IV Evaluation of research results

Data contain errors which are derived from accidental, random, non-systematic and systematic characteristics of analytical methods. Environmental monitoring of chemical substances tends to investigate extremely low concentrations of analytes in various matrices with determination ranges at the ppb (parts per billion) level or less, so it is necessary to pay attention to the accuracy of the obtained values and the degree of precision by which they are obtained. Such details are described in the chapter about quality control. This chapter describes methods for the generalisation of the reality of pollution or symptoms, behaviour analysis, and risk assessment. The results which are dealt in this chapter are described on the assumption of data collected with guaranteed accuracy.

- Generalisation means processes which clarify the distribution of chemical substances, the character of any change, and find out the cause and regulation of determination of the concentration in the environment. This data treatment may make values which have no quality control problems unexplainable in reality, and this connects to processes of refining data.
- Behaviour analysis is the process used to understand data based on behavioural mechanisms of chemical substances in the environment. Here concepts such as material balance (incoming and outgoing) are also considered, mutual inspection between data and mathematical modelling is conducted, then matured mathematical modelling makes accurate prediction of future pollution possible.
- Risk assessment is the process used to clarify the reality of the kinds and sizes of risk of pollution caused by a chemical substance. Outlines of risk assessment to human health reported by NAS/NRC (National Academy of Sciences / National Research Council) have nearly reached international agreement, and they have been being used for indexing and the introduction of an index. The results gained from environmental monitoring are of particular use in policy decisions and implementation designed to decrease pollution, i.e. to develop risk management.

IV.1 Generalisation of research results

The results of environmental monitoring for chemical substances confirm if the target compounds exist in the environment, and at the same time check how much difference there is in

concentrations between survey points and regions, and the difference in concentration between multiple compounds. Environmental monitoring tries to understand in which media concentrations of target compounds will be large, e.g., water, air, living things, sediment, or soil. Furthermore, environmental monitoring aims to understand the essential features of concentration changes, and search for the causes by making temporal (time dependent) data plots, checking physiochemical characters such as water solubility and vapour pressure, and the relationship between data and environmental features such as wind direction, salt constituent, organic matters, etc. Such discussions are best dealt with by performing basic statistical procedures on the data, and visualising the data using graphs, bar charts and scatter plots, and also describing the reality of pollution by more convincing methods based on mathematical reasoning, comparison and correlation analysis etc.

Today, it has become easier to deal with complex data by the recent increase in personal computer memories and faster operating systems, the development and diffusion of superior spreadsheet, graphical, and statistics software. It is important to remember that data should be collated in an appropriate manner using software such as a spreadsheet. This not only facilitates data analysis but also accessing information on samples and field data such as sampling dates, water temperature, air temperature, climate, appearance, laboratory data such as the existence of interference, etc. and information on compounds such as molecular weight, boiling point, vapour pressure, water solubility etc..

IV.1.1 Feature of research results of environmental monitoring

Essentially, the results of environmental monitoring research is a collection of data. The data has a range. Data are usually shown as concentrations, but they are shown as “ND”, rather than given a numeric value, if they are less than detection limits of the analytical methods. Thus the data becomes a mixture of numeric concentration values and NDs. If the form of the distribution of each group of data cannot be assumed beforehand, it is possible to use normal distributions, logarithm normal distributions, or irregular distributions. However, data points termed outliers, “outside” and “far out” values, which are far apart from the general pattern of data distribution may have significant meanings. In addition, the number of data points is sometimes limited because of time and financial restrictions. Therefore, it is possible that data evaluation may change dramatically depending on the methods of data treatment, so it is often necessary to pay attention to data input to statistical methods and discard of huge amount of data.

IV.1.2 Basic statistical management

It is important to be able to grasp the shape of the distribution of data within a group in order to prevent the over- or under- estimation of the research results. Features of the data group have to be expressed by determining appropriate representative values and the degree of spread based on the shape.

IV.1.2.1 Making histogram

Divide the range between the biggest and smallest data points in a group into several even sections, and list how many data points are found in each section in a frequency table. Then make histogram in which the values defining the sections appear on the x-axis as the bases of the bars, and express the frequency of data appearance in each section as length of bars as **Figure IV-1-1**. In general sections are around 5 - 15. If the shape of histogram is symmetric and highest towards the centre, such as in the left figure of **Figure IV-1-1**, it is considered to have a normal distribution (or Gaussian distribution). If the shape of the histogram is symmetric when the values defining the sections of the bases of the bars in the histogram are logarithm transformed, the histogram has a log-normal distribution. Not only a single peak but multiple peaks may appear depending on the results of environmental modelling.

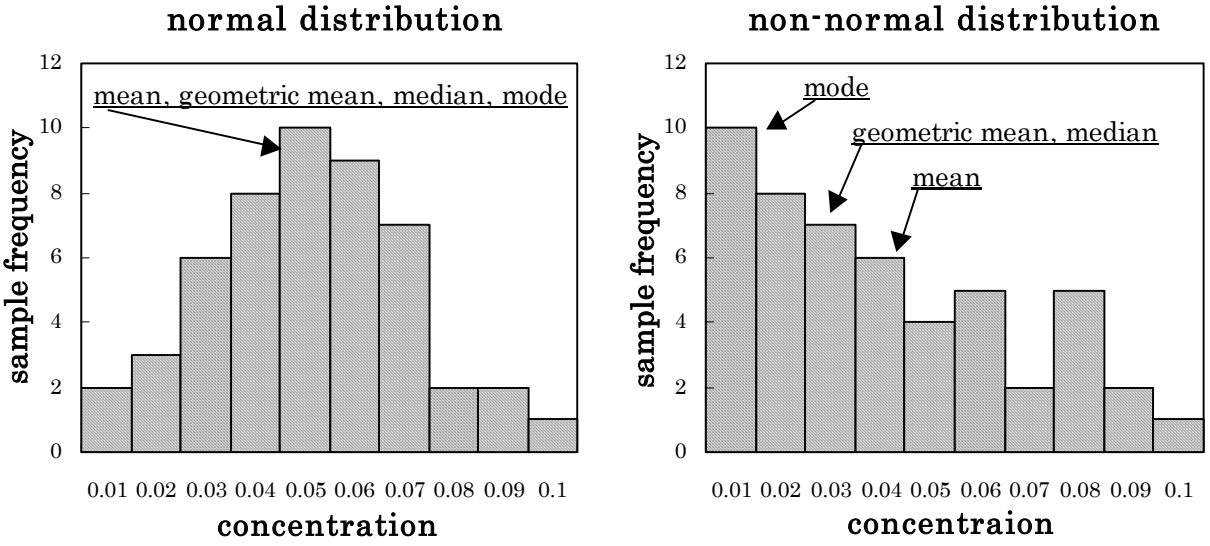


Figure IV-1-1 Example of histogram

IV.1.2.2 Representative values and the degree of spread

Chemical concentration data is often summarised as an average value in conjunction with the detection frequency. In addition, representative values and the degree of spread are used to compare the results obtained at different times, from different areas, compounds or samples. In this case, the kinds of representative values and the degree of spread are issues.

A. Detection frequency

Detection frequency is the percentage of the total number of analysed samples in which a target compound or compounds has been detected. This value is obtained by dividing the number of samples in which an analyte is detected by the number of analysed samples, shown as a percentage. This value becomes an index of the size and range of existence of the target compound in the environment, but doesn't show the range or level of concentration, because whether a chemical is detected or not depends on the determination limit of the analytical method.

B. Representative values

There are some basic, statistical quantities treated as representative values such as mean, geometric mean, median, mode, and trim mean, and these features are listed in **Table IV-1-1**.

Table IV-1-1 Kinds and features of representative values

representative value	definition	feature
Mean	values given by the sum of the data divided by the number of samples $X=(\Sigma x)/n$	values in which the difference to each data point has the smallest value.
Geometric mean	values given by the anti-logarithm of the mean of the logarithm of the data $X=10^{[(S\log)x/n]}$	used when data distribution is tailing towards the right
Median	values at the centre of the distribution of the data when the data is sorted in the size order. When sample numbers are even, take average of n/2 and (n/2)+1.	equal to mean when have symmetric distribution
Mode	the most frequent value or most frequent section	equal to mean when have symmetric distribution
Trim mean	remove values from the largest and smallest sides of the distribution at the same rate and take the average. removal rate is generally about 5 %.	underestimates or overestimates can be avoided

The values of the arithmetic mean, the geometric mean, the median and the mode (generally the 5 % trim mean is used. The 50 % trim mean equals to the median.) are almost the same if data are normally distributed. However, if the histogram is tailing towards the right, these values become "mode < median < mean", and tailing towards the left, "mode > median > mean". This illustrates the dependency of values on the shape of the histogram.

The mean is the value (of concentration, for instance) which shows the typical situation when symmetric normal distribution is assumed, and cannot be used where there is non-normal distribution. The geometric mean is applied to logarithm normal distribution. The median is different from these mean values, and it is a value which doesn't assume any distribution shape of data in the group, i.e. non-parametric value. Therefore it is convenient when distribution is irregular and there are a lot of "ND". The mode can be used as the median, but note that the mode is different depending on the width of section. The trim mean has characteristics of parametric and non-parametric methods, effects of outliers and far out values are small as well as the median because both ends of the distribution has been chopped off.

Occasionally, one must give "ND" a numeric value when calculating representative values, and it becomes a problem whether "ND" should be treated as zero or a certain number. Reality appears to be most appropriately reflected by considering the background level of target compounds in the environment, and to assign a numeric value to "ND" of around 1/2 - 1/10 of the background level when the background level is close to the analytical detection limits, and zero to 1/100 if it can be assumed there scarcely exists any target analyte in the environment at all.

C. The degree of spread

The degree of spread in a data set is the measure of the dispersion of the data, and is directly expressed as the maximum, the minimum, and the range between the maximum and minimum. The most common way to express the degree of spread is to use standard deviations. The standard deviation is the average difference in value of each data point from the mean value. The related basic statistical quantity, the variance, is square of the standard deviation. The coefficient of variation, or the relative standard deviation, is the standard deviation divided by the mean, and is a kind of relative error, and used in order to compare groups whose unit or size are different.

In non-parametric methods, the degree of dispersion is described by the interquartile range which replace the standard deviation, and are usually used with the median. When 'n' pieces of data are sorted in the size order, the data of n/4 and 3n/4 are quartile. The bigger number is called

the upper quartile, and smaller number is the lower quartile. The difference between the upper and lower quartile is the interquartile range, and the half is called the interquartile deviation.

D. Data representation as the box-and-whisker plot

One way to represent data, including outliers (out side and far out values), is the box-whisker plot. This is also called the box graph, and looks like **Figure IV-1-2**. The hinge spread is equivalent to the interquartile deviation. Determine the median and the quartile in the same way as the degree of spread in parametric methods. The upper quartile is called the upper hinge or the 75 % value, and the lower quartile is called the lower hinge or the 25 % value. The gap between the upper and the lower hinges is expressed as a box, divided the box by a line which is median. Stretch whiskers from the box to the data closest to the inner fence which is [the upper hinge]-1.5x[the hinge spread] and [the lower hinge]-1.5x[the hinge spread]. Also, the outer fence is [the upper hinge]-3x[the hinge spread] and [the lower hinge]-3x[the hinge spread]. Data which is outside of the inner fence and inside of the outer fence are termed the 'out side values.' Data which is outside of the outer fence are the 'far out values.'

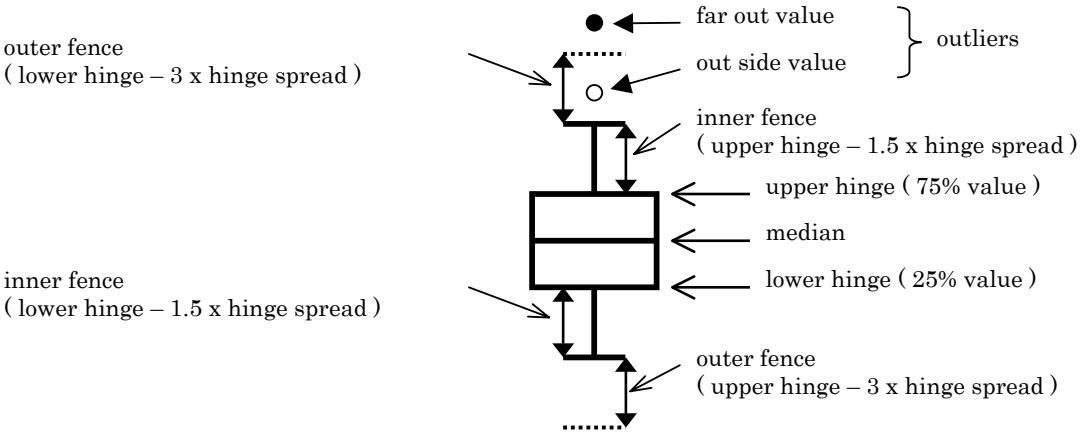


Figure IV-1-2 Box-whisker plot

IV.1.3 Visualisation of the research results

It is very useful to express research results as figures and graphs. This is done to gain an intuitive understanding of the contents. There may be lots of things to show, but in the case of environmental monitoring, observations on the distribution, chronology and correlation of results are indispensable.

