicate values calculated through dividing the no observed adverse effect level (NOAEL), etc., obtained from repeated dose toxicity studies by the product of uncertainty factors, and are equivalent to TDI (Tolerable Daily Intake) or ADI (Acceptable Daily Intake), or alternatively DNEL (Derived No Effect Level) of the REACH.

(ii) Hazard items to be assessment targets

The four hazard items concerning human health that are assessment targets are “general toxicity,” “reproductive and developmental toxicity,” “mutagenicity” and “carcinogenicity.”
Not all of these four items are assessed in relation to the assessment of Priority Assessment Chemical Substances concerning human health. In principle, the following items are the targets; provided, however, that target items can vary depending on hazard information obtained after the designation of relevant substances as Priority Assessment Chemical Substances.

- The items whose priority levels are “High” in the screening assessment, and
- In relation to the reproductive and developmental toxicity or carcinogenicity to which no hazard class was assigned as there was no information obtained, the items for which information of high priority or of a similar value is obtained after the designation of the relevant substances as Priority Assessment Chemical Substances.

In Assessment I, hazard assessment values of general toxicity and reproductive and developmental toxicity are used for Risk Estimation I. For mutagenicity and carcinogenicity, no risk estimation is conducted; they are considered in the process of setting priorities.

(iii) Handling of oral and inhalation routes

In principle, hazard information presumes oral and inhalation routes.
In Assessment I, oral route and inhalation route are not distinguished. Convert hazard data such as NOAEL into the daily amount of intake per body weight unit[1]. Where data from toxicity tests involving inhalation route are used, convert such data into the amount of intake according to the respiration rate and body weight of the test animal species.

[2] Derivation of hazard assessment values

In Assessment I, the hazard assessment values used for assigning hazard classes in the screening assessment are used for general toxicity and reproductive and developmental toxicity.
Where there is new information obtained after the designation of the substance concerned as a Priority Assessment Chemical Substance, assign a reliability rank to each piece of data, and sort out available data from the data. If multiple, available (reliable) pieces of data are obtained, select a key study in line with the rules separately stipulated in the reliability criteria.
If information obtained after the designation of the substance concerned as a Priority Assessment Chemical Substance becomes a key study, set the product of relevant uncertainty factors in the manner below, and derive a hazard assessment value by dividing the NOAEL, etc.[2], by the product of the uncertainty factors.

For derivation of hazard assessment values in the hazard assessment for general toxicity and reproductive and developmental toxicity, use NOAELs obtained from animal testing, etc.

[1] Risk estimation is conducted through comparing the hazard assessment value from the hazard data used for intake conversion, with the estimated total intake obtained by adding the intakes via both oral and inhalation routes figured out in the exposure assessment.
[2] Even where NOEL assessment is used, it is handled in the same way as how a NOAEL is handled at the stage of Risk Assessment I.

A hazard assessment value is obtained through dividing a NOAEL, etc., by the product of uncertainty factors. In so doing, the uncertainty factors for general toxicity are, in principle, as follows[1]:

Inter-species difference: 10
Individual difference: 10
Testing period of less than 90 days: 6
Between 90 days or more and less than 12 months: 2
Testing period of 12 months or more: 1
Adoption of LO(A)EL: 10
Significance of effect: ..... 1 to 10

An uncertainty factor is added for a significant effect with the time length of the effect or the testing period taken into consideration. In a 28-day repeated dose toxicity study, which is a short-term screening toxicity test, an uncertainty factor is to be added where one of the effects below is applicable[2]:

- Where there is an onset of toxicologically important change, such as change in neurobehavioral toxicity or serious histopathological change, in the assumed grounds for NOAELs, etc., or other toxicity developed; or
- In relation to the effects in the recovery period, where there is a toxicologically important change, such as a change in neurobehavioral toxicity or serious histopathological change, and also where one of the following applies:
  a. the effect that generates a histopathological change that is not recovered within the recovery testing period;
  b. the effect that generates delayed toxicity; or
  c. the effect that generates a biochemical change that is not recovered within the recovery testing period.

Regarding effects in the recovery recovered, take account of the degree of reversibility, residual toxicity in the recovery recovered, the presence/absence of delayed toxicity, and whether the change involved is a biochemical one attributed to histological change.

In relation to reproductive and developmental toxicity, the uncertainty factors for deriving hazard assessment values are, in principle, as follows:

Inter-species difference: 10
Individual difference: 10
Adoption of LO(A)EL: 10
Testing quality/Significance of effect: 10

In relation to "Testing quality/Significance of effect," add 10 as "Testing quality" in the case of a simple reproductive toxicity test/one generation reproduction study including the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test using rodents. In the case where the endpoint is teratogenicity/offspring mortality that is caused with a lower dose than maternal toxicity, add 10 as "Significance of effect." However, where both of these cases apply to "Testing quality" and "Significance of effects", respectively, add 10 altogether.

[1] "Testing Methods and Determination Criteria for Determining Newly Registered Chemical Substances and Whether They Fall Under Monitoring Chemical Substances (April 22, 2011)
http://www.meti.go.jp/policy/chemical_management/kasinhou/files/information/ra/criteria_110422.pdf

[2] As the derivation of hazard assessment values with regard to carcinogenicity is not assumed to take place in Assessment I, it is not mentioned herein. Where information on carcinogenicity is available in Assessment II or a subsequent assessment, check the presence/absence of a threshold. If there is a threshold for carcinogenicity, add the uncertainty factor for significance of effect (see III. 7.1 (3) [2] (ii)).

(3) Hazard assessment for the environmental effects

[1] Premises and basic concepts

(i) Hazard information to be used

As is the case for human health, the information for the hazard assessment is one of the following:

- The information used in the screening assessment;
- The information reported from business operators after the designation of the relevant substance as a Priority Assessment Chemical Substance; or
- The information collected by the government after the designation of the relevant substance as a Priority Assessment Chemical Substance.

The handling of testing data is as follows:

- Regarding organism species, use the recommended species for the testing methods under the Japanese Chemical Substances Control Act and the methods of the OECD, etc.
- For chronic toxicity, the endpoint is No Observed Effect Concentration (NOEC). For acute toxicity, it is 50% Lethal Concentration (LC_{50}) and 50% Effective Concentration (EC_{50}).
  Where a NOEC cannot be obtained for chronic toxicity, it is possible to utilize a 10% Effective Concentration (EC_{10}) or a Maximum Acceptable Toxicant Concentration (MATC), etc.

(ii) Target organisms for the assessment

In relation to the environmental effects, both the terms of “animals and plants” and “animals and plants in the human living environment” are used differently in the Japanese Chemical Substances Control Act. The concept of the former term is wider than the latter, and the latter is considered to apply to those “animals and plants that have close connection with human life (for example, useful animals and plants).” The subjects for the risk assessment of Priority Assessment Chemical Substances are animals and plants in the human living environment; they are aquatic organisms and sediment organisms.

(iii) Target toxicity effects for the assessment

The assessment target toxicity effects on the environment are long-term toxicity effects on animals and plants in the human living environment. Hence, in assessments using acute toxicity values, the Acute to Chronic Ratio (ACR)[1, 2] is applied as specified in the following paragraph [2] to extrapolate it to chronic toxicity values.
Freshwater organisms and organisms in seawater are treated in the same manner, and their sensitivity to hazards is assumed to be at the same level among them.

[1] Information Material 2-3 from the 4th Committee on Safety of Chemical Substances, Pharmaceutical Affairs Committee, Pharmaceutical Affairs and Food Sanitation Council; the 56th Review Committee by Subcommittee on Chemical Substances and Chemical Substances Council; the 59th Chemicals Evaluation Subcommittee, Environmental Health Committee, Central Environment Council (all in the fiscal year 2006)
http://www.env.go.jp/council/05hoken/y051-59b.html

[2] Reference Material 2 from the Second Expert Committee Meeting on the Reform of Chemicals Evaluation and Regulation by the Committee on Chemicals System Reform, the Health Science Council; and the Joint Meeting of the 9th Subcommittee on Chemical Management Policy and Planning, Chemicals and Bio-industry Committee, Industrial Structure Council and the Second Subcommittee on Chemicals Evaluation and Regulation, Environmental Health Committee, Central Environment Council
http://www.env.go.jp/council/05hoken/y053-02.html

[2] Derivation of PNECs for aquatic organisms

In Assessment I, the PNECs used for assigning hazard classes in the screening assessment are utilized.
Assign a reliability rank to each piece of new information obtained after the designation of the relevant substance as a Priority Assessment Chemical Substance, and sort out available data from such data in accordance with the reliability criteria separately stipulated. Where multiple pieces of available (reliable) data are obtained, select a key study in line with the selection rules of the relevant items.
Where information obtained after the designation of the relevant substance as a Priority Assessment Chemical Substance is selected as a key study, derive a PNEC through figuring out the product with uncertainty factors as shown below.

Table 6 shows uncertainty factors for deriving PNECs, and Figure 7 shows the derivation flow of PNECs.
In the derivation of PNECs, use chronic toxicity values on a priority basis in cases where both a chronic toxicity value and an acute toxicity value are obtained in relation to the same trophic level.

Table 6 Uncertainty Factors for Deriving PNECs for Aquatic Organisms

Toxicity values to be adopted			UF for inter-species extrapolation	UF (ACR) from acute to chronic	UF from indoor to outdoor testing	Uncertainty factor product, UFs
Lowest NOEC if chronic toxicity test results are available for three trophic levels			—-	—-	10	10
Lower NOEC if chronic toxicity test results are available for two trophic levels			5	—-	10	50
The NOEC if a chronic toxicity test result is available for a trophic level			10	—-	10	100
Lowest L(E)C50 if acute toxicity L(E)C50s are available for three trophic levels			—-	ACR	10	10×ACR
Lower L(E)C50 if the acute toxicity values of the trophic levels without chronic toxicity test results do not match			10	ACR	10	100×ACR
ACR	Algae			20		
	Daphnia	Amines		100		
		Other than amines		10		
	Fish			100		

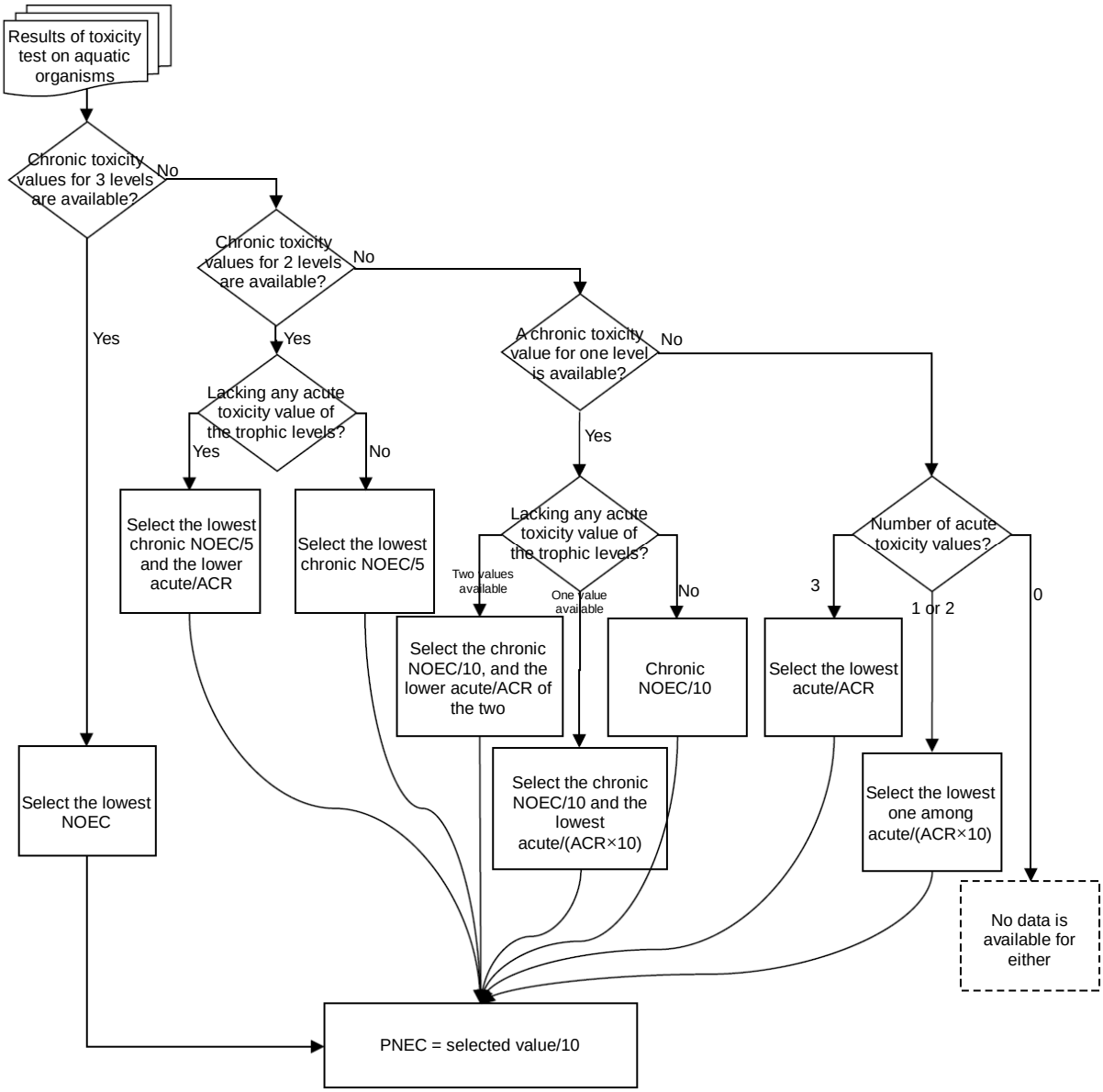


Figure 7 The Derivation Flow of PNECs of Aquatic Organisms

6.2 Exposure Assessment I

(1) Purpose of the Exposure Assessment I

The purpose of the Exposure Assessment I is to estimate the exposure amount (or exposure concentration) (for human health, amount of intake; for the environmental effects, PEC[1]) through the environment for use in Risk Estimation I. In relation to Priority Assessment Chemical Substances without hazard information for Risk Estimation I, their released quantities are estimated in order to use such quantities as an indicator in determining whether submission of hazard information is required.

[1] PEC: the abbreviation for Predicted Environmental Concentration

(2) Premises and basic concepts

[1] Applicable scope of the exposure assessment

As is the case for the assessment stages, in principle, the exposure assessment involves estimating exposure amounts through the environment that are attributable to the manufacture and use of chemical substances, with attention to the applicable scope of the Japanese Chemical Substances Control Act. Carry out risk assessments with consideration for such chemical substances as those below that are outside the scope of the Japanese Chemical Substances Control Act (see Figure 2)[1].

