

# Basic Concepts of the Risk Assessment of Priority Assessment Chemical Substances under the Japanese Chemical Substances Control Act (Draft)

## 1. Background

On the basis of the international goal agreed 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 come fully 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 material organizes the basic concepts of the risk assessment implemented on Priority Assessment Chemical Substances.

## 2. Objectives of 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 damaging human health or the population and/or growth of flora and fauna in the human living environment, due to environmental pollution 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 flora and fauna 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 at 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 promptly as possible on substances in order of priority, given that it takes considerable time to implement long-term toxicity tests etc. based on the instructions on hazard investigation.

From the advancement of the risk assessment by the government at the same time as the collection of information from business operators on chemical hazards and substance handling, a further development is expected in voluntary chemical management by business operators.

\* 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.

### 3. Methods for risk assessment

#### (1) Basic premises of risk assessment

##### [1] Scope of risk assessment

In principle, the risk assessment under the Japanese Chemical Substances Control Act is conducted with the scope of the control under the Act taken into consideration. Regarding the scope of chemical substances subject to the Act, the control subjects of 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 under the Act, special attention should be paid to the following points in conducting risk assessment: Use for food etc. under the Food Sanitation Act, use for agricultural chemicals under the Agricultural Chemicals Regulation Law, and use for drugs etc. under the Pharmaceutical Affairs Law are excluded from the scope.

##### [2] Targets of risk assessment (human beings and the ecosystem)

Basically, implement risk assessment on each of the Priority Assessment Chemical Substances, on those target substances classified as having “High” priority in the screening assessment, and those target substances which are classified as having “Medium” priority in the screening assessment and required to be designated as Priority Assessment Chemical Substances (human health or the ecosystem). Accordingly, there are the following three types of Priority Assessment Chemical Substances. However, assessment targets may vary depending on hazard information obtained after the designation of 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 ecosystem is implemented
- The Priority Assessment Chemical Substances on which the risk assessment in relation to both human health and the ecosystem is implemented

### [3] Unit of substances for risk assessment

In principle, the substance unit for risk assessment is the unit used in designating the relevant substance as a Priority Assessment Chemical Substance. However, substances should be grouped as the occasion arises on the basis of information obtained in the processes of the risk assessment.

## (2) Concepts of risk assessment

### [1] Precautionary approach and transparent, science-based risk assessment

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

#### a. 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 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 disclosed. Further, if business operators etc. offer information to reduce the uncertainty, its reliability needs to be confirmed before use of the information is considered.

## b. 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 risk assessment, it is stipulated in the Japanese Chemical Substances Control Act that a council among the Three Ministries 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 copyrights taken into consideration. Hazard information collected by the government is also disclosed with careful consideration of copyrights, after the government has completed examination of the information.

Moreover, the methods for risk assessment need to be established on the basis of scientific grounds and movements abroad, and to be disclosed as technical guidance for securing transparency.

## [2] Stepwise procedures of risk assessment

Aiming to advance risk assessment promptly and thereby 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 hazard investigations etc. and collecting 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 risk assessment are basically divided into two parts from the aspect of hazard information: "Risk Assessment (Primary)" in which data on long-term toxicity have not been obtained; and "Risk Assessment (Secondary)" in which such data has 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 using notified information, such as manufacturing/import quantities only; "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.

### [3] Concepts of hazard assessment

Basically, the hazard information used for classifying substances into hazard classes in the screening assessment and subsequent hazard information are used for the hazard assessment. In principle, the same uncertainty factors as those used in the screening assessment are used for deriving hazard assessment values or PNECs. In so doing, examine, as required, hazard information of those substances that have not undergone individual expert determinations in the screening assessment. Further, where new hazard information is obtained, use available information for risk assessment as such information has become available, in accordance with the data reliability criteria stipulated by the government.

### [4] Concepts of exposure assessment

Although 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 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, 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 amounts to a Class II Specified Chemical Substance, make a decision on the basis of a comprehensive consideration with other detailed information taken into account.