IV.1.3.1 Distribution chart

Draw a distribution chart in order to understand how concentrations vary depending on the sampling point or region. Indicate data as circles or bars at the sampling point in the map. Connect sampling points (samples) which have the same concentration by curved lines (equal concentration lines).

IV.1.3.2 Chronological graph

There is the chronological graph in order to understand chronological, seasonal or yearly tendency of concentration level to change. The basic chronological graph is shown as the distribution chart which is plotted time, month or year on the x axis and concentration on the y axis.

IV.1.3.3 Correlation graph

This is mainly used when searching for the causes of concentration change. Plot data on the xy coordinates to determine the relationship of two parameters which may causes the change in concentration, e.g. two substance concentrations, or a single substance concentration and another parameter. These parameters are considerable: production and use quantity, distance from the expected pollution source, physiochemical characters such as water solubility, octanol partition coefficient, Henry's constant etc., environmental information such as temperature, water temperature, wind direction, salt amount, amount of organic matters etc., and furthermore, as useful parameters, biological measurement data such as body weight, body length, age, fat containing amount etc. Draw a line or curve through the data points, an obtain an appropriate regression formula. In general, the best method to gain the regressive of a straight line is to minimise the sum of the squares of the residuals. There amy be important cases where the regressive is a function other than that of a straight line. In this case, the function has to be explained to be applied.

IV.1.4 Significance test

There are many instances of comparison and data sorting, such as concentration levels and regional comparison of distribution situation etc., during evaluation of the research results of environmental monitoring. If there are no duplicate significant errors in representative values

and the degree of spread, it is easy to discover the size relationships. However, there is a problem when the representative values are different and the degree of spread has doubled. In such cases, statistical methods are needed to make data comparison convincing. Therefore, go back to the distribution of data within a group again. The shape of histogram can be categorised like **Figure IV-1-3**.

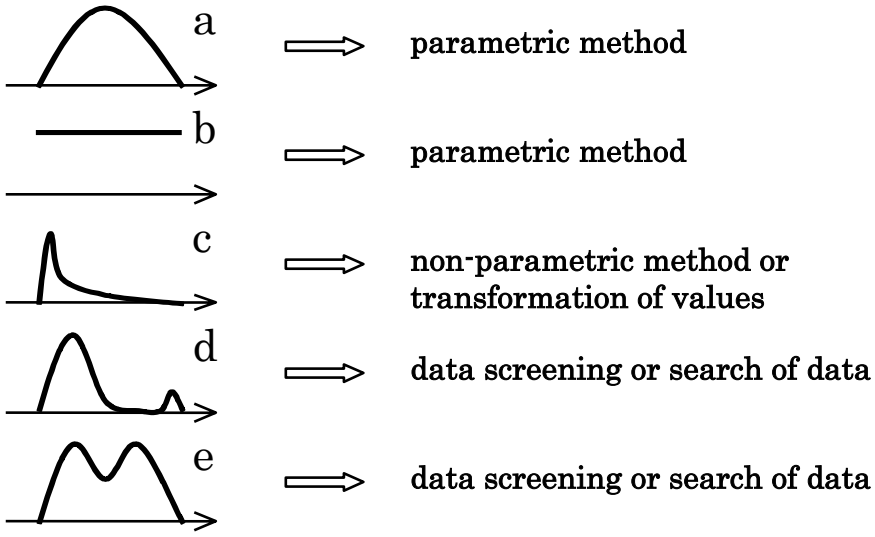


Figure IV-1-3 Classification of histogram and the application for statistical analysis

IV.1.4.1 Test of comparison of data group

The parametric method may be applied if the data has a normal distribution or there is no difference in the distribution like a) and b) in **Figure IV-1-3**. Although c) is for non-parametric methods, their normality has to be checked after changing data to its logarithm values. The geometric mean comes into existence when symmetry is gained. In cases where outliers or multiple peaks exist, like d) and e), it is necessary to re-check data , including repeating the research, and investigate the causes such as conditions of sampling, pollution sources etc.

Therefore, the flow chart of comparison test of two data groups is shown in **Figure IV-1-4**. **Figure IV-1-5** shows comparison test of more than three data groups.

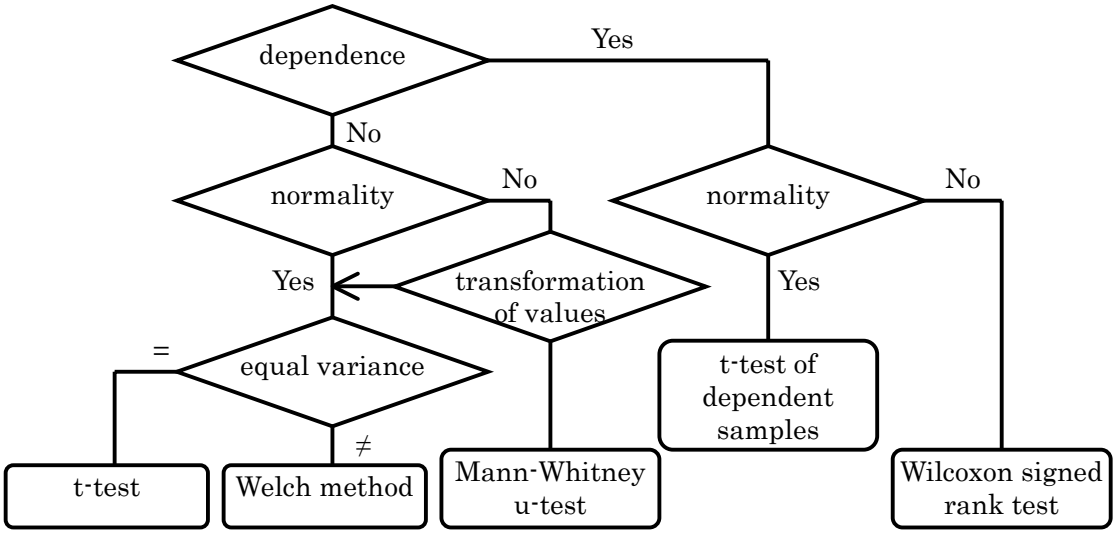


Figure IV-1-4 Flow chart for comparing two groups of data

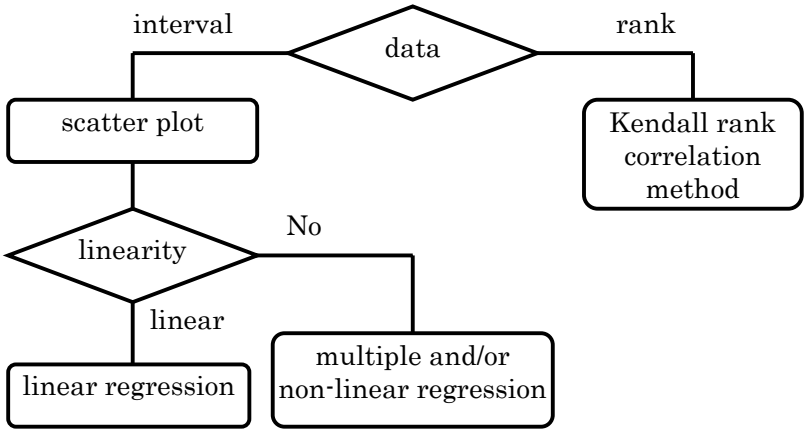


Figure IV-1-5 Flow chart for comparing multiple groups of data

IV.1.4.2 Correlation and regression

Regression formula which is obtained by correlation analysis and correlation coefficients also must be tested for significance (**Figure IV-1-6**).

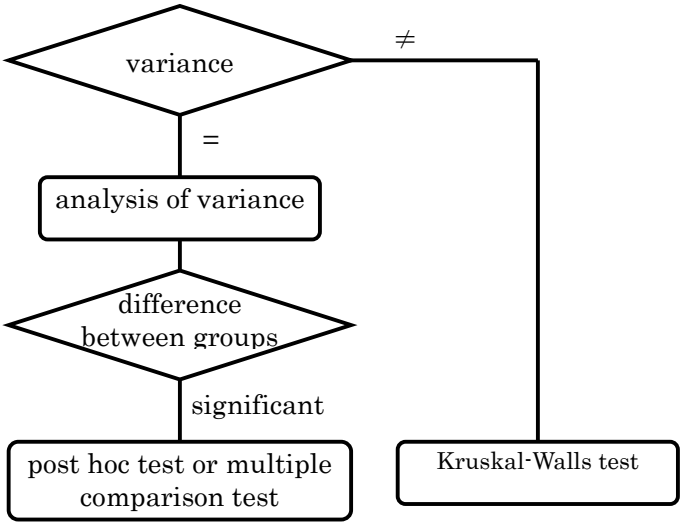


Figure IV-1-6 Flow chart of correlation analysis

IV.2 Behaviour analysis

Chemical substances which enter the environment move and diffuse between the atmosphere, water, soil and sediment, degrading gradually, and finally distribute themselves in the lowest energy levels (see **Figure IV-2-1)**. This movement is determined by reciprocal actions between such factors as human action, materials and the environment, and has a certain regularity. For example, chemicals in water are partitioned e.g. adsorbed onto suspended particles, accumulated by fish or other aquatic organisms, depending on their solubility in water and octanol-water partition coefficients, and the ratios of the concentrations in the various matrices become relatively stable values. Conversely, for water and biological samples taken at the same time, if the results show extremely different concentration ratios, it may be that the data from the water or the biological samples are wrong. In addition, the concentration of a chemical in a matrix can be estimated even if data has not been obtained for such samples or media, if the regularity is obtained. In this section, we show factors related to effects which are estimated to be happening

in the environment. Mentioned under the heading of generalised correlation analysis, it makes it possible to evaluate research results more accurately by examining data which have been obtained from environmental monitoring by referring each effect to the behaviour of chemicals.

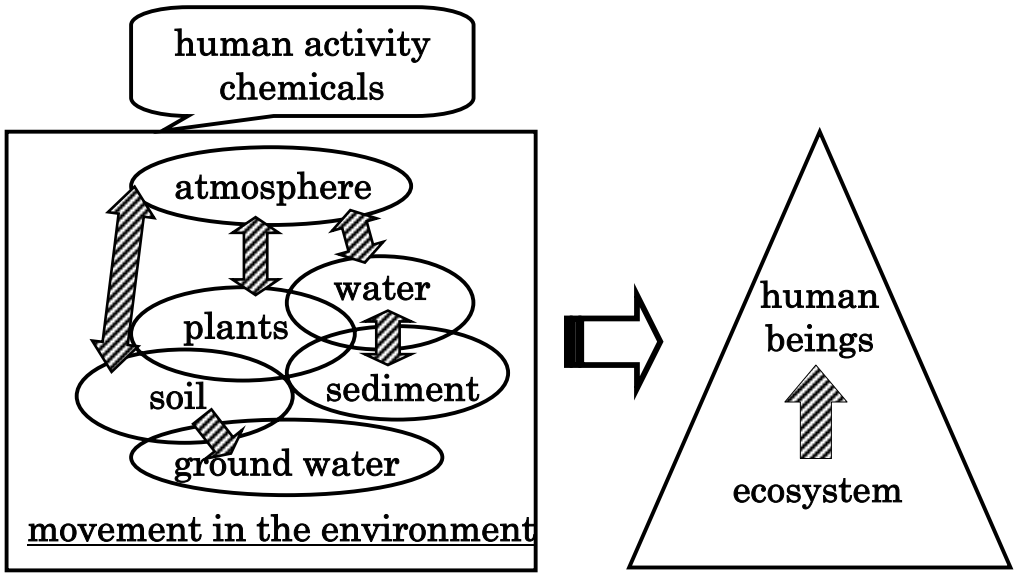


Figure IV-2-1 Concept of chemical movement in the environment and risk flow

IV.2.1 Information needed for behaviour analysis

Though it is very difficult to collect all pertinent information, parameters about chemical behaviour are listed. In the section covering risk assessment, useful resources are listed e.g. data bases and documents etc.

IV.2.1.1 Human action or social factors

Basically this information becomes useful for estimating, directly or indirectly, the flow or amount input into the environment.

- production and use amount
- use and purpose
- situation of use and abolition : distinction of open + closed system, raw materials + products, burning + reclamation etc.

IV.2.1.2 Substance factors

These are physical, chemical, and biological characteristics peculiar to chemical substances, can be used to estimate a compound's movement, partition, and degradation character in the environment.