- Exposure to compounds that are not "chemical substances"
  Example: exposures to natural sources (volcanoes, constituents in food, etc.)
- Exposure attributed to sources outside the scope of "control of manufacture, etc."
  Example: exposures due to exhaust fumes from moving vehicles (products of combustion), emissions due to accidents such as an explosion, exposures attributed to domestic and overseas environmental pollution sources, etc.
- Exposure not "via the environment"
  Example: indoor exposure, direct exposure when using consumer products, occupational exposure
- Exposures related to use outside the applicable scope of the Japanese Chemical Substances Control Act
  Example: exposures from use subject to the Food Sanitation Act, the Agricultural Chemicals Regulation Law, the Pharmaceutical Affairs Law, etc.

[2] Exposure Routes of human beings

There are three routes of human exposure to chemical substances: inhalation, oral and dermal routes. As the risk assessment of Priority Assessment Chemical Substances targets exposure via the environment, inhalation and oral routes of exposure, which are considered to be the main routes of exposure via the environmental, are the targets; the dermal route is not considered herein.
In Assessment I, the inhalation route and oral route of exposure are not differentiated, and the total exposure amounts via both the routes is calculated by converting the amounts of intakes via the routes into mg/kg/day and adding them up. This is on the assumption that the inhalation rate (bioavailability) is 100% for both the oral and inhalation routes.

[3] Concept of time in estimating human exposure quantity

The exposure assessment of Priority Assessment Chemical Substances is an assessment and a future prediction on the premise that, "the exposure concentration based on the actual quantities notified continues for a long period of time without a time variation."

[4] Handling of degradability

Chemical substances are degraded by various mechanisms, such as degradation by microorganisms in the environment, hydrolysis and photolysis. Under the Japanese Chemical Substances Control Act, the degradation test with microorganisms is employed as a testing method for assessing "degradability."
In Assessment I, degradability in the environment is handled in the manner provided below.

[1] In the case of those substances for which PRTR information is available, it is possible that the estimation of exposure amounts may include released quantities from use outside the scope of the Japanese Chemical Substances Control Act. Further, the extent of contribution of various release sources to exposure amounts (exposure concentrations) is not clear, where environmental monitoring information is available. For this reason, in using such information, it may be necessary to interpret the level of contribution subject to the Japanese Chemical Substances Control Act.

- Only the conclusive results regarding biodegradability (Not readily degradable/Readily degradable) under the Japanese Chemical Substances Control Act are used, and degradability by other mechanisms is not taken into consideration.
- In the case of "Readily degradable," multiply the factors on the assumption of the eliminating rate at the sewage treatment plant in the estimation of the released quantity to the water area in relation to the use through which the release into the environment via a sewage treatment plant occurs.
- The foregoing factors are not to be multiplied in the case of "Not readily degradable" or where degradability is unknown.

(3) Methods of Exposure Assessment I

[1] Constituent elements of the exposure assessment

The exposure assessment using notified information such as manufacturing quantities is constituted by the elements exemplified in Table 8.
Among the constituent elements in Table 8, prearrange Items 1 and 2 uniformly[1]. Items 3 to 5 are implemented for each substance in each fiscal year the assessment is carried out.

Table 8 Constituent Elements of the Exposure Assessment

Constituent elements		Overview	Reference
1	Setting exposure scenarios	Assume a series of routes, etc., from the release source of the chemical substance to the exposure of human beings and animals and plants in the human living environment.	6.3(3) [2]
	a Setting emission scenarios	Set the number of release sources, receiving media, the coefficient of emission factors, etc., according to specific use.	(i)
	b Setting exposure scenarios (other than emissions)	Set the exposure population, environment scale (setting the distance from the release sources, the assessed area, etc.), intake media/routes, etc.	(ii)
2	Setting mathematical models, etc.	Select mathematical models, and set parameters to be input into the selected models.	[3]
	a Selecting mathematical models	Select and adjust mathematical models appropriate for exposure scenarios.	(i)
	b Setting model parameters	Set environmental parameters (climate conditions such as wind speed, flow rate, etc.) and exposure factors (respiration volume, food intake, etc.) for estimating human intake.	(ii)
3	Estimating the released quantity	- Estimate the released quantity from notified information such as manufacturing quantities for each of the environmental media.	[4]
4	Estimating the environmental concentration	Calculate this by inputting the environmental parameters in 2b and the released quantity data in 3 (and data on physicochemical properties, etc.) into the mathematical models selected in 2a.	[5]
5	Estimating the amount of human intake	Calculate this on the basis of the environmental concentration calculated in 4 and the exposure factors set in 3b.	[6]

[2] Setting of exposure scenarios

The flow of the estimation of human intake from notified information such as manufacturing quantities is shown in Figure 9.

[1] At the detail stage, changes may be made to the exposure scenarios depending on cases.

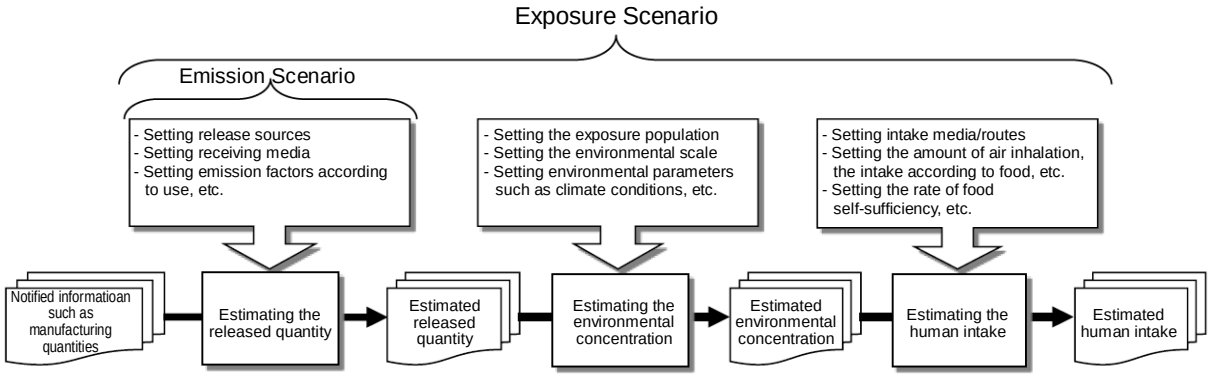


Figure 9 The Flow of the Estimation of Human Intake from Notified Information such as Manufacturing Quantities

As shown in Figure 9, the estimation of human intake from notified information such as manufacturing quantities is based on a series of assumptions. In this section, the series of assumptions for the estimation of released quantities from notified information such as manufacturing quantity is called an "emission scenario." An "exposure scenario" is a series of assumptions for the estimation of a human intake or an exposure concentration of animals and plants in the human living environment, and it includes emission scenarios.

(i) Setting emission scenarios

In relation to emission scenarios, the concepts in setting target release sources, basic emission scenarios and emission scenarios according to use are shown below.

❑ Target release sources

In principle, target release sources of the risk assessment are assumed to relate to the manufacture or use stipulated in the Japanese Chemical Substances Control Act, and thus to be one of the following (a) to (c). (a) and (b) are dealt with in the following item, "Basic emission scenarios," and (c) is covered in, "Emission scenarios according to use":

(a) Manufacturing establishments for Priority Assessment Chemical Substances;
(b) Business establishments to which Priority Assessment Chemical Substances[1] are delivered and used in (for preparation or industrial use), or
(c) A release source involving the end use of Priority Assessment Chemical Substances (e.g., home use, use of products for long-term use).

❑ Basic emission scenarios – a scenario for each release source -

Figure 10 shows the basic emission scenarios based on notified information such as manufacturing quantities.

In the manufacturing stage, release sources are the manufacturing establishments notified. Regarding ship-to destinations, shipment quantities from multiple registered manufacturers are aggregated according to prefectures and specific use. Subsequently, for each of the prefectures, two hypothetical release sources, for the preparation stage and for the use stage[2], are set according to specific use[3]. This scenario is called a "scenario for each release source."

[1] This excludes those chemicals used for and contained in imported products. The definition of "product" under the Japanese Chemical Substances Control Act is as provided for in the "Implementation of the Act on the Evaluation of Chemical Substances and Regulation of Their Manufacture, etc."

[2] The method concerned here sets five stages as the life-cycle stages of chemical substances: the manufacturing stage, preparation stage, industrial use stage, home use stage and use stage of products for long-term use. Among these, three of the manufacturing stage, preparation stage and industrial use stage are the targets of the exposure assessment for each release source.

[3] Depending on specific use, there can be more than one hypothetical release source for each of the preparation stage and the industrial use stage. For example, the presence of intermediates is not assumed in the preparation stage but is set in the industrial use stage. As above, the life-cycle stages are prearranged for each way of use.

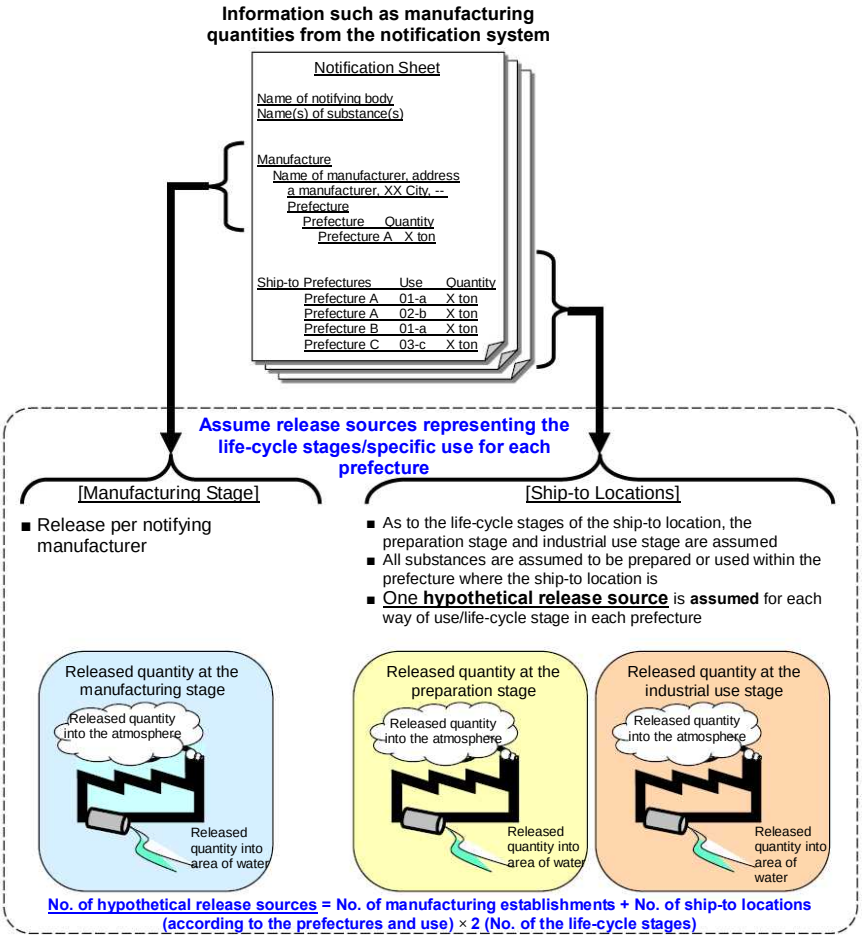


Figure 10 Basic Emission Scenarios - Scenario for each release source -

This emission scenario is set on the basis of the following two concepts.
One of the concepts is based on the Ordinance on the regulation of notification of details such as manufacturing quantities[1]. The Ordinance stipulates that "the name, address of the manufacturing business establishment, the manufacturing quantities according to prefectures, import quantities according to exporting countries and regions, shipment quantities according to the prefectures and specific use" are the matters to be notified for the purpose of estimating the quantities released into the environment. The methods in this document comply with this; the manufacturing quantity of each manufacturing establishment and shipment quantities according to the prefectures and specific use are regarded as the minimum unit and used as a unit of release source in estimating released quantities into the environment.

Another concept is related to the setting of one hypothetical release source for each of the life-cycle stages, the prefectures and ways of use in the handling of shipment quantities. In this estimation of the released quantity, the total quantity of Priority Assessment Chemical Substances handled in the country for manufacture and import is understood, and released quantities into the environment are estimated at locations from upstream in the supply-chain. It is difficult to understand the extent of the area downstream business operators cover from notified information such as manufacturing quantities. Consequently, the concept of "hypothetical release source" according to the prefectures/use is devised. This concept means, "Where there is no concern for risk due to release from hypothetical emission sources, the released quantities of individual release sources are definitely lower than those released quantities of the hypothetical release sources, even if the actual number of release sources grows larger. For this reason, basically, it is possible to consider that there is no concern for risk in this case" (see Figure 11). This is a means to efficiently and uniformly assess Priority Assessment Chemical Substances from limited, notified information such as a manufacturing quantity. As above, the assessment result of this is an estimate greater than a risk that can be generated from actual release sources. Where there is a concern for risk, this leads to

[1] The Ordinance for Enforcement of the Act on the Evaluation of Chemical Substances and Regulation of Their Manufacture etc., as the Act Relates to the Ministry of Economy, Trade and Industry

a stepwise approach for re-assessment through gathering information in a subsequent stage. Moreover, before a final decision as to the instructions on hazard investigation or designation of Class II Specified Chemical Substances, this serves as an assessment of release sources that reflects actual situations rather than hypothetical ones through collecting information such as reports on substance handling.

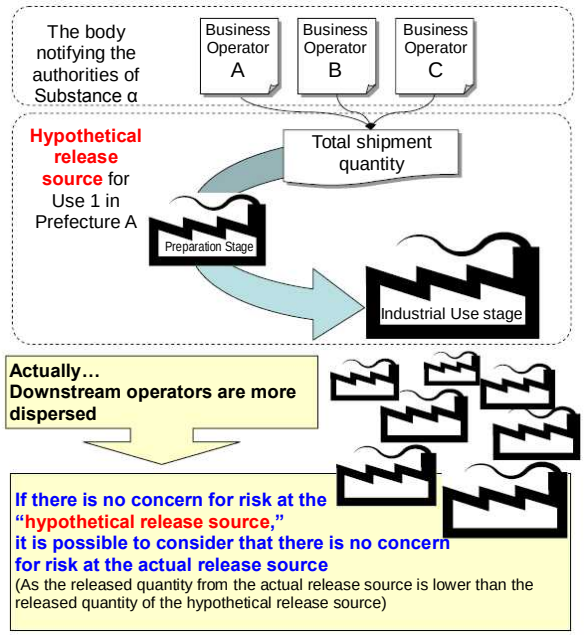


Figure 11 The Concept of Emission Scenarios to Which Hypothetical Release Sources Are Set

❑ Emission scenarios according to use

Apart from the emission scenarios for each of the basic release sources, set emission scenarios according to use. These, together with the details of exposure scenarios, are described below.

(ii) Setting exposure scenarios

❑ Basic exposure scenarios - exposure scenario for each release source -

A basic exposure scenario is a scenario like the one below.

Those release sources under the control of the Japanese Chemical Substances Control Act are treated as the targets of this scenario, and people residing (or animals and plants growing in/inhabiting the human living environment) around each release source are exposed in the assessment area to the chemical substances emitted from the release source through environmental media (for human beings, this includes food).