### [5] Concepts of risk assessment

With the view of one of the requirements of Class II Specified Chemical Substances, “concern over risk in a considerably wide area,” results of risk assessment are basically shown in terms of the nationwide distribution of 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 risk assessment on each of release sources.

### (3) Procedures for risk assessment

In light of (1) and (2), risk assessment is implemented according the following procedures (see Material 2-3).

#### [1] Risk assessment (Primary) Assessment I

In this stage, implement risk assessment on all Priority Assessment Chemical Substances as assessment targets, basically with the use of notified information (manufacturing and import quantities, use, etc.) under paragraph (1) of Article 9 of the Japanese Chemical Substances Control Act and hazard information used in the screening assessment.

The hazard assessment of Assessment I generally involves 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 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 a relevant risk concern (the number of locations of risk concern) and the nationwide total area of effect regions of risk concern (the effect area of risk concern) in the case of human health. In the case of ecological effects, results show the number of locations posing a risk concern as an indicator.

On this basis, the purpose of Assessment I is to set priorities on those Priority Assessment Chemical Substances which proceed to the 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 of a Priority Assessment Chemical Substance whose nationwide total of the manufacturing/importing quantities is 10 tons or less, and in the case of a Priority Assessment Chemical Substance whose nationwide estimated released quantity is one ton or less, generally such substances do not proceed to Assessment II; its manufacturing/import quantities to be notified in the subsequent years are to be monitored.

#### [2] Request for reports on hazard information

If necessary, the Three Ministers shall require, under paragraph (1) of Article 10 of the Japanese Chemical Substances Control, business operators to report on hazard information regarding those Priority Assessment Chemical Substances which have been assigned high priority in Assessment I. When business operators obtain new hazard information, they are obliged, under paragraph (1) of Article 41 of the Japanese Chemical Substances Control Act, to report the information to the Three Ministers, and under paragraph (3) of the same Article, to endeavor to report to the Three Ministers on existing hazard information they have already

been in possession of.

### [3] Risk assessment (Primary) Assessment II

In this stage, implement risk assessment on those Priority Assessment Chemical Substances in order of priority defined in Assessment I so as to determine whether to designate them as Class II Specified Chemical Substances. Further, implement risk assessment on those Priority Assessment Chemical Substances which are given low priority in Assessment I, 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 system of the Japanese Chemical Substances Control Act, and environmental monitoring data (for substances to which monitoring was previously performed).

In the hazard assessment of Assessment II, derive hazard assessment values for which each endpoint is examined. In exposure assessment, estimate environmental concentrations and intakes in the same manner as in Assessment I, refine them as much as possible on the basis of accessible information such as PRTR data and environmental monitoring data, and add, as necessary, exposure scenarios according to use etc.

Assess risk through comparing results of the hazard assessment with refined results of the exposure assessment, clarify as much as possible the geographical distribution of regions of risk concern and the substance use and life-cycle stages relevant to release sources, and specify uncertainty factors involved in the relevant exposure through the processes above.

Accordingly, the purposes of Assessment II are to specify substance handling statuses which those business operators under [4] are required to report on, and regions for which additional monitoring should be implemented. Further, risk assessment II is basically 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. are determined without going through one or some of [4] to [7].

#### [4] Request for reports on substance handling, additional monitoring, etc.

On the basis of Assessment II, where necessary, the Three Ministers and the minister with jurisdiction over the business concerned shall require, under Article 42 of the Japanese Chemical Substances Control Act, business operators handling substances to report on their handling statuses. Furthermore, additional monitoring is to be implemented at the Ministry of the Environment.

Even where such operators are not subject to the request for a substance handling report, any voluntary reports on substance handling from business operators are to be considered in the risk assessment.

#### [5] Risk Assessment (Primary) Assessment III

In this stage, implement risk assessment on those target substances regarding which handling reports and additional monitoring results have been obtained in [4], with the use of newly gathered hazard information and exposure information obtained from [4], in addition to the information used in the Assessment II.