- ultraviolet-visible absorption spectrum : determination of wavelengths which may be affect photodegradation
- melting point / melting point range : a factor which is affected by the condition of the chemical
- boiling point / boiling point range : a factor which is affected by the condition of the chemical
- vapour pressure (curve) : probability of phase change to air, estimation of evaporation rate, and atmospheric concentration
- water solubility : amount of elution to aqueous phase, concentration in water, estimation of adhesion and adsorption
- soil adsorption / desorption : exudation and evaporation from soil, adsorption to soil, the amount partition to the soil, and estimation of speed of travel in soil
- octanol-water partition coefficient : indicates the potential of a chemical to accumulate into living things
- Henry's law constant : estimation of evaporation from water surface to the atmosphere
- photodegradation character : possibility of decomposition by light in the atmosphere, soil and water surface
- hydrolysis character : possibility of decomposition in water
- microorganism decomposition (biodegradation) character : possibility of decomposition by microorganisms in soil or water
- bioconcentration coefficient : degree of bioaccumulation

IV.2.1.3 Environmental factors

These are the characteristics of the environmental conditions and the samples at sampling, and become information showing sample characteristics

A. Water quality

- climatic condition
- water temperature
- water flow (flow speed)
- water depth

- sampling point (surface - bottom)
- general water quality (pH, salt, suspension particles, organic pollution)
- location of discharge source, discharge condition etc.

B. Atmospheric air quality

- climatic condition (temperature, wind direction, wind speed, humidity, rainfall, weather forecast etc.)
- floating suspended particles
- location of discharge source, discharge condition etc.

C. Soil and sediment

- climatic condition
- temperature
- general character (pH, water content, organic matters content, oxidation-reduction potential etc.)
- soil character
- particle size distribution
- existence of living things
- use history, etc.

D. Living things

- biospecies
- biomeasurement data (body length, body weight, etc.)
- eating habits and feeding activities
- habitat, character of activity
- nutrition stages
- life and death and health conditions
- life expectancy, age
- sex
- growth stages
- reproduction conditions
- lipid amount and composition of tissues and organs
- location of discharge source, discharge condition etc.

IV.2.2 Mechanisms of chemical movement in the environment

Figure IV-2-2 shows the movement of chemicals in and between each environmental phase. Bearing these processes in mind, behavioural analysis is used to understand how each of the factors mentioned in the previous section are related, and to find out the regularity between single or multiple factors and data. In addition, it makes it possible to estimate the environmental fate and concentration of chemicals beforehand by using models of generalised behaviours.

It must be understood that chemicals discharged into the environment after production, use, and abolition follow processes of movement, transport and decomposition peculiar to the substance , which are influenced by various environmental conditions, and shift to a distribution equilibrium in which the more stable forms of the material form. As the result, the concentration and distribution of chemicals are determined, but the media making up the environment, such as the atmosphere and water, is always changing, and many processes related to chemical movement and disappearance in the environment exist. Furthermore, the environmental behaviour of chemicals changes in time and space because these process depend on various environmental conditions.

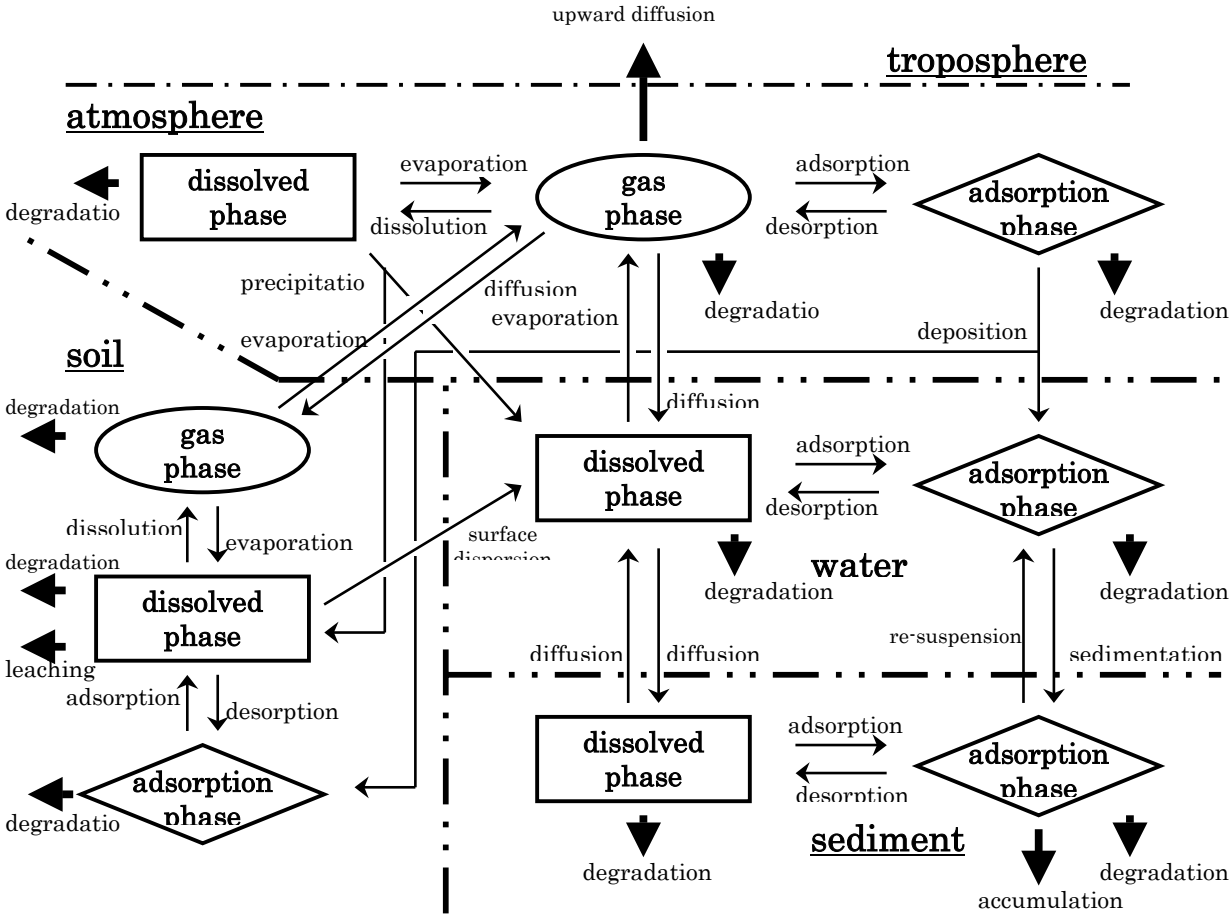


Figure IV-2-2 Movement and fate of chemicals in the environment

IV.2.3 Process of transport, movement and decomposition in the environment

There are many process which affect chemical behaviour in the environment. The degree of effect on chemical behaviour of each process in the environment depends on the character of the chemicals, the medium into which the bulk of the material is discharged, and environmental conditions. Therefore, it is important to understand environmental chemical behavioural processes and the conditions which control the speed of chemical movement.

IV.2.3.1 Transport processes

Transport processes relates to chemical movement in the environmental media, mainly advection and dispersion in the atmosphere, water, and soil. Function of these advection and dispersion in these media are basically the same.

A. Advection

Advection plays an important role in the environment. Chemicals in the gas phase and dissolved phase in the media are transported by advection. The speed of transport of chemicals by advection is given by the following formula.

$$N = G \times C$$

where G is the flow rate of environmental media (m^3/h), and C is the chemical concentration in the media (mol/m^3). Measurement of flow rate can be used for the calculation of the advection speed of a river or lake. Atmospheric flow rate calculated from wind speed etc. is used for air. Advection of substances in the gas phase and dissolved phase in soil is controlled by the vertical flow of air and water. Generally, the flow of air and water in soil is very small, but contributes to chemical transport which is controlled by the air and water compartments in the soil.

B. Turbulent flow dispersion

Turbulent flow dispersion plays an important role in the dilution of chemicals in the environment, and it is more important in the environment than molecular diffusion. Dispersion speed depends on the relative size of a turbulent flow swirl and plume which contains many chemicals. If the plume passes a place of advection, the speed also contributes (on what?). Dispersion speed is affected by wind speed and temperature etc., and is of the order 10 - 1,000 m^2/s. Turbulent flow dispersion is defined as the amount of chemical advection (J) in proportion to

concentration slope (C).

$$J = D \times \Delta C$$

or

$$dc/dt = d(Di \times dc / di) / di$$

where i is defined as the x, y, or z planes, and Di is the dispersion coefficient of these directions (m^2/s). The formula above can be integrated exactly, but in this case a simplified formula is used. Although there is a basic formula for turbulent flow dispersion in the atmosphere, it is impossible to predict chemical dispersion in the atmosphere accurately. In practice, distribution of chemical concentration by turbulent flow dispersion in the environment is shown by a Gaussian normal distribution using a dispersion width (standard deviation) which is a function of distance from the source and climatic conditions.

In surface water, the speed of movement of substances (Ri) by turbulent flow dispersion is shown by the following formula.

$$Ri = \Delta C \times Di \times Ai / i$$

where, i is defined as the x, y, or z planes, Di is the dispersion coefficient of these directions (m^2/s), A is exchange sectional area, l is the distance, and ΔC is the concentration slope of the x, y, and z directions. Dispersion happens in underground water, but is regarded to be a very small contribution to chemical transport.

C. Leaching

Leaching is a chemical transfer process which accompanies water flow in a vertical direction in the soil. The amount and direction of movement of underground water in soil is determined by the soil osmosis coefficient. The smaller the diameter of soil particles are, the smaller the coefficient is, and the smaller the permeation character. Therefore, when a clay layer which contains small diameter particles stays in the ground, ponding on the surface can be observed. Generally, the leaching coefficient (Kpe) is given by following formula:

$$Kpe = E \times ADS^2 \times g \times \rho / \mu$$

where E is a coefficient related to the air capacity of the soil, ADS is the average particle diameter of the soil, g is the acceleration due to gravity, and ρ and μ are the density and viscosity

of water, respectively.

IV.2.3.2 Transfer processes

Transfer processes between environmental media are important processes which control the distribution of a chemical in the environment. For example, if a system consists of surface water and sediment, evaporation, adsorption, sedimentation of suspended particles, re-suspension, sedimentation rate etc. are the main transfer processes. The main problem with transfer processes is how obtain representative velocity data for these processes. Estimation of such data for still water and slow flowing rivers is relatively straightforward, but river mouth and coastal zone processes are often difficult.

A. Evaporation from water

The thermodynamic equilibrium of chemicals between the surface of the water and the atmosphere is well understood, but the dynamics of volatilisation from inside the bulk of the water to the atmosphere has not yet been clarified. When chemicals in the air and water are in an equilibrium state, the chemical concentration in water (C_{wat}) can be related to the concentration of the same chemical in the air (C_{air}) by Henry's law.

$$C_{air} = H \times C_{wat}$$

where, H is a dimensionless value known as Henry's law constant. This Henry's law constant can be measured, and estimated fairly accurately from a chemical's vapour pressure and solubility in water. The speed of evaporation of a substance from inside a body of water depends on not only the nature of a substance, but also on the turbulent flow of water and the atmosphere. Various theories have been suggested, but the double thin layer theory of Whitman is most often used. This theory assumes two thin layers border both sides of the atmosphere and the water, and chemicals pass through the border layers by molecular diffusion. Therefore, the speed of evaporation depends on the nature of molecular diffusion in water and the atmosphere, and thickness of the border layers. In addition, the speed of evaporation can be determined by comparison with oxygen which is well investigated about evaporation from inside of water. The relations between flow speed or wind speed and evaporation speed.

B. Evaporation from soil

Evaporation from soil to the atmosphere is more complicated than evaporation from inside water, and it is dependent on chemical partitioning between air, water and particles in soil, and the

speed of diffusion from soil air to the atmosphere. When the water content of soil covers all of the soil particle surface, partitioning between air and particles in soil can be expressed as the two processes of partitioning between air and water, and between water and particles.

$$C_{air} = H \times C_{wat}$$

and

$$C_{sol} = Kd \times C_{wat}$$

where, C_{sol} is the concentration in particles, and Kd is the adsorption constant between particles and water. From these formulae, the equilibrium partition coefficient between air and particles in the soil can be expressed as the ratio of H and Kd..

$$C_{air} = H/Kd \times C_{sol}$$

Because there is no convenient formula to describe the speed chemical partitioning in soil, assuming partial equilibrium in the soil phase evaporation from soil is expressed by considering that chemicals partitioned into the soil air move into the atmosphere diffusively. The speed of evaporation from soil is largely affected by wind speed, soil temperature and gap ratio?.

C. Adsorption to soil and sediment

The adsorption of nonpolar chemicals to soil or sediment particles is regarded as partitioning to the organic materials in the particles, and the partition equilibrium is expressed using the adsorption constant, Kd, defined above. An adsorption constant (Koc) which takes into account the soil organic carbon ratio (%oc, %) can be used as a standard value, and can be applied to soil whose organic carbon content is known. Koc and Kd can be related by the following formula.

$$Koc = Kd \times 100/\%oc$$

Koc of chemicals such as pesticides have been reported, but those of most of chemicals are unknown. Therefore, for most models, Koc has to be estimated from the octanol-water partition coefficient and water solubility of the compounds of interest. Koc should not be applied to soil with low organic carbon content or high clay content because in such cases adsorption to inorganic matter becomes important.