The assessment area around a release source is the area with "a radius of 1 to 10 km (in units of 1 km) from a release source (however, the area within a radius of 100 m is excluded). The following points were considered in setting this assessment area.

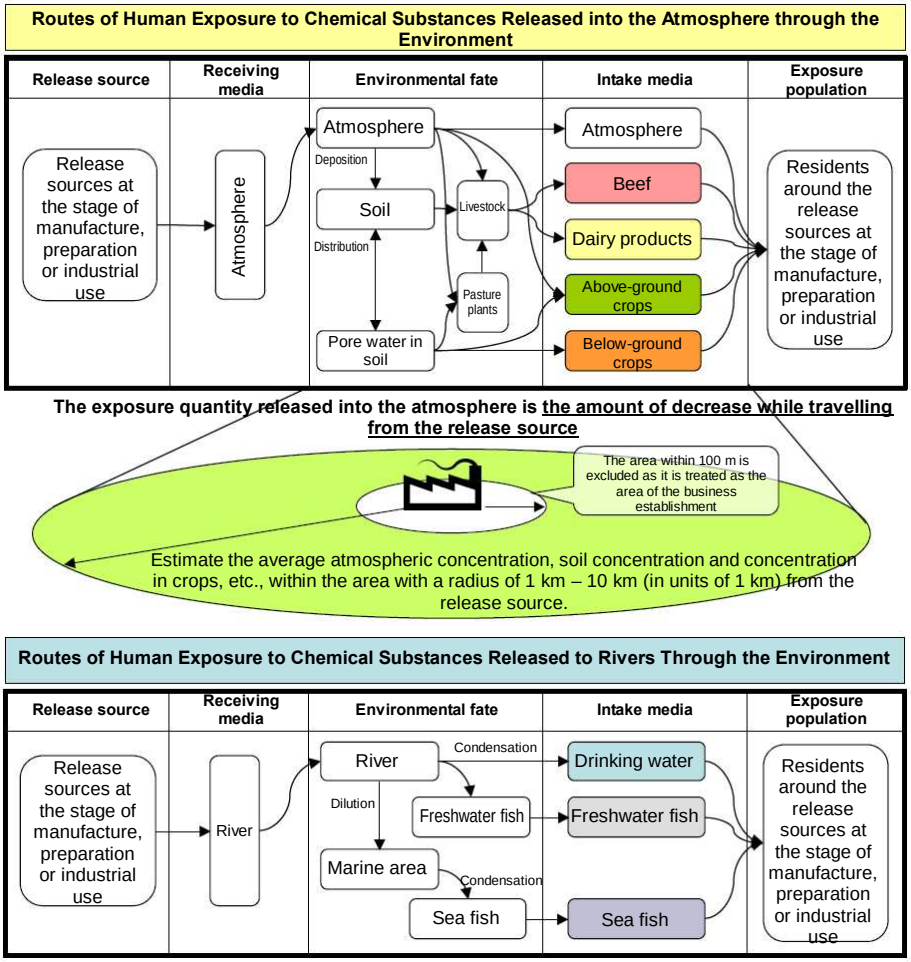
(a) As the area is for estimating an average, long-term, human exposure concentration, the area must be a living area.
(b) The size of the area must be consistent with the minimum unit of a release source (according to the prefectures/use); this unit is based on information, including manufacturing quantities, obtained through the system of notification.

(c) The area must be the one expected to be affected significantly by individual release sources.

The point (a) relates to the fact that the environment where an exposure concentration is estimated is not a spot but an area. As the method concerned herein is to be employed to conduct the risk assessment on long-term toxicity[1], the use of the method supposes a long-term, continuous exposure period in the exposure assessment (see (2) [3]). For the estimation of the average of a long-term exposure concentration through an environmental route, it is appropriate to base the estimation on a living area. Hence, the environment for the estimation of an exposure concentration is not a spot distant from the release source but an area of a certain size. This area is supposed to be the one where residents have breathed the air for a long period of time (from a few decades to a lifetime) and have had food produced in the area. The area concerned here is with a radius of 1 to 10 km and a size of approximately 3 to 300 square kilometers; its size is equivalent to that of a municipality.
Regarding the point (b), the minimum unit of a released quantity in the estimation is for each prefecture/use, and thus the scope of the released quantity and exposure concentration to be estimated is at least smaller than the prefecture under assessment. It is possible that the area is further divided into parts according to use. The area with a radius of 1 to 10 km can be up to approximately 300 square kilometers in size; it is equivalent to a certain percentage of the smallest prefecture (approximately 1,900 square kilometers). On this basis, the area is considered to be consistent with the unit of a release source based on notified information such as manufacturing quantities.
The point (c) relates to the specifications of the mathematical models used for estimating environmental concentrations. In the method concerned herein, the mathematical models are employed to estimate an atmospheric concentration of chemical substances emitted into the atmosphere, and a deposition amount of substances from the atmosphere into the soil. The models are to analyze how chemicals emitted from a point source, such as a business establishment, spread around the area according to climate conditions. They aim to cover an area within 10 km (a radius of 5 km)[2]. Further, the formula to calculate spread parameters, which are used with the estimation formula for an atmospheric concentration, is defined to cover a distance within 10 km from the release source[3]. Therefore, the range of assessing the spread of chemical substances emitted into the atmosphere is roughly limited to a radius of 10 km.

Exposure scenarios focusing on the surrounding area of release sources are set on the basis of the two concepts below. One of the concepts relates to the exposure requirements that are the criteria to determine whether Priority Assessment Chemical Substances are Class II Specified Chemical Substances. As a condition under which the exposure requirements apply, the method concerned herein is based on the case, “local environmental contamination is scattered around release sources nationwide.”
The second concept relates to the detection sensitivity for environmental pollution statuses. In cases where a contamination that poses a concern for risk extends over the general environment, for instance, such contamination starts off as a local contamination. Hence, an exposure assessment focusing on the surrounding area of release sources is considered to be effective for monitoring the contamination status in the general environment.
Figure 12 shows the exposure routes of human population through the environment in the assessment area.

[1] The sentences on long-term toxicity in the Japanese Chemical Substances Control Act are “A chemical substance that is likely to pose a risk of impairing human health if ingested continuously” or “A chemical substance that is likely to pose a risk of interfering with the population and/or growth of animals and plantsanimals and plants in the human living environment if the animals and plants ingest or are exposed to said chemical substance continuously.”
[2] J. Nakanishi, S. Hanai, H. Higashino, H. Yoshikado, and K. Yoshida (2007) Pearls of Wisdom on Risk Assessment Series 1, Atmospheric Dispersion to Exposure, ADMER/METI-LIS, Maruzen
[3] Investigative Commission on Measures Against Suspended Particulate Matter, Supervised by Air Pollution Control Division, Air Quality Bureau, the Environment Agency (1997) Manual for Predicting Pollution by Suspended Particulate Matter, Toyokan



The exposure quantity released into the river = (the released quantity / default flow rate)×BCE, etc., and the amount not dependent on the distance from the release source (constant for each release source)

Figure 12 Routes of Human Exposure in the Scenario for Each Release Source

❑ Exposure scenarios according to use

Where there are those ways of use that cause exposures related to the main release into the environment, and where basic exposure scenarios, on their own, cannot cover such exposures, set exposure scenarios according to such use in addition to the existing basic exposure scenarios. Table 13 shows the overview of this.

Table 13 Overview of Exposure Scenarios According to Use (Including Emission Scenarios)

Scenario name	Main corresponding use	Corresponding life-cycle stages	Outline
Scenario for an aquatic non-point source	- Aqueous cleaning agents [for home use, professional use] - Wax - Biocide, etc.	At the stage of home use/ professional use	The assumed exposure population is those exposed to chemical substances released into rivers as such chemicals are accumulated in sewage treatment plants after being used in houses, etc., and flow through sewerage. The scenario is to convert the nationwide total shipment quantity for the relevant use into the per-capita use/released quantity, and to estimate a representative concentration on the basis of the basic unit. For the extraction rate at the sewage treatment plant, the same value as the one used in the screening assessment is used. In that case, the riverine water concentration level via the sewage treatment plant is assumed to be higher than the concentration level of the riverine water in the area where the sewerage system is not developed. For this reason, the exposure assessment is conducted with the riverine water concentration level via the sewage treatment plant in Assessment I.

Scenario name	Main corresponding use	Corresponding life-cycle stages	Outline
Scenario for an atmospheric non-point, source	- Fragrance, air freshener - Biocide - Fuel, fuel additive, etc.	At the stage of home use, professional use	This scenario is to estimate an exposure quantity via the atmosphere regarding the use from which an atmospheric release at a non-point source (houses, moving bodies, etc.) is assumed. In Assessment I, a hypothetical release source is set, and the exposure quantity is estimated with the same method as the one used for the scenario for each release source.
Scenario for antifoulants for ship bottom paint/fish nets	- Antifoulants for ship bottom paint - Antifoulants for fish nets	At the stage of use of products for long-term use	As antifoulants for ship bottom paint and for fish nets are released into the marine area at the use stage of products for long-term use, a separate scenario is employed. In Assessment I, rank the relevant substance according to the estimated released quantity for the applicable use at the use stage of products for long-term use.

[3] Setting of mathematical models

(i) Selection of mathematical models

The mathematical models for estimating environmental concentrations in Exposure Assessment I are based on various models employed in chemical substance management systems in Western countries or the Japanese versions of such models. In relation to the method concerned herein, the concepts of selecting mathematical models for estimating environmental concentrations are as follows;

(a) Those mathematical models with a record of actual applications for chemical substance management systems in Japan or foreign countries; and
(b) Those simple mathematical models that do not require much information for input parameters and for application.

(ii) Setting of model parameters

It is necessary to set model parameters for environmental conditions and exposure factors[1] in order to estimate environmental concentrations and human intakes by using mathematical models. As specific, individual release statuses and exposure statuses are unknown at the stage where notified information such as manufacturing quantities is used, the default setting is applied to these model parameters. Table 14 shows examples of model parameters and the points to consider in applying the default setting.

Table 14 Model Parameters

Types	Examples	Points to consider in setting
Environmental conditions	- Climate conditions - Riverine flow rate - Dilution rate in marine area	- Generalize them to enable the application of them with information obtainable under the system of the Japanese Chemical Substances Control Act - Set them on the basis of long-term statistics to render them appropriate for assessments of the effects under the Japanese Chemical Substances Control Act (effects of long-term toxicity from a long-term exposure through the environment) - Use as much statistical information in Japan as possible to adjust them to the situation in Japan.
Exposure factors	- Human weight - Amount of atmospheric inhalation - Intake (crops, animal products, fishery products and drinking water)	- Set the intake speed, such as the atmospheric inhalation speed, and weight of each medium on the basis of an adult and of existing knowledge in the country. - The intakes of food items are to be set with attention to the domestic self-sufficiency rate, the domestic intake and the ratio of local products ingestion*, in line with the exposure scenario.

* Ratio of local products ingestion: the ratio of ingestion of agricultural products grown by the residents in a certain area of the region surrounding the release source.

[1] Exposure factors: various parameters for estimating exposure quantities of human beings or other living organisms, for example an individual respiration volume, amounts of intakes according to types of food, water consumption, frequency of ingestion, etc.

[4] Estimation of released quantity

To estimate an environmental concentration, etc., with mathematical models, it is necessary to use released quantity data to input into the models. The details of the estimation of released quantities on the basis of notified information such as manufacturing quantities are explained in (i) to (iv).

(i) Basic premises

The basic premises for estimating a released quantity on the basis of notified information such as manufacturing quantities are listed below.

(a) Basic concept:
Those chemical substances with the same attributes in the life-cycle stages, specific use and physicochemical property divisions are deemed to have the same emission factor into the environment.

(b) Life-cycle stages:

(c) The stages of manufacture, preparation, industrial use, home use (for certain use only), and use of products for long-term use (antifoulants for ship bottom paint/fish net only) are required to be taken into consideration. There is a further explanation in Emission factor (ii):
- An emission factor is the ratio of the quantity released from the quantity handled, and is set for each of the life-cycle stages, specific use and physicochemical property divisions (corresponding to (a) above).
- The environmental media of release are the atmosphere and water area, and an emission factor is set for each of them separately.

(d) Estimation of released quantities (explained in (iii) below)
- In accordance with the emission scenarios mentioned above (see 6.2 (3) [2] (i)), for each of the prefectures, life-cycle stages and hypothetical release sources according to use, multiply the notified quantity, which is from the system of notification of details such as manufacturing quantities under the Japanese Chemical Substances Control Act, by the corresponding emission factor to figure out each released quantity.
- The release into water from a hypothetical release source is assumed to be released into a river not via a sewage treatment plant.

(ii) Emission factors

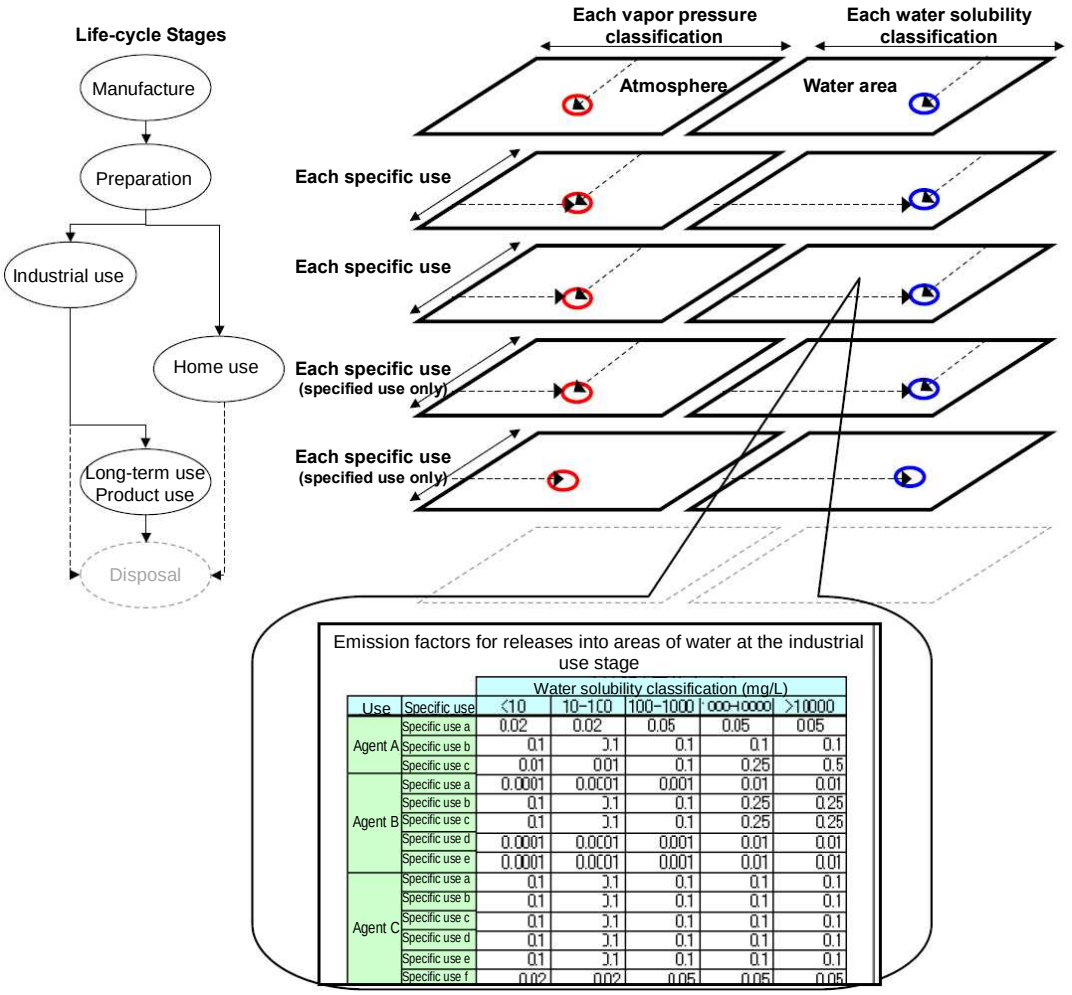
Emission factors employed in the method concerned herein for releases into the atmosphere and water area[1] are set for each life-cycle stage, each way of use and each physicochemical property division, and organized in the manner shown in Figure 15.