In the hazard assessment of Assessment III, derive hazard assessment values in the same manner as in the Assessment II. In the exposure assessment, make improvements and refinement through, for example, reviewing release factors and exposure scenarios on the basis of reports on substance handling and results of additional monitoring.

Hence, the purpose of Assessment III is to give the instruction on hazard investigation. Further, in accord with results of Assessment III, determine whether it is necessary to rescind designation of Priority Assessment Chemical Substances. However, if long-term toxicity information under the Japanese Chemical Substances Control Act has already been obtained, make a determination on designation of Class II Specified Chemical Substances without going through [6] or [7].

#### [6] Instructions on hazard investigation etc.

On the basis of results of Assessment III, where necessary, the Three Ministers shall give, under paragraph (2) of Article 10 of the Japanese Chemical Substances Control Act, the instructions on hazard investigation.

Moreover, as voluntary activities of business operators are expected to be reinforced by the instructions on hazard investigation, make further requests for substance handling reports and implement additional monitoring according to [4], where necessary.



#### [7] Risk Assessment (Secondary)

In this stage, implement risk assessment on those target substances for which knowledge of long-term toxicity is obtained through [6].

In the hazard assessment of the Assessment (secondary), derive hazard assessment values by using hazard information obtained in [6] with regard to long-term toxicity. For the exposure assessment, the same methods as those used in Assessment III are basically employed. However, where new information has been obtained, make improvements and refinement through, for example reviewing release factors and exposure scenarios, on the basis of the new information.

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

#### 4. Current criteria for risk assessment

On the basis of the purpose of the 2020 Goal, which is "to use transparent science-based risk assessment procedures," it is desirable that the most specific criteria possible are indicated for determining to take control measures such as designation of Class II Specified Chemical Substances and rescission of designation of Priority Assessment Chemical Substances.

However, given that it is difficult to indicate conclusive criteria as of this moment before the start of the risk assessment, the following is the criteria for risk assessment which are considered to be appropriate criteria at the moment, with reference to the provisions of the Japanese Chemical Substances Control Act and the past management of the Act.

Hereafter, the criteria are to be reviewed as needed with the latest scientific knowledge found in the processes of the risk assessment, while the risk assessment is set forward. Further, actual decisions are to be based on the criteria and expert opinions and to be made flexibly in light of individual cases.

##### (1) Designation of Class II Specified Chemical Substances

Pursuant to paragraph (3) in Article 2 of the Japanese Chemical Substances Control Act, the Three Ministers shall designate substances as Class II Specified Chemical Substances where as a result of risk assessment, the following two exposure conditions are applicable and also where there is a risk to human beings or flora and fauna in the human living environment: the hazard condition of long-term toxicity on human beings or flora and fauna in the human living environment; and the presence or a firm estimate of a considerable residual amount in a considerably wide area of the region concerned.

Where it is determined that more than a certain number of regions of risk concern (\*) exists, or there is a risk concern extending over more than a certain size of area, as a result of the risk assessment, this situation constitutes designation of the relevant substance as a Class II Specified Chemical Substance.

Furthermore, where the quantity of manufacture or import of the relevant substance, or the ratio of a substance use with a high emission factor, tends to increase and is firmly predicted to lead to the aforementioned situation within about one to two years, this case constitutes designation of the relevant substance as a Class II Specified Chemical Substance.

The actual values for "more than a certain number" and "more than a certain size" are to be further examined in the future on the basis of the future status of risk assessment.

\* Basically, a "concern for risk" is considered to exist, when the  $HQ \geq 1$  in relation to effects on human health, and when the  $PEC/PNEC$  quotient  $\geq 1$  in relation to effects on the ecosystem.

## (2) Instructions on hazard investigations

If hazard information on long-term toxicity cannot be obtained, extrapolate results of the toxicity screening (in relation to effects on human health) or results of the hazard assessment on acute toxicity (in relation to effects on the ecosystem) to the long-term toxicity value, and implement the risk assessment to make a determination in the same manner as the determination with regard to the designation of Class II Specified Chemical Substances in (1).