The details of the dynamics of movement between water and particles have not yet been elucidated. One can consider adsorption dynamics being proportional to the concentration difference between solution and adsorbent, but this does not coincide with experimental data which generally shows rapid initial intake, followed by equilibrium.

The partitioning behaviour of ionic compounds, including materials such as metals and phenols, is not as clear as that of nonpolar compounds. Salt concentrations and pH are considered to affect the partitioning of ionic compounds between water and particles, but a complete partition theory doesn't yet exist. When the environmental fate of ionic compounds is explained by modelling, it is necessary to pay attention to these limits.

D. Bioconcentration

Bioconcentration is evaluated by comparing how high chemical concentrations are in living things with the concentration of chemical in the environmental media which surrounds the living things. Bioconcentration occurs by chemical uptake directly from media and/or via the food chain. Bioconcentration rate (BCF) is defined by the following formula:

$$BCF = C_{biota} / C_{wat}$$

where, C_{biota} is the concentration of chemical in living things. For nonionic compounds, BCF can be estimated from the compounds' octanol-water partition coefficients. However, the BCF of compounds which are easily metabolised and/or biologically decomposed, and high molecular compounds (>700 g/mol) can be overestimated. In general, the degree of bioconcentration is controlled by a compound's physiochemical character and its stability at the low nutrient stage, and an organisms' food habit, life span, degradation and metabolism ability, and physiological conditions.

E. Transfer accompanied with precipitation

Gaseous chemicals in the atmosphere are dissolved in rain drops and fall to earth with precipitation. The air-liquid equilibrium or transfer efficiency of such processes for nonpolar compounds can be estimated from Henry's law. Raoult's law can be applied for water soluble compounds. The half life of removal from the atmosphere by precipitation ($R_{1/2}$) can be determined from a chemical's concentration in rain drops obtained from chemical's vapour pressure (p, torr) and water solubility (x) expressed as mole fractions, and concentration ratio in the atmosphere (a).

$$R_{1/2} = 2310 / a$$

Generally, the smaller Henry's law constant is, the more compounds are dissolved in rain drops, and the more easily the compound moves from the atmosphere to the ground.

F. Transfer associated with deposition of particles in the atmosphere

Gaseous chemicals in the atmosphere are adsorbed to particles and move to earth when particles are deposited on the ground. Generally, deposition of particles larger than 1 μm is basically the result of gravity, and the speed of fall can be determined from Stokes law. The average life span of particles in the troposphere is said to be about 7 days. When the adsorption rate of atmospheric chemicals to atmospheric particles is ϕ, the life span of the chemicals in the atmosphere becomes 7/ϕ.Unfortunately, the adsorption rate ϕ is almost never measured, but only approximately estimated by the following formula:

$$\phi = \chi \times \theta / (\chi \times \theta + p)$$

where, θ is surface area of particles (cm^2) per 1 cm^3 of atmosphere, and χ is a coefficient (cm x torr) which is determined from the following equation:

$$\chi = 5.05\ (D/M)^{2/3}$$

where, D and M are density (g/cm^3) and molecular weight (g/mol), respectively. The smaller the vapour pressure of a compound is, the more the compound is adsorbed to particles and moves from the atmosphere to the ground. Generally, any compound with a vapour pressure less than 10^{-7} torr is easily adsorbed to particles and is deposited.

G. Dry deposition

Gaseous chemicals in the atmosphere also move from the atmosphere to other media by being adsorbed by soil, surface water, or terrestrial plants after coming into contact with them. Such a process is called dry deposition. Dry deposition occurs because adsorption onto, for instance, the earth's surface causes a layer of low concentration of compounds, and thereafter a concentration gradient is formed which causes further molecules of the compound to flow vertically downwards. The speed of this dry deposition is dependent on characteristics such as the ground surface, climatic conditions, and the nature of the chemicals, and varies quite considerably

H. Transfer associated with settling of suspended particles

Settling of suspended particles in water is an important process involving chemical transfer towards sediments for chemicals which are readily adsorbed by the particles. The settling speed of suspended particles can be estimated by using Stoke's law, in the same manner as deposition of

particles from the atmosphere. Partitioning of chemicals in water towards suspended particles is dependent on the chemical adsorption constant K_{oc} and the organic carbon content ratio of the particles.

I. Resuspension

Resuspension of sediment particles is an important transfer process that re-introduces chemicals into the water column. Particles attached to the sediment a the sediment-boundary layer resuspend if they obtain sufficient energy from water flow or biological disturbance. However, it is extremely difficult to estimate the speed of resuspension. If the accumulation speed is known, resuspension can be estimated form the difference between the rates of sedimentation and accumulation.

J. Burial

The surface of sediment is mixed by biological disturbances. The thickness of this region of sediment mixing is dependent on the degree of biological activity. Burial is the difference between the speed of sedimentation of suspended particles and the speed of resuspension. If sedimentation speed is bigger than resuspension, sediment particles are accumulated and the sediment layer becomes deep enough to avoid biological disturbance. Chemicals adsorbed by particles in this sediment layer do not readily re-enter the water column. Burial speed is slow, usually of the order of mm per year. The method which is the most commonly used to estimate burial speed is an ageing measurement.

K. Transfer diffusion between water and sediment

Diffusive transfers of chemicals can not only be by such processes as dry deposition from the atmosphere to soil, but also in the reverse direction i.e. evaporation from soil to the atmosphere, or between sediment pore water and the water column. The speed of diffusive transfer from sediment to water is dependent on nature of the surface of the sediment, the rate of water flow, the character of chemicals, etc. On the other hand, diffusion from sediment to water is dependent on partitioning between sediment pore water and chemicals within particles, and the speed of diffusion from pore water to the water column.

L. Surface runoff

Chemicals partitioned in soil pore water and adsorbed on particles are moved by rain into aquatic environments such as rivers. Surface runoff is a transfer process associated with flow from soil to the water system. Generally, in soil chemicals are partitioned between the soil air, soil water, and soil particles. The water content of the soil increases after rain fall. Water is held in soil up to the soil's saturation point, but if this limit is exceeded, water starts to flow on the surface of soil towards lower geographical points. at saturation, chemicals adsorbed to soil particles dissolve into water, and flow into rivers etc. with the water. It is not easy to estimate the fraction of water in soil, but usually such parameters are obtained by equating rain fall with an amount of water that equals the sum of the amount of water evaporating from the soil, surface runoff, water intake by plants, and ground water leaching.

M. Erosion

Erosion is a transfer process that generally has water assisting the movement of soil particles into rivers etc. Such particulate transfer is more common for small diameter clay particles than silts and sands. The degree of chemical transfer by erosion is dependent on intensity of rain fall and diameter of soil particles etc.

IV.2.3.3 Degradation Processes

Degradation is an important means by which chemical resides in the environment are controlled.

A. Biodegradation

Biodegradation of chemicals is a metabolic process, and is important in many situations. In general, if biodegradation of chemicals is confirmed in the laboratory, it will also occur in the wider environment. However, many of the dynamics of such processes are unknown, and biodegradation rate constants determined in the laboratory are not always applicable in the field. Many fate and exposure model users arbitrarily assign a value to the rate constant or use the following formula:

$$rb = \mu_{max} \times C \times X/(kb + C)$$

where, rb is the rate constant, μ_{max} is the highest growth speed, X is microorganism

concentration, kb is the concentration of substrate which causes a growth of half the highest growth speed, and C is chemical concentration. Under normal environmental conditions, the concentration C is very small, and the above formula can be simplified to:

$$rb = kb' \times C$$

In aqueous, soil, and sediment phases, biodegradation is the most important process. The rate of biodegradation is related to the structure of chemicals, the density of microorganisms, their carbon content, temperature, and also humidity in soil. It is difficult to estimate biodegradation rates accurately, but it is generally assumed in models to be a pseudo linear reaction. When, under special conditions such as in the deep soil or sediment, or surface water, oxygen content is extremely high anaerobic biodegradation is important, and growing microorganisms utilise nitric acid and sulphuric acid as an oxygen source. However, the dynamics of this process is little understood.

B. Hydrolysis

Hydrolysis is defined as the fission of organic molecules by reaction with water, for instance in the following formula:

$$RX + H_2O = ROH + HX$$

Typical functional groups which can be hydrolysed are halogenated alkyl groups, amides, amines, carbamates, epoxides, and esters. Hydrolysis can be separated into three different processes i.e. neutral, acidic, and alkaline reactions. Humic substances, metal ions, Brønsted acids, bases, etc. catalyse hydrolysis. In soils and sediments, hydrolysis is affected by adsorption onto particle surfaces. Because hydrolysis is pH dependent, data on the dynamics of hydrolysis at different pH is required for making models. In general, the pH of river water is in the range 4.5 - 8.5, sea water, 7.5 - 8.5, and soil, 4.5 - 6.5, but sometimes the pH can be as low as 3, or as high as 10 depending on the places.

C. Photodegradation

Photodegradation is categorised into direct and indirect reactions. Direct photodegradation occurs when chemicals absorb sunlight (>295 nm) directly, and react in the resulting excited states. Direct photodegradation reactions occur in many places in the environment, and with a range of the speeds. Indirect photodegradation occurs when chemicals react with unstable compounds, such as hydroxyl radicals, which have themselves been produced by the energy of sunlight.

In the troposphere, indirect photodegradation by reaction with hydroxyl radicals is the most important reaction. The reactivity of many chemicals with hydroxyl radical has been measured. For compounds for which there is no data, reactivity can be estimated by Atkinson's method. For some groups of compounds, reaction with ozone and nitric acid radicals is also important.

In water, direct photodegradation is important. Direct photodegradation is a result of compounds absorbing sunlight, and becomes an important process for compounds which have high quantum yields in water. Reaction rates depend on pH, chemical concentrations, dissolved oxygen, and especially transparency to light. Transparency to light is a function of water depth, concentration of suspended particles, and the colour of the water. Direct photodegradation rates in water are can be calculated using the following equation：

$$rp = kp \times C$$

where, rp is the photodegradation rate, kp is a pseudo linear reaction kinetic constant, and C is the chemical concentration in water.

For compounds which react with oxygen, such as compounds containing sulphur, indirect photodegradation is the more important process. High reactivity compounds in water are produced by photochemical reactions with dissolved humin. Oxygen, hydrated electrons, peroxides, and hydroxyl radicals are the main reactants. Hydroxyl radicals are also produced by light e.g. by irradiation of nitrate or nitrite solutions in the presence of metal catalysts.

In soil photodegradation is not regarded as important degradation process because it happens only at the soil surface.

IV.2.4 Behaviour evaluation model

As previously mentioned, the behaviour of chemical substances in the environment is associated with their transport, transfer and degradation mechanisms. In addition, the velocity or equilibrium status of each process is enormously affected by not only the chemical characteristics of substances, but also by the environment or climatic conditions. Models evaluate such behaviour by inserting environmental discharge data into chemical material (or mass) balance equations. By solving these equations, it is possible to obtain chemical concentration and distribution data, or residue information which are changeable in time and space. Data from single or multiple models of environmental discharges, behaviour / path ways in the environment, and exposure routes are used in early stage exposure analysis for the evaluation of potential chemical distribution in the environment. Such analysis is useful when estimating exposure concentrations under different environmental conditions, for the preparation of monitoring plans, or analysis of research results.

Furthermore, the importance of models is increasing, with several models of chemical behaviour and exposure in the environment having been developed and used with toxicity data to evaluate risk to humans and the harmfulness to other organisms in the environment. The problem is how accurately data related to each behaviour process, such as equilibrium constants or velocity constants, can be obtained. Even if the model is theoretically superior, results obtained using inaccurate data are meaningless.

Several of the models of environmental behaviour which have been already developed differ in their treatment (description) of the environment, and the processes which are considered. For instance, the methods of estimating equilibrium constants and velocity constants are sometimes different, because they rely heavily on the purposes of the models or developers' ideas. These differences ultimately appear as differences in the data output for each model.

Currently, there are many proposed models for the evaluation of chemical behaviour in the environment. When these models are classified by their target environmental media, they can be divided into two categories - single and multi-media models. The former aims to evaluate chemical behaviour in a single medium such as atmosphere, water or soil, while the latter evaluate chemical behaviour in more complex, multiple media (or compartment) environments. When applying these models, one must consider not only the media, but also sources of the target chemicals and the size of the environment. From this point of view, multimedia models often look at a wide range of behaviours on national or global scales. Therefore, sources of chemical discharges into the environment are naturally generalised, and the results themselves become more generalised. On the other hand, single media models aim for a more detailed evaluation of chemical behaviour in a localised environment, such as places close to discharge sources. Environmental modelling of chemicals basically seeks to discover whether targeted compounds exist in the environment at the national scale. Therefore, this chapter will focus on multimedia models, and, adopting the classification, criteria and composition of multimedia models, the MNSEM (Multi-phase Non-steady state Equilibrium Model) which was developed in Japan is introduced.

IV.2.4.1 Basic composition of models

Models generally consist of three programs - data input, calculation and output.