Emission factors are set by basing them on an emission factor list, so-called the A-table of the EU-TGD[2], making them correspond to the use category list, which is also used for the system of notification regarding manufacturing quantities, etc., and adjusting them by using data on the substance emission status in Japan[3].

[1] http://www.meti.go.jp/policy/chemical_management/kasinhou/haishutsu-keisu.html

[2] ECB (2003) Technical Guidance Document on Risk Assessment. Part II, Appendix I Emission factors for different use categories. A-tables Estimates for the emission factors (fractions released).

[3] National Institute of Technology and Evaluation (2010) The FY2009 Report on Environment-Responsive Technology Development (Investigation into the Risk Assessment Scheme for Chemicals under the Amended Japanese Chemical Substances Control Act), the Third Chapter: the Setting of Emission Factors According to the Classifications of Specific Use of Chemicals http://www.meti.go.jp/policy/chemical_management/other/files/21FY_Report.pdf



Use	Specific use	<10	10–100	100–1000	1000–10000	>10000
Agent A	Specific use a	0.02	0.02	0.05	0.05	0.05
	Specific use b	0.1	0.1	0.1	0.1	0.1
	Specific use c	0.01	0.01	0.1	0.25	0.5
Agent B	Specific use a	0.0001	0.0001	0.001	0.01	0.01
	Specific use b	0.1	0.1	0.1	0.25	0.25
	Specific use c	0.1	0.1	0.1	0.25	0.25
	Specific use d	0.0001	0.0001	0.001	0.01	0.01
	Specific use e	0.0001	0.0001	0.001	0.01	0.01
Agent C	Specific use a	0.1	0.1	0.1	0.1	0.1
	Specific use b	0.1	0.1	0.1	0.1	0.1
	Specific use c	0.1	0.1	0.1	0.1	0.1
	Specific use d	0.1	0.1	0.1	0.1	0.1
	Specific use e	0.1	0.1	0.1	0.1	0.1
	Specific use f	0.02	0.02	0.05	0.05	0.05

Figure 15 Image of Emission factor Organization

(iii) Formula for estimating released quantities

In the system of notification of information such as manufacturing quantities, the notification form requires the manufacturing quantity and shipment quantity to be notified separately (see Figure 10). According to this format, calculate the released quantities at the stage of manufacture and at the ship-to locations separately as shown by the formulae below.

Released quantities at the stage of manufacture

The released quantity into the atmosphere at the stage of manufacture =

Manufacturing quantity × the emission factor for atmospheric release at the stage of manufacture

The released quantity into area of water at the stage of manufacture =

Manufacturing quantity × emission factor for release into area of water at the stage of manufacture

Released quantities at ship-to locations (omitting to mention that the formulae below are according to the prefectures)

The released quantity into the atmosphere for Use i at the stage of preparation =

Shipment quantity for Use i × the emission factor for atmospheric release for Use i at the stage of preparation

The released quantity into area of water for Use i at the stage of preparation =

Shipment quantity for Use i × the emission factor for release into area of water for Use i at the stage of preparation

The released quantity into the atmosphere for Use i at the stage of industrial use =

(Shipment quantity for Use i - the released quantity for Use i at the stage of preparation) × the emission factor for atmospheric release for Use i at the stage of industrial use

The released quantity into area of water for Use i at the stage of industrial use =

(Shipment quantity for Use i - the released quantity for Use i at the stage of preparation) × the emission factor for release into area of water for Use i at the stage of industrial use

[5] Estimation of environmental concentrations

Figure 16 illustrates the overall flow in estimating environmental concentrations and human intakes from notified information such as manufacturing quantities. The Figure expresses that the item from which an arrowed line starts is an input value for estimating the item at the end of the line.
Concentrations in media including food are estimated through inputting the applicable release quantities and physicochemical properties, etc., into the mathematical models selected in the manner set forth in III. 6.2 (3) [3].

[6] Estimation of human intakes

Calculate human intakes of chemical substances with the applicable estimated concentrations in environmental media by using the following formula.

Human intake of chemical substances =
$\sum$ (concentrations in media × intake from each medium) / body weight

Human intake of chemical substances:	the intake of chemical substances of an adult who ingests a constant amount of the air and agricultural and animal products in the assessment area surrounding the release source, the water and freshwater fish from the river into which the chemical substances are released, and the sea fish in the area of sea into which the river flows.
Concentrations in media:	a concentration in each of the air, below-ground crops, above-ground crops, beef, dairy products, riverine water, freshwater fish and sea fish.
Intake from each medium:	an adult's intake from each medium
Body weight:	an adult's body weight

For each release source, prepare ten estimates of intake.
Set exposure factors for each medium's intake speed, etc., such as its air inhalation speed, in line with the manner in Table 14. Further, drinking water originated from riverine water is assumed to have no water purification rate (elimination rate) pertaining to chemical substances.

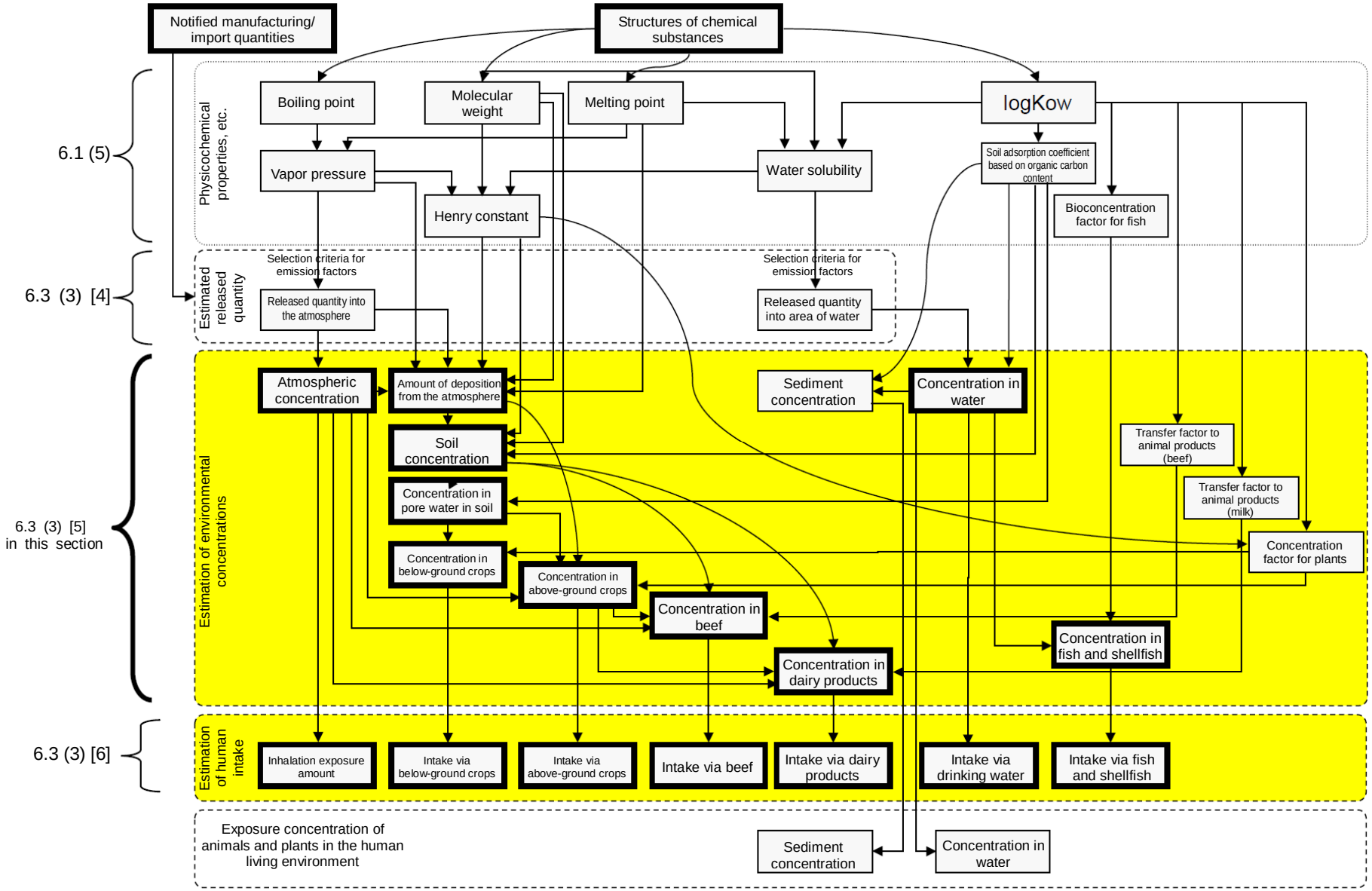


Figure 16 Flow of the Estimation of Environmental Concentrations and Human Intakes

6.3 Risk Estimation I and Prioritsing

(1) Purposes of Risk Estimation I and setting prioritising

This section is the final step in Assessment I with the same purpose as the one for Assessment I; this section aims to set a priority order for implementation of the subsequent stages (Assessment II, the Request for Hazard Information Submission, etc.).

(2) Risk Estimation I

[1] Basic concepts

(i) Definition of the concern for risk

In the method concerned herein, a "concern for risk"[1] is considered to exist where an exposure amount (or an exposure concentration) (in the case of assessments on human health, it is an amount of intake; in the case of assessments on the environmental effects, it is a PEC) exceeds the hazard assessment value (for the environmental effects, the PNEC).

- ✓ Estimation of a risk in the case of human health
  Amount of Intake ≥ Hazard assessment value There is a concern for risk
- ✓ Estimation of a risk in the case of the environmental effects
  PEC ≥ PNEC There is a concern for risk

In the estimation of a risk regarding human health, calculate a Hazard Quotient (HQ) (amount of intake/hazard assessment value); in the estimation of a risk regarding the environmental effects, calculate a PEC/PNEC quotient. On the basis of the definitions above, if the quotient of these is one or more, a concern for risk is considered to exist.

(ii) Expressions for risk with a geographical distribution as an indicator

In the risk estimation for Priority Assessment Chemical Substances, calculate a hazard quotient (in the case of the environmental effects, a PEC/PCEC quotient) for each release source, in relation to the exposure scenario for each release source. By using the result from this, the risk indicator can be expressed in the following two types of geographic distribution[2].

(a) The number of locations of risk concern: the number of nationwide release sources of risk concern
(b) The effect area of risk concern: the nationwide total area of the effect regions of risk concern

The risk estimation for human health employs two expressing indicators of (a) and (b)[3]. Human exposure routes via the environment are based on the scenario that people become exposed through various routes to both chemicals emitted into the atmosphere and those emitted into water. With regard to substances released into the atmosphere, an exposure quantity becomes larger as it is closer to the release source area. Accordingly, where there is a concern for risk in the area surrounding the release source, it is possible to express this concern in terms of the effect area.

[1] This is a synonym of "Hazard Quotient (HQ) ≥ 1" or "PEC/PNEC ≥ 1," and "Margin of Exposure (MOE) ≤ the product of uncertainty factors (UFs)"

[2] As an indicator of risk, a HQ and a PEC/PNEC quotient can be used. In the method concerned herein, in the assessment of atmospheric release (e.g., an assessment of effects on human health), the size of a HQ reflects the size of the effect area of risk concern.

[3] The amount of release into an area of water cannot be expressed in terms of area. For that reason, in a human exposure assessment to suppose the exposure from quantities released into both the atmosphere and an area of water, two cases exist concurrently: the case where a region of risk concern can be calculated in terms of an area size; and another case where the region can be expressed only in terms of the number of locations. The handling of such cases is explained in III. 6.3 (2).

In the risk estimation for the environmental effects, the expressing indicator of (a) is used. With aquatic organisms and sediment organisms as targets, conduct the risk estimation with regard to chemicals released into an area of water. Unlike atmospheric release, risk estimation results cannot be converted into an area size; such results indicate whether there is a concern for risk with regard to each release source, and shows only the number of locations of risk concern at the national level.

The concepts above are illustrated in Figures 17 and 18.