## (3) Rescission of Priority Assessment Chemical Substances

Where it is found, from the results of the risk assessment, that there is "no risk of damage attributable to environmental pollution either on human health or on the population and/or growth of flora and fauna in the human living environment" in accordance with Article 11 of the Japanese Chemical Substances Control Act, the Three Ministers shall rescind the relevant substance's designation as a Priority Assessment Chemical Substance.

The specific criteria for this determination are to be considered in the future on the basis of the future status of the risk assessment etc.

However, where taking account of the consistency with the special measure in the examination of Low Production Volume Chemicals, the nationwide total of the manufacturing or import quantity is 10 tons or less for the past three years, or where taking account of the consistency with the special measure regarding the notification of Newly Registered Chemical Substances in Low Quantity, the estimated released quantity is one ton or less, the case is to be determined to constitute a rescission of the designation of the relevant substance as a Priority Assessment Chemical Substance.

Furthermore, where Priority Assessment Chemical Substances are confirmed to be equivalent to polymers of low concern, to those substances which are judged as "White" in the Polymer Flow Scheme, or to those substances which do not require notification, the situation constitutes a rescission of the designation of the relevant substance as a Priority Assessment Chemical Substance.

Even after rescission of designation of a Priority Assessment Chemical Substance, the notification of the manufacturing/import quantity of the substance is required as a General Chemical Substance. Further, its re-designation as a Priority Assessment Chemical Substance remains possible depending on results of the screening assessment. In this screening assessment, a determination is to be made on the basis of results from the risk assessment in addition to evaluations using the priority matrix.

## 5. Other

### (1) Consideration on the utilization of QSAR and category approach with regard to hazards

When introducing QSAR and category approach regarding hazards, it is necessary to promptly consider in what situation of the operation of risk assessment QSAR and category approach are utilizable according to the steps below. Trial runs are aimed to be conducted at the same time as the implementation, for the part of the assessment for which QSAR and category approach are deemed to be utilizable.

1. Consider in what situations during risk assessment QSAR and category approach are utilizable. In so doing, [1] do not underestimate hazards and [2] consider QSAR and category approach with the view to contributing to efficient implementation of the risk assessment.
2. For candidate QSAR models for human health and the ecosystem, organize the estimation precision (the accuracy rate and statistical data) for which validation has been conducted in relation to testing data with the use of Newly Registered Chemical Substances and existing inspections.
3. Take account of the estimation precision in 2. in the situations for the utilization considered in 1., and utilize usable QSAR models and categories. Possible actual applications are, for example, "Substitute for the case where hazard information is not obtainable" and "Setting an order of assessment implementation." In the latter application example, apply QSAR and category approach actively as the estimation precision does not necessarily require to be high.
4. Build up the track record of the application, and pay attention to international movements and domestic and overseas developments of QSAR models to broaden the scope of application .

The Three Ministries are to develop their considerations on 1. to 4. separately in light of opinions from toxicity experts, and to organize specific use methods in turn in councils among the Three Ministries.

With regard to physico-chemical properties, degradability and accumulative properties, utilize QSAR to advance risk assessment.

## (2) Notification to relevant ministers

In the process of risk assessment under the Japanese Chemical Substances Control Act, a considerable volume of information on substances is considered to be accumulated. As a result, where a more effective regulation is determined to be implemented under an Act other than the regulation under the Japanese Chemical Substances Control Act, or where no regulation is scheduled under the Japanese Chemical Substances Control Act, the minister with jurisdiction over the enforcement of the other Act is to be notified of the relevant information under Article 47 of the Japanese Chemical Substances Control Act in order to promote an appropriate regulation for the purpose of achieving the 2020 Goal.

The knowledge of hazards etc. of individual substances obtained in the risk assessment under the Japanese Chemical Substances Control Act is to be shared among the Ministries responsible for other applicable Acts so as to promote the use of such knowledge.

## (3) Revisions

Review the basic concepts and technical guidance of risk assessment on the basis of the latest scientific knowledge, international movements and results of risk assessment on Priority Assessment Chemical Substances.