Input data comprises chemical characteristics, environmental conditions, and environmental discharge data. The chemical characteristics required for many models are physiochemical characters such as molecular weight, water solubility, vapour pressure, octanol-water partition coefficient, etc., and the degradation kinetic constants of biodegradation, hydrolysis, oxidation and photodegradation, etc. Physiochemical characteristics can be obtained from experiments, the

literature, or structure and activity relationships, but sometimes reliable data is difficult to find.

The environmental conditions required are such things as the capacity of media, height / depth, temperature, organic carbon content in particles, wind speed, rain fall amount etc. Chemical behaviour in the environment becomes complex if these environmental conditions change significantly in time and/or space. Many models use data which are averaged across time and space, but it is necessary to understand that these averaging may render uncertain important environmental chemical behavioural characteristics. In general, models which target local areas requires more environmental data.

The environmental discharge data required includes the rate of chemical discharge speed into the wider environment or each local medium. However, data covering chemical discharge into different environmental media are often inaccurate, estimated values. In many cases, discharge is not constant but discrete and often discontinued, so practical, averaged values are used.

Models calculate the distribution, chemical persistence, and chemical concentration in the environment by solving material balance formulae using input data. Therefore, models are advantage able to evaluate behaviour at various points by putting in different environmental conditions data.

Material balance formulae in the models are generally expressed using the following differential equation:

$$Dmi/dt = Qi - \Sigma jAi,j - \Sigma krecMi + \Sigma jIj,i$$

where, the left hand side of the equation is the time dependent change in chemical quantity (Mi) in a medium (I), and on the right hand side of the equation, Qi is the amount of chemical discharge into the medium, ΣjAi,j is the amount of chemical transferred into the adjacent media, ΣkrecMi is the amount of chemical disappearance by degradation in the medium, and ΣjI,j is the amount of in-flow for the adjacent media.

In general, equations which are used for the calculation of material balances are sometimes essentially empirically derived. Some of them have been widely verified by experiments, and are very reliable. On the other hand, there are some equations which are based on little data, and which are not reliable.

Data output from environmental behaviour models is in the form of displayed calculation results, or output to a printer or to floppy disks. Calculation results are shown in the form of figures or numbers. Output figures are simple and useful as a summary of calculation results. However, numeric output cannot be omitted if one wishes to discuss and utilise the model's calculation results in detail.

IV.2.4.2 Multimedia models

A. Construction

Multimedia models look at the behaviour of chemicals on a large scale. Chemical distribution and concentration in each environmental medium are evaluated from the mass balance of chemicals in the total, multi-media environment. An environment with useful, generalised character is used to make chemical behaviour in the environment understood. They are called "evaluative environments", "generic environments", or "unit worlds". Generally, evaluations of chemical behaviour in the environment is possible by just using chemical characteristic data. Multimedia environments in many models consist of the following four or six compartments – the atmosphere, water, soil, and sediment, with perhaps also suspended substances and aquatic organisms. There are other models which add further compartments, such as atmospheric particles and terrestrial organisms to the six compartments. Chemical substances are often assumed to be evenly distributed in each compartment that makes up the multi-media environment.

B. Classification and criteria

Generally multimedia models can be classified from the type of environmental processes they consider into a) mass-conserving / non-mass-conserving, b) equilibrium / non-equilibrium, and c) stationary state / non-stationary state.

a) **mass-conserving / non-mass-conserving models**

Chemicals discharged into the environment generally degrade by biological and chemical processes, and are then transported out of the system. However, mass-conserving models evaluate chemical distribution in the environment according to transport process between media without considering chemical decomposition. Therefore, chemical mass will be conserved in the environment which this model targets. These kinds of models are used at the very beginning of environmental chemical behaviour evaluation, such as when evaluating the behaviour of a chemical whose decomposition rates are unknown. On the other hand, non-mass-conserving models consider each transport, transfer, and degradation process, and chemical mass isn't conserved in the environment.

b) **equilibrium / non-equilibrium models**

Equilibrium models are models which describe transport between media as using equilibrium constants such as Henry's rule, hypothesising that thermodynamic equilibrium distribution is

achieved. On the other hand, non-equilibrium models describe transport between media, such as evaporation from water to atmosphere, or deposition from atmosphere to water, as rate processes. These models don't hypothesise distribution equilibrium, since in reality, it is rare that chemical distribution between media reaches equilibrium.

c) **stationary state / non-stationary state models**

It has already been mentioned that material, or mass balance equations expressed by evaluation of chemical behaviour in the environment can be generally expressed using the differential equation :

$$dMi/dt = Qi - \Sigma jAi,j - \Sigma krecMi + SjIj,i$$

For many general industrial chemicals, discharge into the environment is continuous, and it may be considered that a stationary, or steady state is established. Therefore, it becomes easier to gain answers because material balance formulae become simultaneous equations of the following form :

$$Qi - \Sigma jAi,j - \Sigma krecMi + \Sigma jIj,i = 0$$

Non-stationary state type models evaluate chemical behaviour and concentration with time by solving differential equations. In other words, the difference between non-stationary and stationary state models is that whether differential equations are solved or not. The processes by which material balance equations are formulated is the same. In the multimedia models, at the time of model calculation some select stationary states, some non-stationary states.

Based on these criteria, actual multi-media models are further categorised into four levels : level I, II, III, and IV. Levels I - IV of the fugacity model, which is the most popular and basic multi-media models, are equivalent to the following classifications:

Level I model categorisation may be applied to mass conserving, equilibrium and stationary state models. As mentioned above, chemical decomposition processes are not considered, and theoretical distribution of chemicals between compartments based on thermodynamic equilibrium calculated from equilibrium distribution coefficients and compartment capacities. Level I is useful for confirming which environmental media should be studied in more detail. For calculation, the following parameters are needed : chemical discharge amount into the environment, Henry's law constant, adsorption constant of soil and sediment, and bio-concentration factor. In the case of hydrophobic compounds, these distribution coefficients can be calculated from solubility and vapour pressure data.

Level II model categorisation may be applied to equilibrium and stationary state models that

are non-mass-conserving because they consider processes of transport and decomposition. The Level II model gives the same results for the environmental distribution of chemicals as Level I, because the Level II model is also an equilibrium type. Although the persistence of chemicals in the environment is evaluated, the estimates are suspected to be far from the reality. For calculation, decomposition ratio constants and discharge ratio data are needed, as well as the equilibrium constants needed for the Level I model.

Level III model categorisation may be applied to non-mass-conserving, non-equilibrium and stationary state models. Like the Level II model, Level III evaluates chemical distribution in the environment, concentration in each environmental media, and the persistence. However, transfer dynamics between compartments are also considered. For Level III non-equlibrium models, material balances between each compartment are needed. By solving these, level III models evaluate environmental behaviour much more accurately than level II models. For calculation, discharge rate data for each media are needed, as well as the same parameters required for level II. In addition, level III models require of data transfer rates between compartments, although many transfer processes are automatically estimated within the model.

Level IV model categorisation may be applied to non-mass conserving, non-equilibrium, and non-stationary state models. Level IV models can evaluate how long is needed for environmental purification after termination of chemical discharge into the environment, or how long is needed to reach stationary state in the case of continuous chemical discharge, or environmental behaviour when discharge is intermittent, eg pesticide use. The parameters required for the calculations are the same as level III model.

IV.2.4.3 Examples of multimedia models

It is difficult for users to choose which model to use from the many multimedia models available. To begin with, the reason for using the model has to be clarified. For example, when it is necessary to estimate chemical distribution in the environment, it is important to choose only Level I and II models, because less parameters are required, and the models are easy to use. However, if one must evaluate behaviour close to reality, it is important to choose Level III and IV because they have more parameters to be put in the models. Models classified into Level II should be used for general chemical behaviour in a fairly realistic environment.

In general, multimedia models are suitable for the evaluation of background concentrations and average concentrations of chemicals in environments located far from the discharge sources, and the evaluation of chemical behaviour in the wide range of environment. One must be careful with calculate results from calculations which deviate from these applications. The accuracy of the results from multimedia model relies on input parameters, especially environmental conditions

and ratio constants. Which parameter significantly affects chemical behaviour in the environment can be clarified by sensitivity analysis. As the result of sensitivity analysis, to check adequacy of the values is indispensable as for parameters which are expected to have big effects on chemical behaviour in the environment.

Here after, a few typical models will be outlined. They are all almost equivalent with respect to being based on experimental data, and because they are already developed and available, they are expected to be highly practical models. Thereafter, MNSEM is described. This model has been developed in Japan. It has an improved distinguishing feature which fits the environmental character of "generic environment" with the character of the region, and makes behaviour evaluation more accurate in the target region.

A. Fugacity models

Fugacity models are the most commonly used multimedia models. By using from Level I to IV models, one can distinguish between simple distribution equilibrium in the environment and the behaviour of easily degradable compounds in the stationery and non-stationery states. This model then becomes the basis of a number of other models. A Level III fugacity model is suitable for the stationery state evaluation of the behaviour of continuously discharged organic chemical, and the distribution, concentration, persistence, and main transfer routes of the chemicals. Level III models deal with four kinds of bulk compartment - air, water, soil and sediment. Each bulk compartment consists of sub-compartments of air, water and organic materials, and it is assumed that a distribution equilibrium is set up inside the compartment. By solving material balance equations which consider the amount of environmental discharge, diffusive or non-diffusive transfer, advection, and degradation process, the fugacity of each compartment is obtained. Thereafter, the concentration and amount of chemicals are determined from the fugacity. Necessary input data are environmental conditions, chemical / substance material, degradation rate, and discharge data.

B. Enpart (Environmental Partitioning Model)

Enpart is a fugacity model which was developed by US EPA for application to organic chemicals. It evaluates residue persistence, and the possibility of bioconcentration by comparing concentration ratio between environmental media. It is used as screening method for selection of chemicals which need detailed evaluation.

C. EEP (Environmental Exposure Potentials)

This model aims to evaluate the behaviour of new chemicals in the environment. This belongs to Level II of fugacity models, and is applied to compounds which are imported, or of which there is more than one ton per year produced in the EC countries. It evaluates distribution into environmental media and the possibility of chemical persistence, but doesn't evaluate environmental concentration. It considers only degradation by micro-organisms.

D. SIMPLESAL

This is a fugacity model which evaluates the concentrations of organic compounds and heavy metals in the stationary and non-stationary state. This has been developed in the Netherlands in order to regulate environmental discharge of existing and new organic compounds, and a screening method to conduct evaluation under various conditions. This model considers such processes as transport, transfer, and degradation in the atmosphere, water, suspended particles, aquatic living things, sediment, and soil.

E. GEOTOX

This model have been developed by US Department of Energy, and considers chemical distribution, degradation, diffusive and non-diffusive transfer processes in the atmosphere, living things, soil, surface water, and sediment. Soil is categorised into three layers : top soil, sub-soil, and under ground water. The calculated concentrations in each environmental media are correlated with inhalation rate, intake rate and absorption ratio to evaluate human body exposure. Chemical bio-concentration in terrestrial plants is given by the concentration in soil and plants / soil partition coefficient, and this is used for estimation of the amount of human body exposure. This model was developed using the environment of south east area of the United States. However, it can be applied to other areas by changing environmental conditions. In addition, this model can be applied not only when chemical discharge rate is constant, but also when the rate changes over time.

F. MNSEM

MNSEM is a model which has been developed in order to evaluate the environmental behaviour of organic chemicals in the stationary state in Japan. Chemical discharge rate is

estimated using annual production figures, usage data, and physicochemical characteristics. Based on this, the amount of human body exposure is evaluated from chemical partition, persistence, typical concentration in the Japanese environment, purification period when environmental chemical discharge stops, concentrations in various environmental media, inhalation rate, and intake rate. The environment consists of the following four media : the atmosphere, water, soil, and sediment, and each phase consists of air, water and particle compartments. Partition equilibrium is set up not between phases but between each compartment within phases, and expressed as equilibrium constants. Processes of transport, transfer, and degradation are expressed as rate constants. Precipitation, surface effusion, sedimentation of suspension particles, and soil leaching are considered. Hydroxy radical oxidation in the atmosphere, photodegradation, hydrolysis in water, and biodegradation in water system and soil are considered as degradation processes. This model will be described in detail later.

G. SMCM (Spatial Multimedia Compartment Model)

SMCM was developed by UCLA, and evaluates chemical behaviour in an environment which consists of the atmosphere, water, soil and sediment in the stationary and non-stationary states. This model is noted for its ability to evaluate vertical distribution of chemicals in soil and sediment, using equilibrium constants and rate constants in response to environmental temperature without assuming homogeneous media concentrations. Such treatment needs complex modelling calculations, but makes it possible to obtain more realistic evaluations. This model expresses chemical movement between media as mass movement coefficient and diffusion coefficient. Although these coefficients are calculated by models, necessary input parameters are almost the same as fugacity model Level III.

H. Toxscreen

Toxscreen was developed by US EPA, and evaluates the behaviour of chemicals which are released into the atmosphere, surface water, and soil, and the possibility of human exposure. Chemical behaviour in the atmosphere is evaluated using a Gaussian distribution diffusion model, and EXAMS, a water system environment model, and SESOIL, a soil model, are used to evaluate behaviour in aqueous systems and soil. Thus this model is combination of useful single-media models. The atmospheric diffusion model can be applied to all discharge sources, such as point source, linear source, or surface sources. Therefore, this model makes behaviour evaluation in small areas possible. However, a wide range of parameters necessary for the calculation.