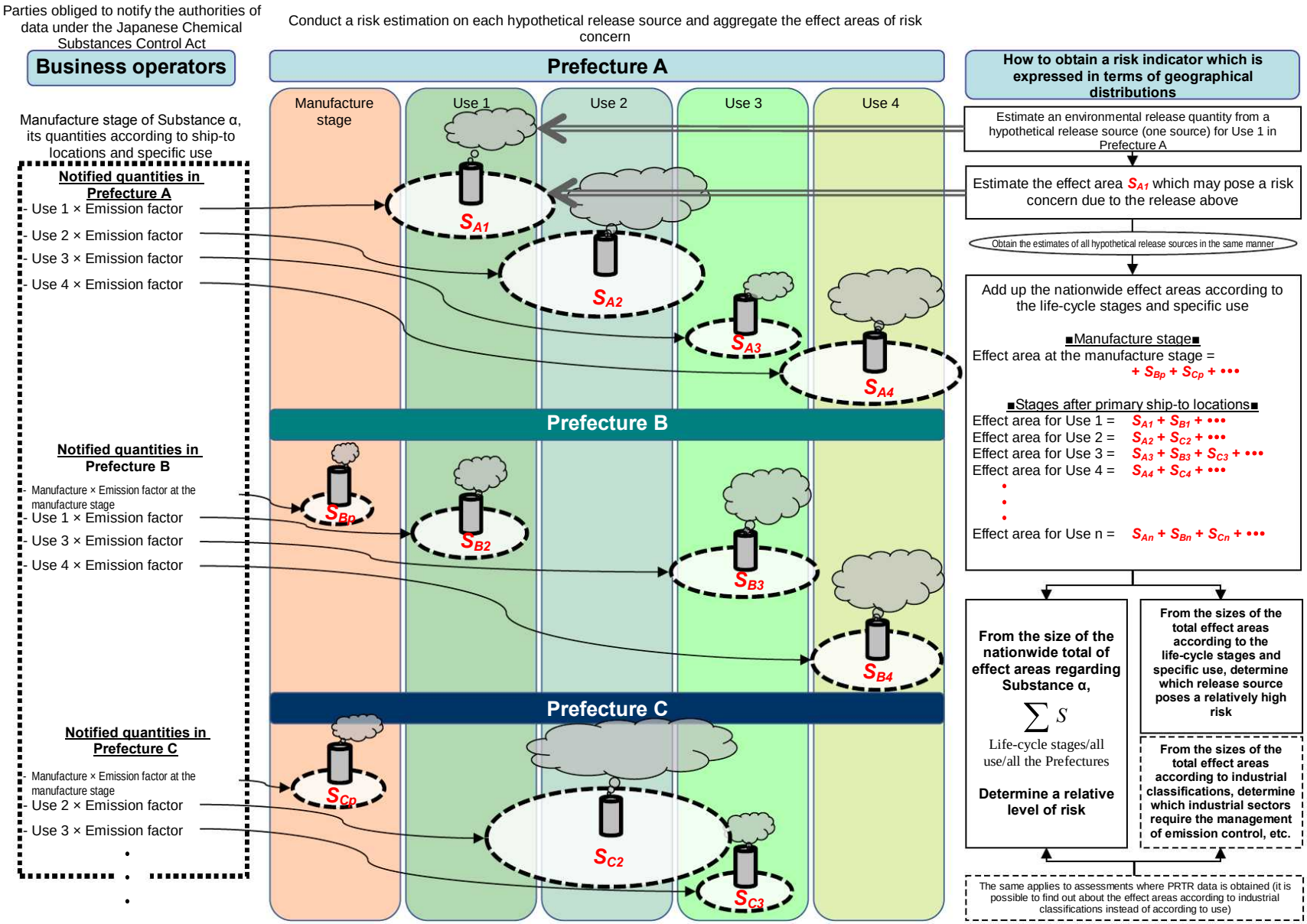


Figure 17 Ways to Express Risk Indicators in the Risk Estimation for Human Health

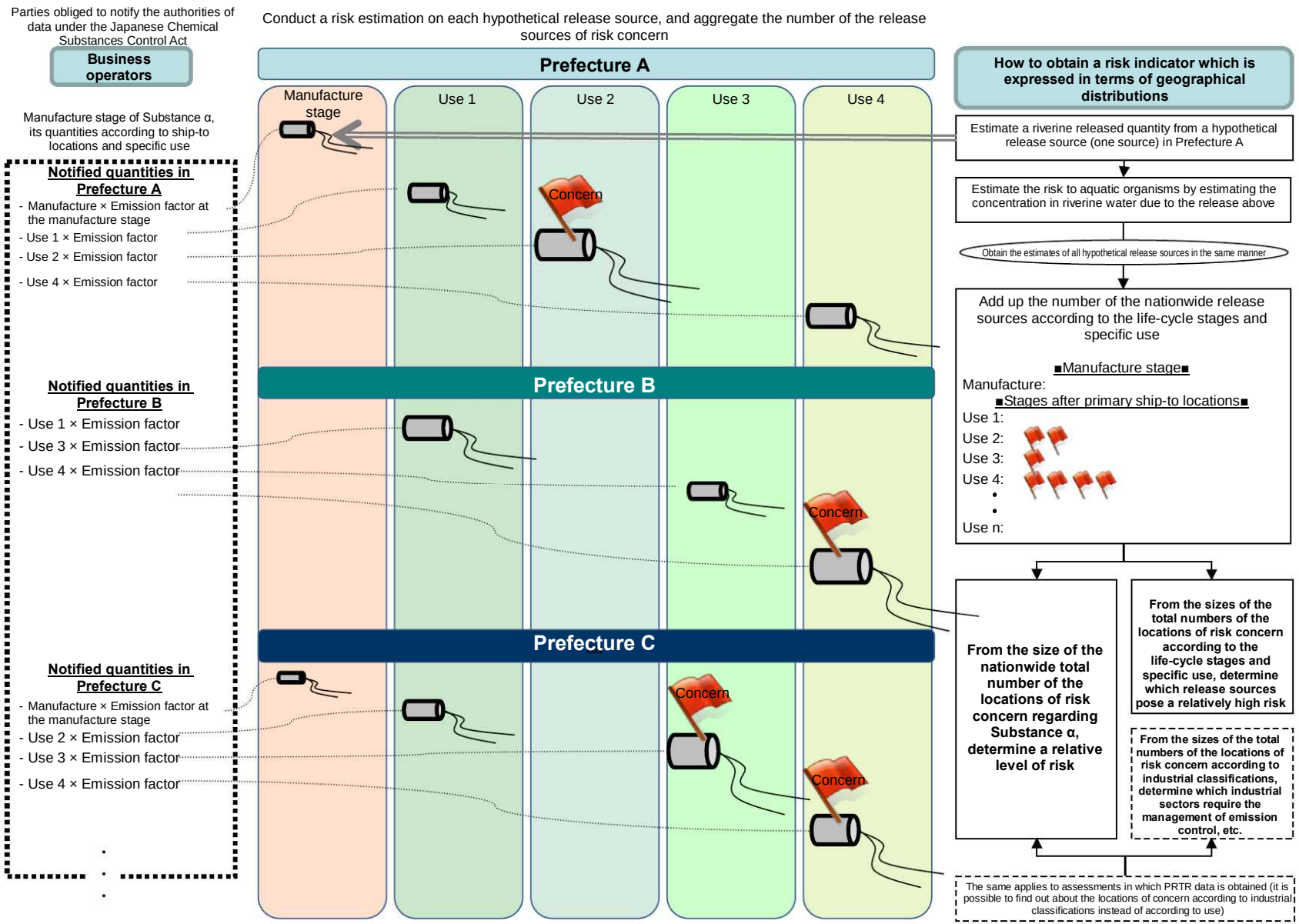


Figure 18 Ways to Express Risk Indictors in the Risk Estimation for the Environmental effects

[2] Risk estimation regarding human health

(i) Risk estimation for human health according to the scenario for each release source

In the scenario of each release source, risk indicators are expressed in terms of the effect area of risk concern. Thus, the assessment area is divided into ten different sizes with a radius of 1 to 10 km from a release source in units of 1 km, and the risk estimation is performed on each of the ten different sizes. For instance, if a concern for risk exists in the assessment area with a radius of 2 km from a release source, the effect area of risk concern is determined as an area with a radius of 2 km (see Figure 19). In this manner, conduct risk estimations on all the release sources, and derive the effect area of the risk for each of the sources. Consequently, the nationwide total effect area and the number of nationwide locations of the risk concern can be obtained (see Figure 17).

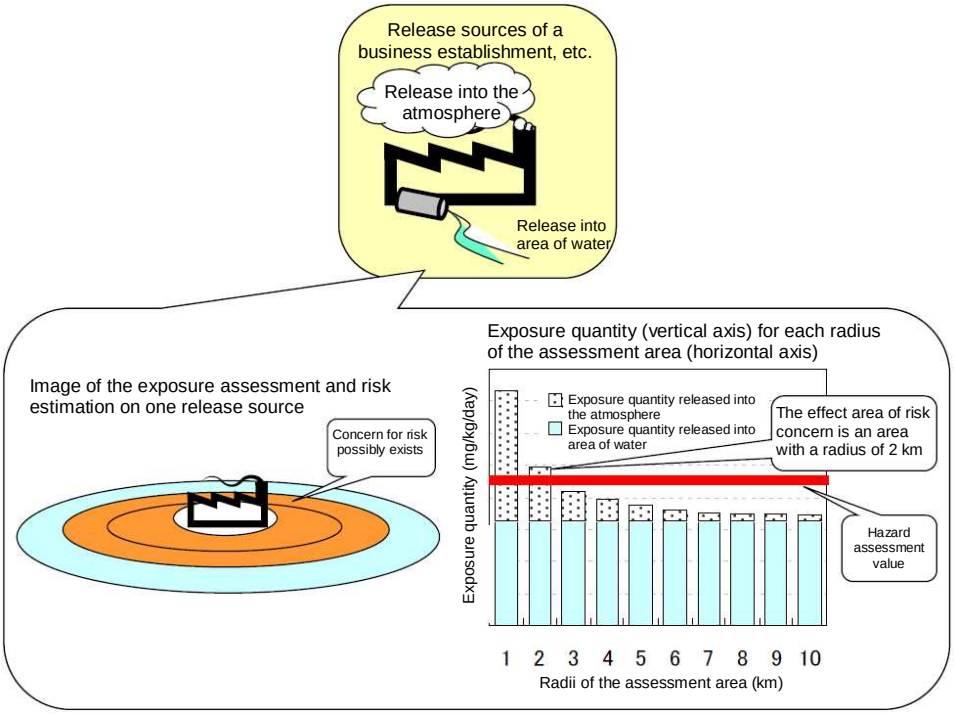


Figure 19 Relation Between the Risk Estimation and the Effect Area of Risk Concern According to the Scenario for Each Release Source

(ii) Risk estimation for human health in scenarios according to use

Among exposure scenarios according to use (see Table 13), conduct the risk estimation on the scenarios for aquatic and atmospheric non-point sources in Assessment I.
In scenarios for aquatic non-point sources, handle the processes from the estimation of released quantities to the estimation of environmental concentrations on the basis of basic units, and estimate an exposure amount for each substance. The comparison of this exposure amount with the hazard assessment value leads to a result for each substance in the risk estimation.
In scenarios for atmospheric non-point sources, set a hypothetical release source for each way of use, and perform the risk estimation on the sources.

[3] Risk estimation regarding the environmental effects

(i) Risk estimation for the environmental effects according to each release source

In a scenario for each release source, a PEC is estimated for each release source, and a PEC/PNEC quotient is obtained in the risk estimation. Perform the risk estimation on all release sources to obtain the nationwide number of locations of risk concern as a result (see Figure 18).

(ii) Risk estimation for human health in scenarios according to use

Among exposure scenarios according to use (see Table 13), conduct the risk estimation on aquatic non-point sources in Assessment I.
In scenarios for aquatic non-point sources, handle the processes from the estimation of released quantities to the estimation of environmental concentrations on the basis of basic units, and estimate a PEC for each substance. The comparison of this PEC with a PNEC leads to an estimation result for each substance in the risk estimation.

(3) Prioritsing

The process of prioritisng is the final step in Assessment I and conducted for both human health and the environemtal effects.
Where the availability status of hazard information for each Priority Assessment Chemical Substance, estimated release quantities and hazard information are on hand as a result of Assessment I, results of the risk estimation can be obtained. Use these kinds of information as indicators for setting an order of priority in order to determine the necessity for subsequent stages (Assessment II or the Request for Hazard Information Submission).

Table 20 Indicators used for Prioritising for Subsequent Stages

Assessment targets	Subsequent stages	Indicators used for prioritising
Human health	Assessment II pertaining to general toxicity and reproductive and developmental toxicity	- Risk estimation result for each release source - Risk estimation result according to use
	Assessment II pertaining to mutagenicity/carcinogenicity	- Estimated released quantity - Relevant hazard information
	Request for Hazard Information Submission	- Estimated released quantity - Items on hazards for which information is available
Environmental effects	Assessment II	- Risk estimation result for each release source - Risk estimation result according to use
	Request for Hazard Information Submission	- Estimated released quantity - Items on hazards for which information is available - Risk estimation result for each release source - Risk estimation result according to use

7. Assessment II of Risk Assessment (Primary)

In this stage, implement the risk assessment in sequence on those Priority Assessment Chemical Substances that are given high priority in Assessment I, so as to determine whether to designate them as Class II Specified Chemical Substances. Further, on the Priority Assessment Chemical Substances that are given low priority in Assessment I, implement the risk assessment to determine whether to rescind their designation as Priority Assessment Chemical Substances. In addition to the information used in Assessment I, this stage utilizes newly obtained hazard information, PRTR data (for PRTR target substances only) as exposure information outside the control of the Japanese Chemical Substances Control Act, and environmental monitoring data (for substances to which monitoring was performed previously).
In the hazard assessment of Assessment II, derive a hazard assessment value for which each of the endpoints is examined. Refine the exposure assessment on the basis of accessible information such as PRTR data and environmental monitoring data, in addition to the estimation of environmental concentrations and amount of intakes in the same manner as in Assessment I, and add, as necessary, evaluations utilizing exposure scenarios and mathematical models according to use, etc.
Assess risk through comparing results of the hazard assessment with results of the refined exposure assessment, clarify, as much as possible, details such as the geographical distribution of locations of risk concern and the substance use and life-cycle stages relevant to the release sources, and specify, through these processes, uncertainty factors involved in the exposure.
Accordingly, the purposes of Assessment II are to determine whether it is possible to immediately designate substances as Class II Specified Chemical Substances or possible to give the instructions on hazard investigation, determine the necessity for Assessment III where such designation or instructions cannot be

made, and specify substance handling statuses that business operators are required to report on and the regions for which additional monitoring should be implemented. Further, Risk Assessment II should basically be conducted only with existing information. However, where sufficient existing information is obtained to implement a detailed risk assessment to determine designation of Class II Specified Chemical Substances, the instructions on hazard investigation or the rescission of designation of Priority Assessment Chemical Substances, such designation of Class II Specified Chemical Substances, etc., should be determined without undergoing the instructions on hazard investigation or the Risk Assessment (Secondary).

From Assessment II onward, it is possible to make decisions on measures such as the instructions on hazard investigation, depending on details of the risk assessment. Organize the information obtained through the processes of the risk assessment and assessment results in risk assessment reports, etc., to render such information useful in making decisions on measures.
In this section, although the methods for "Hazard Assessment II," "Exposure Assessment II" and "Risk Estimation and Summarization" are explained in that order, actual implementation of the risk assessment should proceed flexibly; for instance, repeat the hazard assessment or exposure assessment where necessary, according to information obtained during the assessment processes.

7.1 Hazard Assessment II

(1) Purpose of Hazard Assessment II

The purposes of Hazard Assessment II are the following two points:

(a) derive hazard assessment values (for the environmental effects, PNECs) for the Risk Estimation II; and
(b) where sufficient grounds are obtained for the instructions on hazard investigation, specify investigation items.

The details of (a) are stated in the subsequent sections (2) to (4). In relation to (b), among the items prescribed in those Ministerial Ordinances concerning the instructions on hazard investigation, specify which instruction is to be given in individual cases.

(2) Contrast to Hazard Assessment I

The differences between Hazard Assessment I and II are shown in Table 21.
The contrasting details are printed in bold. In principle, the hazard assessment values used for establishing hazard classes in the screening assessment are used without altering them, as no detailed examination is conducted at the stage of Hazard Assessment I. In Hazard Assessment II, a detailed examination is conducted, including examination on existing knowledge. However, no detailed examination may be necessary in Assessment II, provided that detailed examination, including examination on existing knowledge, has been conducted at the stage of the screening assessment, and there is no additional information.

Table 21 Differences between Hazard Assessment I and II

Target items, etc. \ Assessment stage		Hazard Assessment I	Hazard Assessment II (III)
Human health	General toxicity and reproductive and developmental toxicity	- Use the information used in the screening assessment (where additional hazard information is available, choose and use the most rigorous data in terms of reliability from usable data). - Use essential uncertainty factors to derive hazard assessment values (regarding the hazard assessment values used in the screening assessment, use them without altering them). - Do not treat oral and inhalation intakes differently from each other.	**- Select a key study through collecting existing knowledge and examining it individually.** **- Derive hazard assessment values through individual examinations (the setting of uncertainty factors and the application of the benchmark dose method, etc., should be determined individually).** **- Depending on details of effects, treat oral and inhalation intakes differently.**
	Mutagenicity/ Carcinogenicity	- Use information on hazard classes in the screening assessment qualitatively to set priority.	**- Carcinogenicity: collect quantitative information (slope factor, etc.). If none is found, derive hazard assessment values.** **- Mutagenicity: collect existing knowledge to determine the presence/absence of a threshold for carcinogenicity, examine it individually and use it for making decisions.**
Environmental effects	Aquatic organisms	- Use the information used in the screening assessment (where additional hazard information is available, choose and use the most rigorous data from reliable data). - Use essential uncertainty factors to derive PNECs (regarding the PNECs used in the screening assessment, use them without altering them).	**- Select a key study through collecting existing knowledge and examining it individually.** **- Use essential uncertainty factors to derive PNECs.**
	Sediment organisms	- Not assessed.	**- Those substances that are likely to stay in sediments are assessment targets.** **- Collect and individually examine existing knowledge. If none is found, derive PNECs.** **- Where existing knowledge is not found, derive PNECs by using equilibrium partitioning**

* The details to be added in a stepwise manner are printed in bold.

(3) Hazard Assessment II for human health

[1] Premises and Basic Concepts

(i) Collection and examination of existing knowledge

Report on the hazard information newly obtained after designation of Priority Assessment Chemical Substances. In addition, investigate the way existing knowledge was collected in the screening assessment and any updates in it, and collect existing knowledge again. Further, where necessary, examine the information used in Assessment I on the basis of considerations on the significance of effects in the screening assessment.

(ii) Items on hazards to be assessment targets

In principle, the target items in Hazard Assessment II are as follows:
Where new pieces of hazard information are obtained in the process of collecting existing knowledge, consider them individually to see whether they are to be regarded as target items.

- General toxicity and reproductive and developmental toxicity: those items posing a concern for risk in Risk Estimation I
- Carcinogenicity and mutagenicity: those items to which hazard classes are assigned in the screening assessment

(iii) Handling of each route

In and after Assessment II, implement the risk assessment for each route depending on hazard details, and

derive a hazard assessment value for each route[1].

[2] Derivation of hazard assessment values

The derivation methods for hazard assessment values are, in principle, as provided for in Table 22 according to the presence and absence of a threshold of toxicological concern. However, it is possible to change the methods depending on any new information, in line with expert judgement [2].

Table 22 Derivation Methods for Hazard Assessment Values According to the Presence and Absence of Threshold

Presence and absence of threshold	Applicable items	Derivation methods for hazard assessment values	Calculation formula for hazard assessment values
Presence of threshold	- General toxicity - Reproductive and developmental toxicity - Carcinogenicity for which a threshold is considered to be present	Calculate it by dividing the NOAEL, etc. obtained from hazard data by the uncertainty factor corresponding to the data	NOAEL, etc.,/ the product of uncertainty factors
Absence of threshold	- Carcinogenicity for which no threshold is considered to be present	Calculate a Virtually Safety Dose with an acceptable risk level of 10^{-5} by using a unit risk or slope factor.	10^{-5}/Unit risk or slope factor

(i) Selection of key study

Prior to the derivation of hazard assessment values, select appropriate toxicity test data (key study) for each item[3]. Where new information is available through collecting existing knowledge, give a reliability rank to each piece of data, and sort out available data. Even with regard to unavailable hazard information, use it for weight of evidence and crosschecking where necessary. From examinations of such information as above, select a key study for each item on the basis of expert judgement.

(ii) Derivation of hazard assessment values pertaining to general toxicity

After addition and examination of new hazard information obtained through collecting existing knowledge, review hazard assessment values if necessary. Although uncertainty factors are, in principle, as provided for in the Hazard Assessment I (see 6.1 (2) [2]), it is possible to alter them in line with expert judgement, depending on new information[4]. Further, add the significance of effect in the case of carcinogenicity for which there is a threshold.

(iii) Derivation of Hazard Assessment Values in the case of carcinogenicity in the absence of a threshold

The assessment of carcinogenicity is conducted in the following cases:

(a) Where a hazard class of carcinogenicity is 1 or 2 in the screening assessment; and
(b) Even where no hazard class is assigned as there was no information in the screening assessment, new information on carcinogenicity is obtained after designation of Priority Assessment Chemical Substances.

The determination on the presence or absence of a threshold is to be made on the basis of expert determination with reference to results of mutagenicity tests and previous assessments.

[1] For example, cases where inhalation route and oral route involve different target organs.
[2] For example, the application of benchmark dose method is possible instead of NOAEL, etc.
[3] Regarding mutagenicity, it does not necessarily mean that a key study is to be selected. Reliable information should be used comprehensively for determining the necessity for subsequent testing and determining the presence/absence of a threshold for carcinogenicity.
[4] For example, possibilities include the changing uncertainty factor for inter-species difference or applying benchmark dose method instead of NOAEL, etc., in accordance with information on inter-species differences between testing animal species and human beings.

In cases where no threshold is regarded to exist[1], check the validity of evaluation values of existing unit risks and slope factors if they are available, and use these values if they are valid. A hazard assessment value is calculated by dividing a carcinogenic risk level at 10^{-5} by a unit risk or slope factor (see Table 22). Hence, a Virtually Safe Dose equivalent to a carcinogenic risk level at 10^{-5} is regarded as a hazard assessment value. Where an existing evaluation value is not available, obtain a unit risk, etc., and derive a hazard assessment value in the same manner. However, it is possible to change these depending on new information on the basis of expert judgement[2].
Where it is difficult to determine the presence or absence of a threshold, this is determined by experts.

(iv) Derivation of hazard assessment values from reference values

In cases where various reference values (such as the water quality criteria of tap water and the environmental quality standard) are used to convert them into hazard assessment values, review whether the conversion methods used in the screening assessment are appropriate as the occasion arises.

[3] The case where only mutagenicity is a target item

Consider the necessity for the instructions on hazard investigation according to individual cases.

(4) Hazard Assessment II for the environmental effects

[1] Premises and basic concepts

(i) Collection and examination of existing knowledge

Report on newly obtained hazard information after designation of Priority Assessment Chemical Substances. In addition, investigate the way existing knowledge was collected in the screening assessment and any updates on it, and collect existing knowledge again.

(ii) Organisms to be assessment targets

In addition to aquatic organisms, sediment organisms are regarded as targets in Hazard Assessment II in cases where "they are likely to be found in sediments and stay there in the environment on the basis of already existing knowledge on their compositions and properties"[3].

[2] Derivation of PNECs

(i) Selection of key study

Where new information is available through collecting existing knowledge, assign a reliability rank to each piece of data, and sort out usable data. Even with regard to unusable hazard information, use it for weight of evidence and crosschecking where necessary. Upon examination of the information above, select a key study for each test item on acute and chronic testing for trophic levels on the basis of expert determination[4].

[1] The derivation of hazard assessment values in the presence of a threshold follows the application methods of uncertainty factors specified in the previous section [2].
[2] Possibilities include the application of benchmark dose method.
[3] The instructions on hazard testing on sediment organisms is made "where relevant chemicals are likely to be found in sediments and to stay there in the environment on the basis of already existing knowledge on their compositions and properties, and also where the contamination of the sediments by the said chemicals are thought to pose a risk of damaging the population and/or growth of animals and plants in the human living environment." [Testing Methods for the Study of the Hazardous Properties of Type III Monitored Chemical Substances (March 25, 2004; MIB No. 6 of March 19, 2004; EHP Announcement No. 040325004)]
[4] There are six types: acute toxicity test on algae, chronic toxicity test on algae, acute toxicity test on daphnia (crustacean), chronic toxicity test on daphnia (crustacean), acute toxicity test on fish and chronic toxicity test on fish.

(ii) Derivation of PNECs for aquatic organisms

After adding and examining hazard information through collecting existing knowledge, review PNECs as necessary. The uncertainty factors are, in principle, as provided for in the Hazard Assessment I (see 6.1 (3) [2]).

(iii) Derivation of PNECs for sediment organisms

With regard to sediment organisms, the assessment takes place where "chemicals are likely to be found in sediments and to stay there in the environment on the basis of already existing knowledge on their compositions and properties." To determine whether "chemicals are likely to be found in sediments and stay there in the environment," use the logKow value. If the logKow is 3 or more, the substance concerned is classified as one which is likely to remain in sediments[1].

If sediment organisms are included as assessment target species, derive $PNEC_{sed}$[2] in the following manner according to the case where existing data can be obtained and to the case such data cannot be obtained (see Figure 23).

Derivation of $PNEC_{sed}$ by using existing data
Where existing information on hazards for sediment organisms is found, set $PNEC_{sed}$s on the basis of the found data. Where multiple pieces of usable data are obtained, prioritize the use of chronic toxicity values. In selecting chronic toxicity values, select uncertainty factors in line with "The number of data pieces sorted out by different inhabiting/dietary conditions" (see Figure 23). These uncertainty factors accord with the setting of the REACH guidance on sediment organisms in freshwater[3].

Derivation of $PNEC_{sed}$ with equilibrium partitioning
Where no hazard information on sediment organisms is obtained, apply equilibrium partitioning which is regarded as an alternative method[4]. This method presupposes the following:

(a) The sensitivity of sediment and aquatic organisms to chemical substances are the same; and
(b) The sediment concentration, concentration in pore water, concentration in sediment organisms are all under an equilibrium condition.

Further, the REACH Guidance takes into consideration substances absorbed into sediments when the logKow is 5 or more, and suggests an addition of 10 as an uncertainty factor ("assessment factor" in the Guidance). In concert with this, when a logKow is 5 or more, the $PNEC_{sed}$ is one-tenth of a logKow with a value of below 5.

[1] This bases itself on the view in the Reach Guidance, "In general substances with a Koc < 500 - 1000 l/kg are not likely sorbed to sediment (SETAC 1993). According to this, a log Koc or log Kow of ≥ 3 is used as a trigger value for sediment effects assessment." ECHA (2008) Guidance on information requirements and chemical safety assessment, Chapter R.7b: Endpoint specific guidance, R.7.8.7 Introduction to sediment organisms' toxicity.
[2] sed in PNECsed is an abbreviation of sediment.
[3] ECHA (2008) Guidance on information requirements and chemical safety assessment Chapter R.10: Characterisation of dose [concentration]-response for environment, R.10.5.2.2 Calculation of PNEC for fresh water sediment using assessment factors.
[4] R.10.5.2.1 Calculation of PNECs for freshwater sediment using equilibrium partitioning in the Guidance above.

On the basis of the assumptions above, convert the $PNEC_{water}$ into a sediment concentration by using the partition coefficient between the particle absorbing bodies in sediments and water, the result of this is the $PNEC_{sed}$. The $PNEC_{sed}$ is a chemical concentration based on the dry weight of sediments.

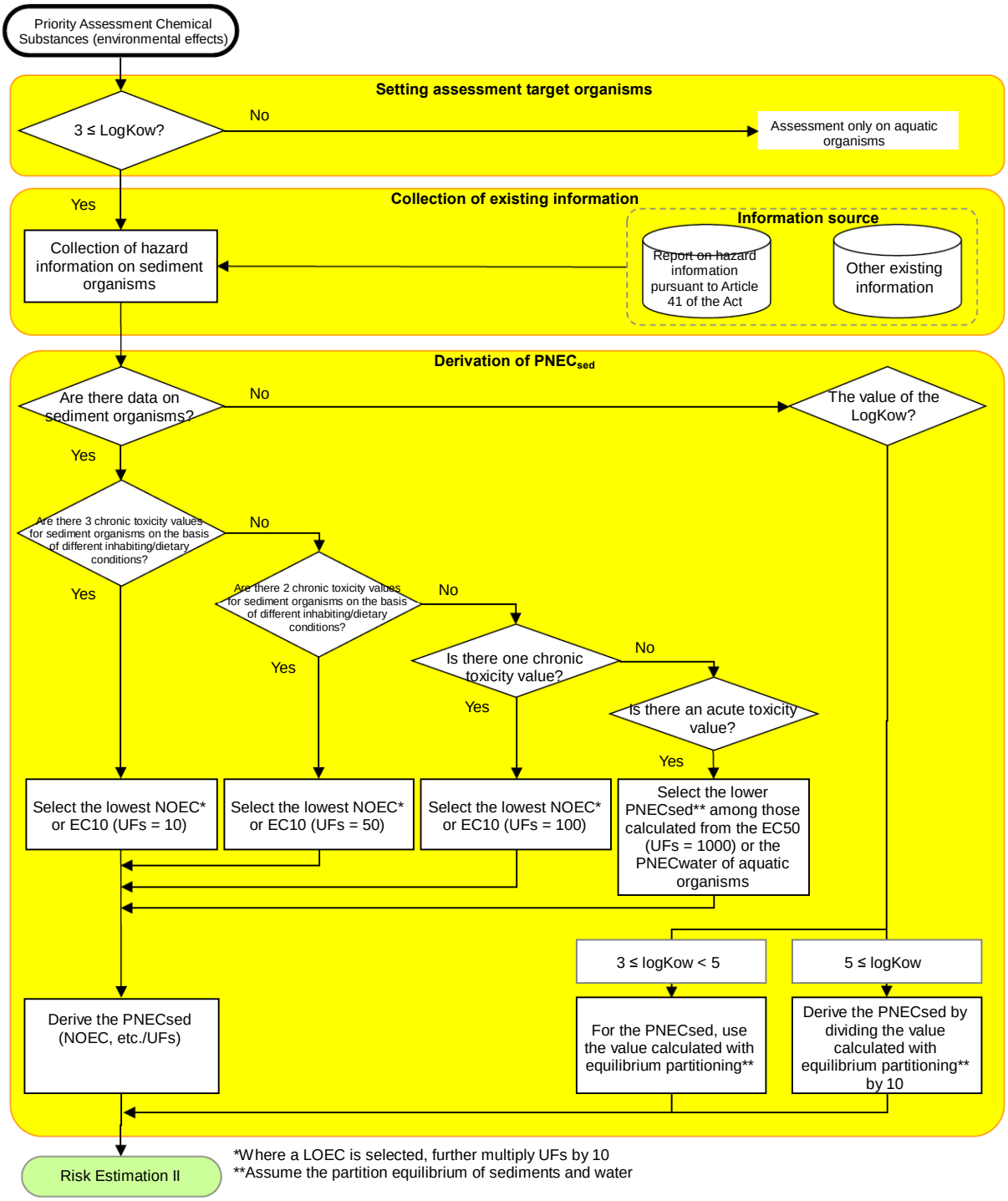


Figure 23 Derivation Flow of $PNEC_{sed}$s of Sediment Organisms

7.2 Exposure Assessment II

(1) Purpose of Exposure Assessment II

The purpose of Exposure Assessment II is to estimate the exposure status of target substances by using available information. In so doing, use PRTR information and environmental monitoring information, where such information is available, concurrently with the estimates obtained with those mathematical models applying notified information such as manufacturing quantities. Further, employ multiple information sources and multiple estimating methods, and collect and organize information necessary for estimation sand analyses.