IV.2.4.4 MNSEM2

The first version of the Multi-phase Non-Steady State Equilibrium Model (MNSEM) was released in 1987. After addition of some improvements, MNSEM145I(Version 1.4.5I) was confirmed as the model which can be used for the evaluation of the amount of indirect human exposure at the OECD Workshop on the Application of Simple Models for Environmental Exposure Assessment (Berlin, Germany) in 1992. MNSEM2 (Version 2.0) is the program which has supplanted the MS-DOS based MNSEM145I onto Windows, and has been further improved by adding new knowledge about material movement between environmental media, and calculated exposure doses which have been reported since 1993. The program of this model is available from database of the National Institute for Environmental Studies through w-chemdb@nies.go.jp.

MNSEM2 basically follows the concept of the former version (MNSEM145I). However, some of the default values and some of the formulae which are used for the calculation of material movement between environmental media and exposure doses were revised based on more recent research results.

A. Input parameters

Weather conditions and the environmental, chemical substances, and discharge feature which are needed for MNSEM2 will be described. The default values of these characteristics are not always suitable for every evaluation. It is recommended that users should wherever possible use values which are suitable for their own evaluation.

a) Weather conditions and the environment

Table IV-2-1 Weather conditions and environmental feature for calculation

Parameters	abbreviation	units	default values
Environmental area for evaluation	SUA	m^2	1×10^{10}
Temperature	TEMPK	°C	20
land area ratio	LLS	-	0.8
wind velocity	AFR	m/sec	3.2
Precipitation	TRF	mm/year	1500
Atmospheric altitude	DEPA	m	200
Concentration of aerosol	CAER	mg/m^3	0.03 [1)]
Density of aerosol	DENAER	kg/m^3	1500 [1)]
Diameter of aerosol	DAER	μm	10
OH radical concentration	OHC	$molecule/cm^3$	1×10^6 [2)]
depth of surface water	DEPW	m	10
Suspended particles	CWSS	mg/L	50
Aquatic organisms	CWB	mg/L	5
ratio of organic carbon content to amount of suspended particles	OCSS	-	0.06
rate constant of surface water advection rate	KWAD	1/day	0.1
sedimentation velocity of suspended particles	KSV	M/day	0.5
decay ratio of photodegradation in water	PAIW	-	0.1
surface water pH	PHW	-	7.0
aquatic microorganisms	AMWW	cell/L	1×10^5
depth of soil	DEPSO	m	0.20
air volume ratio in soil	SOAF	-	0.2 [3)]
water volume ratio in soil	SOWF	-	0.3 [3)]
organic carbon content ratio in soil particles	OCSOS	-	0.04
density of soil particles	DENSOS	kg/L	1.5
pH of water in soil	PHSO	-	7.0
evaporation ratio of water in soil	ETP	-	0.35
soil erosion rate	ERS	m/year	0.0002 [1)]
aquatic microorganisms in soil	AMSOW	cell/L	1×10^5
microorganisms in soil particles	AMSOS	cell/kg	1×10^8
depth of sediment	DEPSE	m	0.05
water volume ratio in sediment	POSE	-	0.75
organic carbon content ratio in sediment particles	OCSES	-	0.06
density of sediment particles	DENSES	kg/L	2.0
pH of sediment water	PHSE	-	7.0
aquatic microorganisms in sediment	AMSEW	cell/L	1×10^5
microorganisms in sediment	AMSES	cell/kg	1×10^8

b) Chemical compound parameters

Table IV-2-2 Chemical compound parameters for calculation

Parameters	abbreviation	units	default values
molecular weight	MW	g/mol	119.4
melting point	TEMPMP	°C	-25
water solubility	WS	mg/L	8000
vapour pressure	Pa	Pa	21332
log Kow	KOW	-	1.97
absorption constant of organic carbons	KOC	L/kg	280
fish bioconcentration factor	BCF	L/kg	15
reaction with atmospheric OH radical	KOH	cm^3/mole/sed	9.7×10^{-14}
photodegradation in water	KPHT	1/day	0
Hydrolysis	KHY	L/mole/dec	0
Biodegradation	KBIO	L/cell/day	0

Note : The default compound is chloroform, and chloroform's characteristics, equilibrium constants and velocity constants are set up.

c) Discharge parameters

Table IV-2-3 Discharge parameters for calculation

Parameters	abbreviation	units	default values
annual production	PM	ton/y	36000
use ratio (closed system utilisation)	FCU	-	0.88
Total Japanese production / evaluation area	EVAI	-	production amount in whole Japan
discharge coefficient (production, atmosphere)	EPRA	-	0.10
discharge coefficient (production, surface water)	EPRW	-	0.00
discharge coefficient (production, soil)	EPRS	-	0.00
discharge coefficient (closed system, atmosphere)	ECUA	-	0.20
discharge coefficient (closed system, surface water)	ECUW	-	0.00
discharge coefficient (closed system, soil)	ECUS	-	0.00
discharge coefficient (open system, atmosphere)	EOUA	-	0.95
discharge coefficient (open system, surface water)	EOUW	-	0.05
discharge coefficient (open system, soil)	EOUS	-	0
background concentration of inflow atmosphere	CBGA	mg/m^3	0.00
background concentration of inflow surface water	CBGW	mg/L	0.00

Note : Default values are those of chloroform.

d) Intake parameters

Data covering human intake parameters are necessary for the calculation. The National Diet Survey classifies vegetables as yellow-green vegetables (carrot, spinach, green pepper, tomato, etc.) and other vegetables (radish, onion, cabbage, cucumber, Chinese cabbage, salted leaf vegetables / radish pickles). However, the model parameters of leaf vegetables and root vegetables don't correspond to these. Therefore, the sum of 300 g of yellow-green vegetables and the other vegetables are assumed as leaf vegetables : root vegetables = 2 : 1 for default values.

Table IV-2-4 Intake parameters for calculation

Parameters	abbreviation	units	default values
body weight (human)	BW	Kg	60
air inhalation rate (human)	INTKA	m^3/day	20
bio-availability from inhalation	BIOAV	-	0.75 [6]
intake of drinking water (human)	INTKDW	L/day	2.0
purification ratio of drinking water source	PFW	-	0
intake of marine products (human)	INTKF	g/day	100 [5]
intake of leaf vegetables and fruits (human)	INTKLC	g/day	320 [5]
intake of root vegetables (human)	INTKRC	g/day	100 [5]
intake of meat products (human)	INTKME	g/day	80 [5]
intake of dairy products (human)	INTKMI	g/day	130 [5]
intake of soil (human, unintentional)	INTKS	g/day	0.05 [7]
air inhalation rate (livestock)	CTKINHL	m^3/day	122 [6]
pasture (dairy cattle, dry)	CTLGRASSL	kg/day	16 [8]
pasture (beef cattle, dry)	CTLGRASSN	kg/day	8 [8]
soil (livestock, unintentional, dry)	CTLSOIL	kg/day	0.41 [6]

B. Detailed description of the models

a) Material movement in the atmosphere

The atmosphere consists of the following compartments : air, rain water, and aerosol. MNSEM treats chemicals distributed into the compartments of air, rain water, and aerosol in the atmospheric phase as chemicals in the gas phase, dissolved phase, and adsorbed phase, respectively.

(1) Mass distribution ratio

The amount (mass) of material in the gas phase (MMA) and the mass of adsorbed material (MAP) are related by the following formula :

$$MAAP = MAA + MAP$$
$$MAA = MAAP \cdot (1 - FP)$$
$$MAP = MAAP \cdot FP$$

where MAAP is the sum of the gaseous and adsorbed phase material, FP is the ratio of the mass of adsorbed material to the sum of the gas phase and adsorbed phase material calculated by the following Junge formula :

$$FP = CJ \cdot SP / (VPL + CJ \cdot SP)$$

where CJ is constant of the Junge expression, SP is surface area of the aerosol, VPL is vapour pressure of the liquid phase (the vapour pressure of supercool liquid phase is used when the melting point of the chemical is higher than environmental temperature.

The ratio (RRT) of total chemical concentration in the gas and adsorbed phase (CAAP) and chemical concentration in rain water (CAW) is determined by the following formula :

$$RRT = CAW / CAAP = (1 - FP) / HENRY + 2 \times 10^5 \cdot FP$$

where, HENRY is Henry's law constant, and 2×10^5 is the trap ratio of aerosol.

When the total chemical volume of the air and aerosol compartment is given as VOLAAP, and the volume of rain water compartment, VOLAAP, then the amount of chemical in the rain water compartment is determined by the following equation :

$$MAW = RRT \cdot MAAP \cdot VOLAW / VOLAAP$$

The total chemical mass in the atmosphere (MSA) is determined by following formula :

$$MSA = MAA + MAP + MAW = (1 + RRT \cdot VOLAW / VOLAAP) \cdot MAAP$$

From the above formula, the chemical mass distribution ratio in air, aerosol, and rain water in the atmospheric phase (FAA, FAP, FAW respectively) can be obtained in the following manner :

$$FAA = (1 - FP) / (1 + RRT \cdot VOLAW / VOLAAP)$$
$$FAP = FP / (1 + RRT \cdot VOLAW / VOLAAP)$$
$$FAW = RRT \cdot VOLAW / VOLAAP / (1 + RRT \cdot VOLAW / VOLAAP)$$

The volume of the rain water compartment is determined by :

$$VOLAW = TRF \cdot SUA \cdot RTRF / 1000 / 365$$

where TRF is annual precipitation (mm/year), SUA is total contact area of the surface water and soil compartment, and RTRF is the standing time of the rain water in the atmosphere. A rain fall rate of 6.5 m/s is adopted, and corresponds to typical rain drop diameter of 1000 μm. Therefore, the first kinetic constant of rain fall (KARF, 1/day) is determined by the following equation, with the reciprocal number being the standing time of the rain water (RTRF).

$$KARF = 24 \times 3600 \times 6.5 / DEPA$$
$$RTRF = 1 / KARF$$

Where, DEPA is altitude of the atmospheric phase.

If the volume of the atmospheric phase (VOLA) is given by

$$VOLA = SUA \cdot SEPA$$

then VOLAAP is determined by the following formula :

$$VOLAAP = VOLA - VOLAW$$

When default values of 30 μg/m^3 for CAER and 1.5 g/cm^3 for DENAER are used, the aerosol volume ratio occupied in VOLAAP is 2×10^{-11}.

(2) Kinetic constant

The kinetic constant of advection (KAAD) is determined from the average wind velocity (AFR) by the following formula :

$$KAAD = 24 \times 3600 \times AFR / (SUA)^{1/2}$$

The kinetic constant of atmospheric dispersion (KAU) is determined by the Thornthwaite-Holzmann formula. It is known that this formula gives appropriate results when the atmospheric stability is either weakly stable, intermediate, or has weak instability where the Richardson number is less than 0.01.

$$KAU = 24 \times 3600 \times 0.412 \cdot AFR / \{\log (DEPA / 0.1)\} / DEPA$$

The kinetic constant of decomposition in the atmosphere (KAT) is determined from the following formula which explicitly considers oxidation by OH radical :

$$KAT = 24 \times 3600 \times KOH \cdot OHC$$

Where, KOH is kinetic constant of reaction with OH radical (cm^3/molecule/sec), and OHC is concentration of OH radical in the atmosphere (molecule/cm^3).

The kinetic constants against diffusive transfer from the atmosphere to surface water phase (KAW) is determined by using the following mass movement coefficient (unit : m/day).

[air phase mass movement coefficient] $KG = 24 \times 36 \times (0.3 + 0.2 \times AFR) \cdot (18/MW)^{0.4355}$
[liquid phase mass movement coefficient] $KL = 24 \times 36 \times (0.004 + 0.00004 \times AFR) \cdot (32 / MW)^{0.4047}$
[air / liquid boundary mass movement coefficient] $KGL = 1 / (1 / KL + 1 / HENRY / KG)$

KAW is determined by the following formula :

$$KAW = KGL / HENRY / (DEPA / LLW)$$

Where, LLW is the ratio of surface water to total surface area (SUA).

The kinetic constants of diffusive transfer from the atmospheric phase to soil phase (KAS) is determined by the double thin layer theory using the following mass movement coefficient (unit : m/day) :

[air in soil mass movement coefficient] $KASLSA = 24 \times 3600 \times 0.00000556$
[water in soil mass movement coefficient] $KASLSW = 24 \times 3600 \times 0.000000000556$

KAS is determined by the following formula :

$$KAS = (KG \cdot KASLSA + KG \cdot KASLSW / HENRY) / (KG + KASLSA + KASLSW / HENRY) / (DEP / LLS)$$

Where, LLS is the ratio of soil to the total surface area (SUA).