(2) Contrast to Exposure Assessment I

The differences between Exposure Assessment I and II are shown in Table 24. The differences in the assessment stages are the scope of information used, the extent of examination and the multiplicity on the basis of levels and cases of detailed assessment contents.

Table 24 Differences Between the Exposure Assessment I and II

Assessment Stages / Implementation items, etc.		Assessment I	Assessment II (Parts added/changed from the Assessment I are stated)
Information to be used		- Notified information such as manufacturing quantities - Physicochemical properties (on the basis on the reliability ranks but not examined yet) - Degradability: distinction of "readily degradable"/"not readily degradable" - Environmental conditions: default settings	- Notified information such as manufacturing quantities **(over time)** **- PRTR information** **- Existing environmental monitoring information** - Physicochemical properties **(select again after examining)** **- Degradability: gather a degradation rate for each environmental medium and reflect it in estimations** **- Where PRTR information is available, investigate the flow rate of the area of water where the relevant substance is released, and the land use around the release sources. Reflect such information in estimations, etc.**
Estimation of environmental concentration, etc.	Exposure scenario for each release source	- Estimate an environmental concentration for each hypothetical release source on the basis of notified information such as manufacturing quantities	**- Examine the "other" use stated in notified information such as manufacturing quantities, and reflect it in the estimation of released quantities.** **- Where PRTR information is available, concurrently estimate an environmental concentration for each PRTR-notifiable business firm.** **- If both PRTR information and environmental monitoring information are available, use them as the environmental concentration for the relevant scenario depending on factors such as the positional relation with the release source.**
	Exposure scenarios taking account of effects from various release sources	-	**- From notified information such as manufacturing quantities, estimate exposure statuses with broad and long-term mathematical models by taking account of the released quantities that include releases caused at the use stage of products for long-term use.** **- Where PRTR information is available, use mathematical models that apply geographical information and estimate the nationwide spatial distribution of environmental concentration.** **- Where environmental monitoring information is available, set it as the environmental concentration for each measurement point.**
	Exposure scenarios taking account of use, etc.	- Estimate environmental concentrations, etc., on the basis of exposure scenarios in line with use, etc.	**- Collect and reflect parameters (the extraction rate at sewage treatment plants, etc.) in estimations.** **- Add a more detailed model estimation corresponding to individual cases in exposure scenarios according to use, etc.** **- Use environmental monitoring information corresponding to the relevant scenario where it is obtainable.**
Estimation of human intake		- Regarding exposure amounts, add up inhalation/oral exposure amonuts to the intake - Point estimation	**- Depending on details of the hazard concerned, estimate the inhalation exposure amounts and the oral exposure amount separately.** **- Allow some latitude in the estimation where necessary**
Assessment of persistence		-	**- Estimate persistency in the environment by using the half-life period of each environmental medium as well as broad- and long-scaled mathematical models.** **- Where environmental monitoring information is available, organize detection statuses over time.**

* The details that are added in a stepwise manner are printed in bold.

(3) Premises and basic concepts of Exposure Assessment II

[1] Information sources for the basis of Exposure Assessment II

(i) Features of information sources and points to consider

The information sources for the basis of Exposure Assessment II have three different types shown in Table 25. Table 25 shows the outline and features of each information source, and Figure 26 shows the differences in the estimation steps in the exposure assessment.

Table 25 The Outline and Features of Information Sources for the Exposure Assessment II

Information sources	Outline	Main features		
		Merits	Demerits/Points to consider	
Notified information such as manufacturing quantities	Under the Japanese Chemical Substances Control Act, each manufacturer's/importer's: - Manufacturing quantities according to the prefectures - Import quantities - Shipment quantities according to the prefectures and specific use	All Priority Assessment Chemical Substances possess.	- The estimation results for which this information has been used are relative quantities as the results have gone through multistage estimation steps. - Additional information, such as handling of individual substances, is required before a final determination is made regarding designation of Class II Specified Chemical Substances.	
PRTR information	Under the Act for PRTR and Promotion of Chemical Management, - Released quantities notified by handling operators - Released quantities estimated by the government	Data on notified released quantities are specific in accordance with individual release sources and media.	- Only some of Priority Assessment Chemical Substances possess. - In some cases, the range of the relevant chemical substances does not match that of Priority Assessment Chemical Substances.	- The range of release sources does not necessarily match the control subjects of the Japanese Chemical Substances Control Act. - Estimated release quantities are according to the prefectures, not necessarily to the media.
Environmental monitoring information	Measured concentrations of chemical substances in environmental media (the atmosphere, riverine water, sea water, sediment, fish and shellfish, etc.) and in food	- This allows a grasp of actual environmental concentration levels to which human beings and organisms are exposed. - This can be evidence of estimated concentrations obtained through the use of mathematical models.		- With this information alone, it is difficult to interpret whether releases are those resulting from the control subjects of the Japanese Chemical Substances Control Act. - It is difficult to understand human intake via multiple exposure routes with this. - Depending on the number of measurements, this does not represent concentrations (long-term average values, etc.) presumed in exposure scenarios.

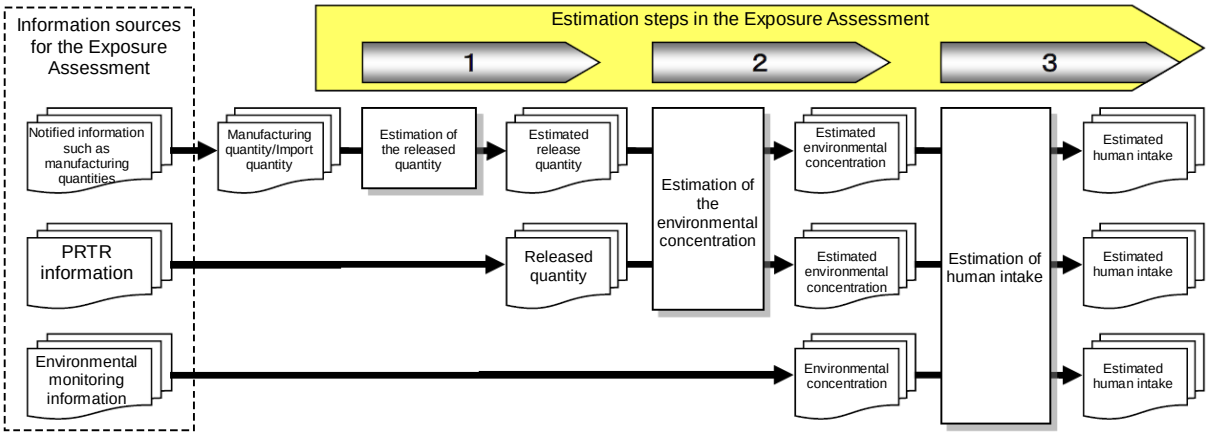


Figure 26 Differences in the Estimation Steps in the Exposure Assessment for Individual Information Sources

As shown in Table 25, the information used in the exposure assessment has various merits and demerits. Hence, determination on the instructions on hazard investigation and the like should not depend solely on the values obtained from the estimation steps in Figure 26, and take account of the merits and demerits of the information for the exposure assessment in utilizing the information.

(ii) Handling of each combination of information sources

In relation to the three information sources for the basis of Exposure Assessment II in Table 25, there are four combinations of the sources according to target substances, as shown in a row in Figure 28. Depending on obtainable information, different methods are applicable.
Further, the target information sources of each information source are different among each other, as shown in Table 27.

Table 27 Differences in the Potential Target Release Sources for Each Information Source

The target release sources when notified information such as manufacturing quantities under the Japanese Chemical Substances Control Act is used

		Types of release source				
		Use subject to the Japanese Chemical Substances Control Act	Use not subject to the Japanese Chemical Substances Control Act	Other release sources (examples)		
				Moving bodies	Natural sources	Contamination outside the country
Life-cycle stages	Manufacture stage	○				
	Preparation/Industrial use stage	○				
	Home use stage	○				
	Use stage of products for long-term use	○				
	Disposal stage					

Release sources that can be targets when using PRTR information

Life-cycle stages	Manufacture stage	○	○			
	Preparation/Industrial use stage	○	○			
	Home use stage	○	○	○		
	Use stage of products for long-term use					
	Disposal stage					

Release sources that may be included when using environmental monitoring information

Life-cycle stages	Manufacture stage		
	Preparation/Industrial use stage		
	Home use stage	○	○
	Use stage of products for long-term use		
	Disposal stage		

Figure 28 Differences in the Estimation Steps in the Exposure Assessment for Individual Information Sources

Scenarios \ Combinations	Information under the Japanese Chemical Substances Control Act	Information under the Japanese Chemical Substances Control Act PRTR information	Information under the Japanese Chemical Substances Control Act Monitoring information	Information under the Japanese Chemical Substances Control Act PRTR information Monitoring information
Exposure scenario for each release source	[Japanese Chemical Substances Control Act] Must estimate	[PRTR] Estimate by using notified information		[PRTR] Estimate by using notified information [Monitoring] Use monitoring information corresponding to the relevant scenario where the information is obtainable
Exposure scenario taking account of effects from various release sources	[Japanese Chemical Substances Control Act] Must estimate	[PRTR] Estimate by using PRTR information	[Monitoring] Regard and use this as monitoring information on the general environment	[PRTR] Estimate by using PRTR information [Monitoring] Use this through matching it with the estimated value for each mesh
Scenario according to use etc. – Scenario for an atmospheric non-point source	[Japanese Chemical Substances Control Act] Estimate the extent of contribution by the non-point source where the applicable use takes place	[PRTR] Estimate this if estimations have taken place regarding the applicable use	[Monitoring] Regard and use this as monitoring information on the general environment	[PRTR] Estimate this if estimations have taken place regarding the applicable use [Monitoring] Use this through matching it with the estimated value for each mesh
Scenario according to use etc. – Scenario for an aquatic non-point source	[Japanese Chemical Substances Control Act] Estimate the extent of contribution by the non-point source where the applicable use takes place	[PRTR] Estimate this if estimation has taken place regarding the applicable use	[Monitoring] Regard and use this as monitoring information on the general environment	[PRTR] Estimate this if estimations have taken place regarding the applicable use [Monitoring] Use this through matching it with the estimated value for each mesh
Scenario according to use etc. – Scenario for ship-bottom/ fish net antifoulants	[Japanese Chemical Substances Control Act] Estimate this when the applicable use takes place	[PRTR] Estimate this if estimations have taken place regarding the applicable use	[Monitoring] Use monitoring information corresponding to the relevant scenario where such information is obtained	[PRTR] Estimate this if estimations have taken place regarding the applicable use

[2] Human exposure routes

In and after Assessment II[1], obtain the exposure amount for each route depending on hazards[2] (see "6.1 (2) [1] (iii) Handling of Oral and Inhalation Routes").

[3] Handling of degradability

In and after Assessment II[3], investigate and estimate the degradation rate for each environmental medium (its half-life time) and eliminating rates at sewage treatment plants. If these are obtained, use them for the estimation of release quantities from sewage treatment plants, and for the estimation of environmental concentrations and the evaluation of their persistence.

(4) Methods of the Exposure Assessment II

[1] Collection and examination of existing knowledge

To implement Exposure Assessment II, collect the various kinds of existing knowledge mentioned in Table 24, and if necessary, examine data on properties, such as physicochemical properties, for estimating released quantities and exposure amounts.

[2] Exposure scenario for each release source

(i) In the case where notified information such as manufacturing quantities is used

Ensure that the methods of the exposure assessment, which are based on notified information such as manufacturing quantities and used in Exposure Assessment I, reflect the following matters. Thereafter, re-estimate exposure quantities according to the scenario for each release source.

(a) In cases where the adopted values are changed as a result of examination of data on physicochemical properties, re-select the emission factor.
(b) In cases where specific use is found for the "Other" use stated in the notification of shipment quantity, review the emission factor.
(c) In cases where the degradation rate constant is obtained for each environmental medium, reflect this in concentration estimation.

(ii) In the case where PRTR information is obtainable

Furthermore, where it is possible to obtain PRTR information under the Act for PRTR and Promotion of Chemical Management, refer to the notified data of each business operator, and use each notifiable business firm's atmospheric released quantity and released quantity to the public water area as input values for the estimation of exposure for each release source.
In contrast to notified data such as manufacturing quantities under the Japanese Chemical Substances Control Act, release sources concerned here are not "hypothetical release sources" but actually existing notifiable business firms. Thus, locations of release sources and receiving media can be identified specifically. Furthermore, non-control subjects under the Japanese Chemical Substances Control Act, such as use outside the scope of the Act and releases due to subgeneration, are covered here.

[1] In Assessment I, inhalation and oral routes are not discriminated; convert both routes into intakes (the unit is mg/kg/day), and add up intakes to calculate the total exposure amount of all the routes.
[2] For example, there may be different target organs for each of the inhalation route and oral route.
[3] In Assessment I, use only conclusive results regarding degradability under the Japanese Chemical Substances Control Act (Not readily degradable/Readily degradable), for the estimation of release quantities from sewage treatment plants.

(iii) In the case where environmental monitoring information can be obtained

If both environmental monitoring information and PRTR information are obtainable, regard the environmental concentration corresponding to "the relevant scenario for each release scenario" as the actual value in the scenario, depending on the positional relation concerned in both pieces of information.

[3] Exposure scenarios taking account of effects from various release sources

In the exposure scenario for each release source, the exposure assessment is conducted for stationary release sources (manufacturing establishments and business establishments for preparation or industrial use) located upstream to midstream of the supply-chain. In Exposure Assessment II, set the scenario concerned here to include effects from not only stationary release sources but also various release sources (houses, moving bodies, etc.).

(i) In the case where notified information such as manufacturing quantities is used

In the scenario concerned here, take account of regional quantities such as those from the stages of home use, business use and use of products for long-term use, in addition to released quantities of the stationary release sources located upstream to midstream of the supply-chain, which are targets of the scenario according to each release source. On this basis, estimate exposure statuses on a broad and long-term scale by using the multimedia model[1].

(ii) In the case where PRTR information is obtainable

Where PRTR information is obtainable, on the basis of released quantities from nationwide release sources including regional release quantities, estimate the spatial distribution of environmental concentration at the national level and thereafter the nationwide exposure amount by using the model for estimating environmental concentrations for plots on the map (meshes). In so doing, effects of release sources outside the scope of the control under the Japanese Chemical Substances Control Act are also analyzed as much as possible. For this reason, carry out the estimation of PRTR information even in those cases in which PRTR information clearly outside the scope of the control under the Act was excluded.

(iii) In the case where environmental monitoring information can be obtained

In the stage of Assessment II, with existing information from environment monitoring conducted by the government as the basis, collect measured data from the past ten years in order to secure a certain level of reliability in relation to measurements and analyses. Furthermore, consider the necessity for collecting other environmental monitoring information, together with the necessity for implementing additional monitoring; such information is to be used in the stage of Assessment III.
On the basis of the collected environmental monitoring information, set the environmental concentration for each measurement point, and thereafter estimate the exposure amount.
Environmental monitoring information includes effects of those release sources not subject to the Japanese Chemical Substances Control Act. As the relations between monitoring information and such release sources are unclear, collect and organize as much necessary information as possible for analyzing the relations between release sources and such information as the locational information of PETR-notifiable business firms and information on those release sources not subject to the Act.

[4] Exposure scenarios according to use, etc.

(i) In the case where notified information such as manufacturing quantities is used

Where an exposure scenario for each release source alone cannot evaluate those ways of use causing exposures associated with releases into the environment, add to this scenario the applicable exposure scenarios shown in Table 29 according to use. If necessary, add also estimation models. In Exposure

[1] Multimedia model: a mathematical model to evaluate the environmental fate of chemicals that are released into the environment and transported/moved or distributed between environmental media, such as the atmosphere, water, soil and sediment, or chemically or biologically degraded.

Assessment II, add existing information and particularize it to a possible extent.

Table 29 Outline of Exposure Scenarios According to Use (including Emission Scenarios)

Scenario names	Main corresponding use	Main corresponding life-cycle stages	Outline
Scenario for aquatic non-point sources	- Aqueous cleaning agents[home/ business use] - Wax - Biocides	Stage of home/ professional use	This supposes the exposure population exposed to chemical substances that were used in houses, etc., and travelled through sewerage to a sewage treatment plant, concentrated in there and released into a river. In Assessment II, choose and use a value for the extraction rate at the sewage treatment according to substances. Further, estimate both the riverine water concentration via the sewage treatment plant and the one in the area where a sewage system is not developed.
Scenario for atmospheric non-point sources	- Fragrance air-freshener - Biocides - Fuel, fuel additives	Stage of home/ professional use	Regarding the use for which a release into the atmosphere from a non-point source (house and moving body) is supposed, in Assessment II, allocate a nationwide released quantity to each mesh unit by using the population, etc., as an indicator. Conduct the exposure assessment with the use of the allocated released quantity.
Scenario for antifoulants for ship-bottom paint and fish nets	- Antifoulants for ship-bottom paint - Antifoulants for fish nets	Stage of use of products for long-term use	On the assumption that antifoulants for ship-bottom paint and fish nets are supposed are released into the sea from ship-bottom paint films and fish nets, in Assessment II, calculate the released quantity of a typical use location in Japan (marine area) from the nationwide shipment quantity for the relevant use, and estimate the concentration in the sea area.
Scenario for the possibility of groundwater contamination	- Detergent solvents for metal - Cleaning solvents	Industrial use stage or home/professional use stage	Only where the use and properties of the substance are under a specific classification, assume the possibility that the Priority Assessment Chemical Substance (human health) is released into the soil, and examine how easily the substance migrates into groundwater by employing the model estimation.

(ii) In the case where PRTR information is obtainable

Where an estimation of a released quantity outside the notifiable PRTR is conducted, add one/some of the exposure scenarios shown in Table 29[1] to the hazard assessment as necessary, and implement the assessment.

[5] Estimation of amount of human intake

In the estimation of amount of human intake on the basis of food, take account of the self-sufficiency rate and the rate of local products intake in a scenario that focuses on effects of a particular source. However, in relation to the general environment, the self-sufficiency rate is to be taken into consideration, but not the rate of local products intake. Where concentrations in the area surrounding the release source and in the general environment are to be separately estimated, estimate the total intake of both these cases.
Further, calculate exposure amounts with some latitude in exposure factors such as the rate of local products intake, as required.

[6] Assessment of persistence

Estimate the steady state reaching time, etc., in the environment by using the multimedia model as an indicator of persistence in the environment.

[1] In relation to scenarios for aquatic non-point sources and atmospheric non-point sources, it is possible that some cases do not require an addition of a scenario where such a scenario is included in the mathematical model using PRTR information of "exposure scenarios taking account of effects from various release sources."

Furthermore, where environmental monitoring information for multiple years is available, organize the detection status of each environmental medium over time.

7.3 Risk Estimation II and summarization

(1) Risk Estimation II

[1] Purpose of Risk Estimation II

The purpose of Risk Estimation II is to quantify risk. Through quantification, estimated risk values can be one of the indicators to be used in decision-making.

[2] Risk Estimation II regarding human health

Implement the risk estimation for human health on hazard items and on each exposure scenario/information source. The expressions used for describing results of the risk estimation are different for each exposure scenario/information source, as shown in Table 30.

Table 30 Expressions for Results of the Risk Estimation for Human Health According to Each Exposure Scenario/Information Source

Exposure scenarios	Information sources	Expressions for risk estimation results
Exposure scenario for each release source	Notified information such as manufacturing quantities	The effect area of, and the number of locations of, a risk concern in relation to hypothetical release sources
	PRTR information	The effect area of, and the number of locations of, PRTR-notifiable business firms regarding a risk concern
	Environmental monitoring information (where PRTR information is also obtainable)	The presence and absence of a risk concern in each assessment area surrounding release sources
Exposure scenario taking account of effects from various release sources	PRTR information	Nationwide distribution of the meshes of a risk concern
	Environmental monitoring information	Nationwide distribution of environmental monitoring measurement points in relation to a risk concern
Exposure scenario according to use, etc.	Notified information such as manufacturing quantities, PRTR information	The presence and absence of a risk concern*

* Although results of Assessment I for each scenario are shown in terms of the presence/absence of a risk concern, results may be shown in terms of regional distributions in and after Assessment II.

[3] Risk Estimation II regarding the environmental effects

The risk estimation for the environmental effects is implemented on target organisms (aquatic organisms and, if necessary, sediment organisms) and on each exposure scenario/information source. The expressions used for describing results of the risk estimation are different for each exposure scenario/information source, as shown in Table 31.

Table 31 Expressions for Results of the Risk Estimation for the Environmental effects According to Each Exposure Scenario/Information Source

Exposure scenarios	Information sources	Expressions for risk estimation results
Exposure scenario for each release source	Notified information such as manufacturing quantities	The number of hypothetical release sources of a risk concern
	PRTR information	PRTR of a risk concern The number of notifiable business firms
	Environmental monitoring information (where PRTR information is also obtainable)	PEC/PNEC quotient for each environmental monitoring measurement points surrounding release sources
Exposure scenario taking account of effects from various release sources	PRTR information	Nationwide distribution of the meshes of a risk concern
	Environmental monitoring information	Nationwide distribution of environmental monitoring measurement points in relation to a risk concern
Exposure scenario according to use, etc.	Notified information such as manufacturing quantities, PRTR information	The presence and absence of a risk concern*

* Although results of Assessment I are shown in terms of the presence/absence of a risk concern, results may be shown in terms of regional distributions in and after Assessment II.

(2) Summarization

Summarize the information and assessment results obtained in the processes of the risk assessment in risk assessment reports so as to enable such information to be used for determining measures such as the instructions on hazard investigation. The details to be summarized in risk assessment reports are shown in the following[1].

[1] Uncertainty factors included in assessment results

In general, uncertainty in risk assessment results exists in both the hazard assessment and the exposure assessment. Uncertainty in the hazard assessment is expressed in "the product of uncertainty factors," and is incorporated into the safety margin representing the lack of knowledge on the toxicity effects of the relevant substance on human beings and animals and plants (see 6.1 (2) [2]).
On the other hand, uncertainty in the exposure assessment has been dealt with by setting assumptions and default values in the exposure assessment. Extract the part to which such assumptions were applied (environmental conditions such as the number of release sources, receiving media, emission factors, the flow rate, etc.) as uncertainty factors, and rank them in order of the degree of their effects on estimation results.

While uncertainty factors that cannot be overlooked are included in assessment results and therefore cannot be utilized for determining the instructions on hazard investigation, etc., repeat the cycle of "Uncertainty analysis → obtaining information → reassessment." Determinations pertaining to the instructions on hazard investigation, etc., are to be made only after the major uncertainty has been reduced by introducing new information.

[2] Nationwide distribution of meshes of risk concern

The nationwide distribution status of areas of risk concern is shown in risk estimation results according to multiple exposure scenarios (see Tables 30 and 31). According to exposure scenarios and information sources, risk estimation results are shown in terms of national distributions of the effect area and number of locations of risk concern, meshes of risk concern, etc.

[1] Regarding the details to be summarized, the definition of "risk characterization" in Harmonization Project Document No. 1 of the WHO (2004) IPCS Risk Assessment Terminology, and the concepts in the U.S. EPA (2000) Risk Characterization Handbook. EPA 100-B-00-002, are used as reference.

As exposure statuses of target chemical substances are understood through different means and from different perspectives according to exposure scenarios and information sources, comprehend and interpret the nationwide distribution statuses of areas of risk concern from multiple aspects by ensuring that such means and perspectives reinforce each other.

[3] Use and industrial classifications in relation to areas of risk concern

Indicate the values related to the nationwide distribution of risk concern areas in the previous section as well as the breakdown of release sources of risk concern. Where these are based on notified information such as manufacturing quantities under the Japanese Chemical Substances Control Act, it is possible to show them according to the life-cycle stages/specific use. Where they are based on notified PRTR information, it is possible to show them according to industrial classifications[1]. This shows whether areas of risk concern are weighted toward particular use/industry sectors, and whether the areas extend to multiple ways of use and sectors.

The breakdown of release sources of risk concern can be used for determining the following:

- In the case where exposure requirements are to be determined:
  Whether exposures are related to the "manufacture, use, etc." under the Japanese Chemical Substances Control Act.
- In the case of proceeding to the subsequent assessment:
  From what type of use and industrial sectors should information be collected?
- In the case of giving instructions and advice:
  To what type of business operators should instructions and/or advice be given?
- In the case of regulating use and sectors
  What types of use and sectors are the targets when the technical guidance is formulated under Article 27 of the Act, in order to prevent environmental pollution?

[4] Information used for assessments

This includes information with regard to the identification of target substances, information on substances' properties, hazard information and information related to exposure. Such information is important for securing the transparency and objectivity of risk assessments.

[5] Conclusion of assessment

The conclusion of an assessment is to be reached through logically considering and summing up the information used for the assessment and the assessment result for each assessment step.
In and after Assessment II, the conclusion is conductive to the determination of the applicability of the conclusion to the exposure requirements and the determination of the effectiveness of the regulation under the Japanese Chemical Substances Control Act. For this reason, considerations on such results must be many-sided and multi-layered: for instance, a comparison of environmental monitoring information on the basis of risk estimation results in which multiple exposure assessment methods were employed in accordance with information obtained through analyses on the residue status in the environment.
In so doing, make interpretations from perspectives such as those mentioned below. In addition, where sufficient information has been obtained for interpretation, derive a conclusion of the assessment. Where such information is not available, organize information necessary for reducing the uncertainty in the following section, rather than deriving a conclusion.

[1] If this is based on PRTR information, it is possible to show the values and breakdown according to individual business operators, as required.

(a) Where results based on multiple information sources are available, which information source should be the basis for ensuring certainty?
- ✓ What about the information sources from the perspectives of the characteristics, limitations and other points of each source (see Table 25)?
  - What about them from the perspective of the inclusion relations of chemical substances?
  - What about them from the perspective of the inclusion relations of release sources?
- ✓ What are the remaining uncertainty factors?

(b) Are there areas of risk concern?
- ✓ If there are, are the areas related to the "manufacture, use, etc." under the Japanese Chemical Substances Control Act?
- ✓ What about the detection status of environmental monitoring data in the areas surrounding the release source?

(c) Is it possible that contamination extends to the general environment?
- ✓ Is there any release apart from the point source of the relevant business operator, etc.?
  - If it is considered that there is,
    is the release related to the "manufacture, use, etc." under the Japanese Chemical Substances Control Act? Its extent of contribution?
- ✓ What is the detection status of environmental monitoring data in the general environment?

Etc.

[6] Information required for reassessment

Information required for re-assessment is assumed to be the one related to the exposure assessment and the one related to the hazard assessment.
Regarding uncertainty factors extracted from uncertainty analyses in the exposure assessment, organize such types of information as the following: information required for reducing uncertainty, the location information of release sources to grasp the nationwide distribution, and information for confirming use purposes and industrial classifications of release sources. In so doing, write down the levels of effects such information as the above has on assessment results, the order of information to be obtained and its priority level through taking into account various cases; for example, where subsequent information is not required upon acquisition of certain information[1].
In the hazard assessment, organize hazard information that is essentially desired to be obtained in cases, for example, where the product of uncertainty factors is very large testing data, where testing data of the administration route related to the main exposure route via the environment is not obtained, and where the reliability of testing data is limited.

[1] Where opinions of a council are sought before the instructions on hazard investigation or designation of Class II Specified Chemical Substances, there is an assumption that information that can legally be obtained has already been obtained and reassessed in order to use it to reduce uncertainty. Therefore, the details of the recommendation indicated at this stage are those still left nevertheless. The loading of resources to reduce such uncertainty is supposed to be determined according to individual cases (see "III. 7.3 (2) [1] Uncertainty Factors Included in Assessment Results").

8. Risk Assessment III (Primary)

In this stage, implement the risk assessment with newly gathered hazard information and exposure information in addition to the information used in Assessment II. The targets of the assessment are those substances on which reports on substance handling and results of additional monitoring have been obtained. In the hazard assessment of Assessment III, derive hazard assessment values in the same manner as in Assessment II. In the exposure assessment, make improvements and refinements through, for example, reviewing emission factors and exposure scenarios on the basis of reports on substance handling and results of additional monitoring.

From this, the purpose of Assessment III is to determine the necessity for giving the instructions on hazard investigation. Further, in accord with results of Assessment III, determine whether it is necessary to rescind the designation of Priority Assessment Chemical Substances, etc. However, if long-term toxicity information under the Japanese Chemical Substances Control Act has been obtained, determine the designation of Class II Specified Chemical Substances without going through the instructions on hazard investigation or the Risk Assessment (Secondary).

9. Risk Assessment (Secondary)

In this stage, implement the risk assessment on those substances, as targets, regarding which knowledge of long-term toxicity is obtained.

In the hazard assessment of Risk Assessment (Secondary), derive hazard assessment values by using hazard information with regard to long-term toxicity reported by business operators on the basis of the instructions on hazard investigation. For the exposure assessment, the same methods as those used in Assessment III are employed. However, if new information is available, make improvements and refinements through, for example, reviewing emission factors and exposure scenarios on the basis of the information.

From this, the purpose of Risk Assessment (Secondary) is to designate substances as Class II Specified Chemical Substances. Further, in accord with results of Assessment III, determine a rescission of designation of Priority Assessment Chemical Substances.