The aerosol deposition kinetic constant (KAEF) is determined from the following formula :

$$KAEF = 2 \times (DAER / 1000000)^2 \cdot DENAER \cdot 9.8 / 9 / 0.000015 / DENAIR \cdot 3600 \times 24 / DEPA$$

Where, DAER is particle diameter (m), DENAER is particle density (kg/m^3), and DENAIR is air density (1.293 kg/m^3).

(3) Average standing time

Average standing (residence) time in the atmosphere (TA) is determined by the following formula combining mass distribution ratio and kinetic constants.

$$TA = 1 / (KAAD + (KAT + KAW + KAS + KAU) \cdot FAA + KARF \cdot FAW + KAEF \cdot FAP)$$

(4) Disappearance contribution ratio

Contribution of advection, dispersion, decomposition, diffusive transport (surface water and soil), precipitation and aerosol deposition to chemical disappearance in the atmosphere is determined by the following formulae :

[advection] $COAAD = 100 \times KAAD \cdot TA$

[dispersion] $COAU = 100 \times KAU \cdot FAA \cdot TA$

[decomposition] $COAT = 100 \times KAT \cdot FAA \cdot TA$

[diffusion (water)] $COAS = 100 \times KAS \cdot FAA \cdot TA$

[diffusion (soil)] $COAS = 100 \times KAS \cdot FAA \cdot TA$

[precipitation] $COARF = 100 \times KARF \cdot FAW \cdot TA$

[particle deposition] $COAEF = 100 \times KAEF \cdot FAP \cdot TA$

b) Material movement in soil phase

The soil phase consists of three compartments : air, water and particles. MNSEM deals with chemicals which are distributed into soil air, water, and particle compartments in the same way as chemicals in gas phase, dissolved phase, and adsorption phase respectively.

(1) Mass distribution ratio

Chemical mass distribution ratios in air, water, and particles in soil phase (FSOA, FSOW, FSOS) are determined by the following formulae :

$$FSOA = HENRY \cdot SOAF / (HENRY \cdot SOAF + SOWF + KOC \cdot OCSOS \cdot (1 - SOAF - SOWF) \cdot DENSOS)$$

$$FSOW = SOWF / (HENRY \cdot SOAF + SOWF + KOC \cdot OCSOS \cdot (1 - SOAF - SOWF) \cdot DENSOS)$$

$$FSOS = KOC \cdot OCSOS \cdot (1 - SOAF - SOWF) \cdot DENSOS / (HENRY \cdot SOAF + SOWF + KOC \cdot OCSOS \cdot (1 - SOAF - SOWF) \cdot DENSOS)$$

Where, SOAF and SOWF are the soil : air volume and the soil : water volume ratios, respectively, and OCSOS and DENSOS are the organic carbon content, and density of soil particles respectively. KOC is organic carbon adsorption constants of the chemicals.

(2) Kinetic constants

The kinetic constant for evaporation from soil phase to the atmosphere is determined by using mass transfer coefficient mentioned above.

$$KSA = 1 / (1 / KG / HENRY + 1 / (KASLSA \cdot HENRY + KASLSW))/(SOAF \cdot HENRY + SOWF + (1 - SOAF - SOWF) \cdot KOC \cdot OCSOS \cdot DENSOS) / DEPSO$$

Where, DEPSO is depth of soil.

Degradation in soil, microbial degradation and hydrolysis in soil water (dissolved state) and microbial degradation in soil particles (adsorption state) are considered.

$$KSOW = KBI0 \cdot AMSOW + 24 \times 3600 \times KHY \times 10\ PHSO - 14$$

$$KSOS = KBIO \cdot AMSOS$$

Therefore, the kinetic constant of degradation (KSOT) is determined by the following formula :

$$KSOT = FSOW \cdot KSOW + FSOS \cdot KSOS$$

Surface effusion and leaching from soil accompanied by precipitation contribute to the disappearance of dissolved substances in soil. The kinetic constants of effusion and leaching are expressed as the following :

[surface effusion] $KSRO = SRF / 1000 / DEPSO / SOWF / 365$

[leaching] $KSLE = RLE / 1000 / DEPSO / SOWF / 365$

Where, SRF and RLE are the amount of water effusing and leaching in both mm/year, respectively. RLE is determined as the product of the penetration coefficient (KPED, mm/day) and the number of days of precipitation.

$$KPED = 0.01 / 96 \cdot ADS^2 \times 980.7 / 0.010038 \times 10 \times 24 \times 3600$$

ADS is average diameter of soil particles (cm).

The number of days of precipitation is considered to be 100 days, or the number of days which have more than 1 mm/day of rainfall. Therefore, SRF is determined by the following formula :

$$SRF = TRF \cdot (1 - ETP) - RLE$$

Where, erosion by precipitation and by wind contribute to the disappearance of substances adsorbed onto soil, the kinetic constants of rainfall and wind erosion are expressed as the following :

[erosion] $KSER = ERS / 365 / DEPSO / (1 - SOAF - SOWF)$

[lofting] $KSRSUP = CAER / 1000 \cdot VOLA \cdot KAEF / VOLSO / (1 - SOAF - SOWF) / DENSOS / 1000000$

Where, ERS is soil erosion rate (m/year) and CAER is atmospheric aerosol concentration (mg/m^3). It is clear from the calculation of KSRSUP that soil particles lofted by wind into the atmosphere is balanced by particle adsorption from the atmosphere.

(3) Average residence time

The average standing time in soil (TS) is determined by the following formula using mass distribution ratio and kinetic constants :

$$TS = 1 / (KSA + FSOW \cdot (KSOW + KSRO + KSLE) + FSOS \cdot (KSOS + KSRSUP + KSER))$$

(4) Disappearance contribution ratio

The contribution of evaporation, degradation, surface effusion, leaching, erosion, and lofting into the atmosphere to the disappearance of chemicals in soil are determined by the following formulae :

[evaporation] $COSA = 100 \times KAAD \cdot TA$

[degradation] $COAT = 100 \times KAT \cdot FAA \cdot TA$

[surface effusion] $COAU = 100 \times KAU \cdot FAA \cdot TA$

[leaching] $COAS = 100 \times KAS \cdot FAA \cdot TA$

[erosion] $COAS = 100 \times KAS \cdot FAA \cdot TA$

[lofting] **COARF = 100 × KARF·FAW·TA**

c) Material movement in surface water phase

The water or aqueous phase consists of three compartments : water, suspended particles, and aquatic organisms. MNSEM treats chemicals which are distributed into water, on suspended particles and in aquatic organisms as chemicals in the dissolved phase, adosrption phase and biological phase respectively.

(1) Mass distribution ratio

Mass distribution ratios of chemicals in water, suspended particles and aquatic organisms in the water phase (FSS, FWSS, FWB) are determined by the following formulae :

$$FWW = VOLW / (VOLW + KOC \cdot OCSS \cdot WSS + BCF \cdot WB)$$

$$FWSS = KOC \cdot OCSS \cdot WSS / (VOLW + KOC \cdot OCSS \cdot WSS + BCF \cdot WB)$$

$$FWB = BCF \cdot WB / (VOLW + KOC \cdot OCSS \cdot WSS + BCF \cdot WB)$$

Where, WSS and WB are the amount of suspended material (ton) and aquatic oranisms (ton) in the surface water phase. The concentration of suspended materials (CWSS, mg/L) and concentration of aquatic organisms (CWB, mg/L) are determined by the following formulae :

$$WSS = CWSS \cdot VOLW / 1000000$$

$$WB = CWB \cdot VOLW / 1000000$$

(2) Kinetic constants

Aqueous phase degradation, photodegradation, hydrolysis and microbial degradation in the dissolved phase must be considered. The kinetic constants of degradation (KWT) are determined by the following formula :

$$KWT = (KPHT \cdot PAIW + KBIO \cdot AMWW + KHV \times 10\ PHW - 14 \cdot 24 \times 3600)$$

Where KPHT is the kinetic constants of photodegradation in water (1/day), and PAIW is decay ratio of photodegradation by light scattering. KBIO and AMWW are the biodegradation kinetic constants (L/cell/day) and microbiological amount in surface water (cell/L), respectively. And KHY and PHW are the hydrolysis kinetic constants (L/mole/sec) and pH of surface water, respectively.

The kinetic constants of evaporation from the water phase to the atmospheric phase (KWA) are

determined by using air/liquid boundary mass transfer coefficients (KGL), and :

$$KWA = KGL / DEPW$$

Where, DEPSW is depth of the surface water phase.

The kinetic constants of diffusion transfer from the water phase to the sediment phase are determined by the double thin layer theory using the following mass transfer coefficients (unit: m/day) :

[surface water side mass transfer coefficients] $KWSW = 24 \times 3600 \times 0.000002778$
[sediment water side mass transfer coefficients] $KWSS = 24 \times 3600 \times 0.00000002778$

KWSE is determined by the following formula :

$$KWSE = KWSW \cdot KWSS / (KWSW + KWSS) / DEPW$$

The kinetic constants of transfer to the sediment phase accompanied by sedimentation of suspended particles in water phase (KWSV) are determined by the following formula :

$$KWSV = KSV / DEPW$$

Where, KSV is sedimentation rate of suspended particles (m/day).

(3) Average residence time

The average residence time in surface water (TW) is calculated by the following formula using mass distribution ratio and kinetic constants. Chemical disappearance by metabolism inside of aquatic organisms is not considered.

$$TW = 1 / (FWW \cdot (KWAD + KWT + KWA + KWSE) + FWSS \cdot (KWAD + KWSV))$$

(4) Disappearance contribution ratio

The contribution of advection, degradation, evaporation, diffusive transfer into sediment and sedimentation to chemical disappearance in surface water are determined by the following formulae :

[advection] $COWAD = 100 \times (FWW + FWSS) \cdot KWAD \cdot TW$

[degradation] $COWT = 100 \times FWW \cdot KWT \cdot TW$

[evaporation] $COWA = 100 \times FWW \cdot KWA \cdot TW$

[sediment diffusion transfer] $COWSE = 100 \times FWW \cdot KWSE \cdot TW$

[sedimentation] $COWSV = 100 \times FWSS \cdot KWSV \cdot TW$

Where, KWAD is the advection kinetic constants of surface water (1/day).

d) Material movement in sediment phase

The sediment phase consists of two compartments : interstitial pore water and particles. MNSEM treats chemicals which are distributed in interstitial pore water and particles as being dissolved and adsorbed chemicals, respectively.

(1) Mass distribution ratio

Mass distribution ratio of chemicals in interstitial pore water and particles in the sediment phase (FSEW, FSES) are determined by the following formulae :

$$FSEW = POSE / (POSE + KOC \cdot OCSES \cdot (1\text{-}POSE) \cdot DESES)$$

$$FSES = KOC \cdot OCSES \cdot (1-POSE) \cdot DENSES / (POSE + KOC \cdot OCSES \cdot (1-POSE) \cdot DENSES)$$

(2) Kinetic constants

Degradation in the sediment phase, hydrolysis and microbial degradation in the dissolved state and microbial degradation in adsorption state must be considered. The kinetic constants of degradation in dissolved state and adsorption state (KSET and KSEST) are determined by the following formulae :

$$KSEWT = (KBIO \cdot AMSEW + KHY \times 10^{PHSE-14} \cdot 24 \times 3600)$$

$$KSEST = KBIO \cdot AMSES$$

Where, AMSEW and AMSES are microbiological amount in sediment interstitial pore water and sediment particles (cell/L or cell/kg). And PHSE is pH of sediment interstitial pore water.

Therefore, the kinetic constant of degradation (KSET) is determined by the following formula:

$$KSET = FSEW \cdot KSEWT + FSES \cdot KSEST$$

The kinetic constant of diffusive transfer from the sediment phase to surface water phase

(KSEW) is determined by the double thin layer theory as mentioned above :

$$KSEW = KWSW \cdot KWSS / (KWSW + KWSS) / (DEPSE \cdot POSE)$$

The kinetic constants of particle re-suspension from the sediment phase to surface water phase (KSERS) is determined by the following formula :

$$KSERS = 0.25 \times KWSV \cdot WSS / VOLSE / (1 - POSE) / SENSES$$

As is clear from the above formula, particle re-suspension from sediment to surface water is assumed to be 25 % of the amount of particle sedimentation.

(3) Average residence time

The average residence time in the sediment phase (TSE) is determined by the following formula involving mass distribution ratio and kinetic constants :

$$TSE = 1 / (FSEW \cdot (KSEW + KSEWT) + FSES \cdot (KSEST + KSERS))$$

(4) Disappearance contribution ratio

The contribution of degradation, diffusion transfer into surface water phase, and re-suspension of sediment particles to chemical disappearance in sediment phase is determined by the following formulae :

[degradation] $COSET = 100 \times KSET \cdot TSE$

[diffusion into water phase] $COSEW = 100 \times FSEW \cdot KSEW \cdot TSE$

[resuspension] $COSERS = 100 \times FSES \cdot KSERS \cdot TSE$

e) Material balance in the environment

Chemical material balances in an environment consisting of four kinds of phases - the atmosphere, surface water, soil, and sediment - is expressed by the following differential equations :

[atmospheric phase] $dMSA/dt = TEMA + A(1,1) \cdot MSA + A(1,2) \cdot MSW + A(1,3) \cdot MSSO + A(1,4) \cdot MSSE$

[surface water phase] $dMSW/dt = TEMW + A(2,1) \cdot MSA + A(2,2) \cdot MSW + A(2,3) \cdot MSSO + A(2,4) \cdot MSSE$

[soil phase] $dMSSO/dt = TEMS + A(3,1) \cdot MSA + A(3,2) \cdot MSW + A(3,3) \cdot MSSO + A(3,4) \cdot MSSE$

[sediment phase] $dMSSE/dt = A(4,1) \cdot MSA + A(4,2) \cdot MSW + A(4,3) \cdot MSSO + A(4,4) \cdot MSSE$

Where, MSA, MSW, MSSO, and MSSE are the amounts of chemical material in the atmospheric, surface water, soil, and sediment phases, respectively. And TENA, TEMW, and TEM are the amounts of chemical discharged into the atmospheric, surface water, and soil phases, respectively. Coefficients A(1,1) - A(4.4) can be expressed by using the mass distribution ratio, kinetic constants, and average residence time in each phase using the following:

$A(1,1) = -1 / TA$

$A(1,2) = KWA \cdot FWW$

$A(1,3) = KSA + FSOS \cdot KSRSUP$

$A(1,4) = 0$

$A(2,1) = KAW \cdot FAA + LLW \cdot (KARF \cdot FAW + KAFE \cdot FAP)$

$A(2,2) = -1 / TW$

$A(2,3) = KSROP \cdot FSOW + FSOS \cdot KSERS$

$A(2,4) = KSEW \cdot FSEW + FSES \cdot KSERS$

$A(3,1) = KAS \cdot FAA + LLS \cdot (KARD \cdot FAW + KAEF \cdot FAP)$

$A(3,2) = 0$

$A(3,3) = -1 / TS$

$A(3,4) = 0$

$A(4,1) = 0$

$A(4,2) = KWSE \cdot FWW + KWSV \cdot FWSS$

$A(4,3) = 0$

$A(4,4) = -1 / TSE$

MNSEM2 assumes that chemical discharge into the environment is continuous and constant and the amount of chemical material in the environment (concentration) is in a stationary, or steady state. That is, it is assumed that dMSA/dt = dMSW/dt = dMSSO/dt = dMSSE/dt = 0. Therefore, the amount of chemical material in each phase in the environment is obtained by solving the following simultaneous equations :

$A(1,1) \cdot MSA + A(1,2) \cdot MSW + A(1,3) \cdot MSSO + A(1,4) \cdot MSSE = TEMA$

$A(2,1) \cdot MSA + A(2,2) \cdot MSW + A(2,3) \cdot MSSO + A(2,4) \cdot MSSE = TEMW$

$A(3,1) \cdot MSA + A(3,2) \cdot MSW + A(3,3) \cdot MSSO + A(3,4) \cdot MSSE = TEMS$

$A(4,1) \cdot MSA + A(4,2) \cdot MSW + A(4,3) \cdot MSSO + A(4,4) \cdot MSSE = 0$

f) Calculation of the amount of exposure

Routes of indirect exposure to humans via the environment include exposure from inhalation of air, drinking of water, eating marine, meat and dairy products, eating root and leaf vegetables, and unintentional intake of soil.

(1) Exposure through inhaled air

The amount of exposure via inhaled air is determined by the following formula :

$$EXPA = CACON \cdot INTKA \cdot BIOAV / BW$$

Where, CACON is the concentration in the atmospheric environment (mg/m^3), and is calculated by the equation as mentioned above. INTKA is daily air inhalation rate (m^3/day), BIOAV is biological use ratio against air inhalation, and BW is human body weight. Default values of these exposure factors are shown in **Table IV-2-4**.

(2) Exposure through ingestion of drinking water

The amount of chemical exposure associated with ingestion of drinking water (EXPDW, mg/kg/day) is determined by the following formula :

$$EXPDW = CW \cdot (1 - PFW) \cdot INTKDW / BW$$

Where, CW is the chemical concentration in surface water calculated by the above formula. PFW is purification ratio of drinking water source, and INTKDW is the daily intake of drinking water (L/day). Default values for these exposure factors are shown in **Table IV-2-4**.

(3) Exposure through ingestion of marine products

The amount of chemical exposure associated with ingestion of marine products (EXPF, mg/kg/day) is determined by the following formula :

$$EXPF = CFISH \cdot INTKF / 1000 / BW$$

Where, CFISH is the chemical concentration in fish in surface water phase (mg/kg) determined by the following formula :

$$CFISH = 1000000 \times CW \cdot FWB / CWB$$

INTKF is the daily intake of marine products (g/day). Default values for these exposure

factors are shown in **Table IV-2-4**.

(4) Exposure through ingestion of meat products

The amount of chemical exposure associated with meat products intake (EXPME, mg/kg/day) is determined by the following formula :

$$EXPME = CMEAT \cdot INTKME / 1000 / BW$$

Where, CMEAT, the chemical concentration in meat of livestock (mg/kg) is calculated by the following formula, and INTKME is daily intake of meat products (g/day). Default values for these exposure factors are shown in **Table IV-2-4**.

$$CMEAT = BCFMEAT \cdot (C\_grass \cdot CONWD \cdot CTLGRASSN + CA \cdot CTLINHL + CSOCON \cdot CTLSOIL \cdot CONVSOIL)$$

BCFMEAT is the biotransfer coefficient into meat products (day/kg) determined from the logarithm value of octanol/water partition coefficient (log Kow : LOGKOW).

$$BCFMEAT = 10^{-7.6 + LOGKOW}$$

Also C_grass is the chemical concentration in pasture, and this is assumed to be equal to the concentration in leaf vegetables (see later). CONWD and CTLGRASSN are the conversion coefficient from pasture wet weight to dry weight, and pasture intake by beef cattle, respectively. Since CTLGRASSN is daily pasture intake expressed as dry weight of grass, C_grass expressed on a wet weight basis is converted into a dry weight concentration by using CONWD. CA and CTLINHL are chemical concentrations in the atmosphere and the air inhalation rate of livestock, respectively. CSOCON, CONVSOIL, and CTLSOIL are chemical concentrations in the soil (mg/kg), the amount of dry soil ingested by livestock, and a coefficient representing the conversion from dry weight soil to wet weight, respectively. As CTLSOIL is dry weight intake amount, it is converted by using CONVSOIL into a wet weight intake.

(5) Exposure resulting from ingestion of dairy products

The amount of chemical exposure associated with ingestion of dairy products (EXPMI, mg/kg/day) is determined by the following formula :

$$EXPMI = CMILK \cdot INTKMI / 1000 / BW$$

Where, CMILK is chemical concentration in cow milk (mg/kg) as determined by the following formula, and INTKMI is daily intake of dairy products (g/day). Default values for these exposure factors are shown in **Table IV-2-4**.

$$CMILK = BCFMILK \cdot (C\_grass \cdot CONWD \cdot CTLGRASSL + CA \cdot CTLINHL + CSOCON \cdot CTLSOIL \cdot CONVSOIL)$$

BCFMILK is biotransfer coefficient into cow milk (day/kg), which is determined from the logarithm value of octanol/water partition coefficient (log Kow : LOGKOW).

$$BCFMILK = 10^{-8.1 + LOGKOW}$$

Also CTLGRASSL is the amount of pasture eaten by dairy cows.

(6) Exposure resulting from ingestion of root vegetables

The amount of chemical exposure associated with ingestion of root vegetables (EXPRC, mg/kg/day) is determined by the following formula :

$$EXPRC = C\_rootplant \cdot INTKRC / 1000 / BW$$

Where, C_rootplant is the chemical concentration in root vegetables (mg/kg) calculated by the following formula, and INTKRC is daily intake of root vegetables (mg/kg). Default values for these exposure factors are shown in **Table IV-2-4**.

$$C\_rootplant = BCFROOT \cdot CSOCON$$

BCFROOT is the magnification of chemical concentration in the root vegetables resulting from soil, and determined by the following formula :

$$BCFROOT = (0.82 + 10^{(0.77 \cdot LOGKOW - 1.52)}) / 1000 \cdot BDCON / KSOIL\_WATER$$

Where, BDCON is soil bulk density per kg/m^3. KSOIL_WATER is the soil/water partition coefficient, and determined by the following formula :

$$KSOIL\_WATER = SOWF + SOSF \cdot KDCON \cdot DENSOSCON$$

Where, KDCON is soil adsorption coefficient per m^3/kg, and DENSOSCON is soil particle density per kg/m^3.

(7) Exposure resulting from ingestion of leaf vegetables

The amount of chemical exposure associated with ingestion of leaf vegetables and fruit (EXPLC, mg/kg/day) is determined by the following formula :

$$EXPLC = C\_stemplant \cdot INTKLC / 1000 / BW$$

Where, C_stemplant is the chemical concentration in the leaf vegetables and which is calculated by the following formula, and INTKLC is daily intake of leaf vegetables (g/day). Default values for these exposure factors are shown in **Table IV-2-4**.

$$C\_stemplant = BCFSTEM \cdot CSOCON + BCFA\_PLANT \cdot CA$$

BCFSTEM is the magnification of chemical concentration in leaf vegetables via soil, and which is calculated by the following formula, and BCFA_PLANT is the chemical concentration magnification of leaf vegetables via the atmosphere.

$$BCFSTEM = TSCF \cdot SCF \cdot BDCON / KSOIL\_WATER$$

Where, TSCF, the partition coefficient between the water flowing in vascular system of the plant and soil water, and SCF, the concentration magnification in stem, are determined by the following formulae :

$$TSCF = 0.784 \cdot EXP \{- (LOGKOW - 1.78)^2 / 2.44\}$$

$$SCF = (0.82 + 10^{0.95 \cdot LOGKOW - 2.05}) / 1000$$

BCFA_PLANT is the magnification of chemical concentration in the leaf vegetables via the atmosphere, and is determined by the following formula :

$$BCFA\_PLANT = FAP \cdot Kaer\_plnt + FAA \cdot Kgas\_plnt$$

Where, Kgas_plnt is bioconcentration of gaseous substances in the atmosphere by plant leaves and stems, and is determined by the following formula using air volume ratio (FPA, v/v), water volume ratio (FPW, v/v), and lipid volume ratio (FPLPD, v/v) in plant.

$$Kgas\_plnt = (FPA + (FPW + FPLPD \times 10\ LOGKOW) / HENRY) / BDPLANTCON$$

Kaer_plnt, the concentration of substances in adsorption phase in the atmosphere into leaves and stems, is 3300.

(8) Exposure resulting from unintentional soil

The amount of chemical exposure associated with ingestion unintentional of soil (EXPSO, mg/kg/day) is determined by the following formula :

$$EXPSO = CSO \cdot INTKS / DENSOS / 1000 / BW$$

Where, INTKS is the daily intake of soil (g/day).

(9) Amount of total exposure

The total exposure to chemicals associated with inhalation of air, intake of drinking water, marine products, meat products, dairy products, root vegetables, leaf vegetables, and unintentional soil (THDOSE, mg/kg/day) is determined by the following formula :

$$THEDOSE = EXPA + EXPDW + EXPF + EXPME + EXPMI + EXPRC + EXPLC + EXPSO$$

IV.3 Risk assessment method

The results of environmental monitoring produce extremely important information which is used to judge the level of exposure to a chemical or chemicals by humans and other organism, and the effects of that exposure. Methods of evaluating the affect of chemicals on environmental organisms are still being developed, but a method which expresses the size of chemical effects on human health as the probability of determining the kinds of possible health effects has almost been established, and is used as an index and for setting guidelines. This risk assessment plays an important role in practically and efficiently taking countermeasures to reduce risk, and to give scientific grounds used control harmful effects to less than tolerable level.

Environmental exposure to chemicals is undoubtedly smaller than direct exposure in the working environment, such as chemical or goods production and processing areas. However, since possible environmentally influenced health risks generally do not include acute toxicity, chronic toxicity effects, such as carcinogenicity, must be considered. Therefore, risk assessment using the results of environmental monitoring is generally regarded as a life-time risk evaluation based on assumptions of continuous human exposure.

This chapter illustrates the concept of risk assessment in a step by step manner, using the risk assessment of dioxin exposure in Japan as a concrete example. In addition, since a wide range of information is needed to conduct chemical risk assessment, such as social information on use patterns, purpose, production volumes etc., physicochemical information such as solubility, character of degradation, accumulation, volatilisation, solubility, and adsorption, movement in the environment, and biological information such as toxicity, bioeffects, movement in the body, bioinfluences etc., this chapter lists sources for such information.

IV.3.1 Structure and concept of risk assessment

The word “risk” as originally used has a meaning of “probability of damage or hazard”. However, the meaning of “risk” when “risk” is used in environmental “risk assessment” indicates “any danger or dangerous things which may have a harmful influence on humans or the environment”, and this definition includes not only the “probability of danger happening and the size of its influence” but also “how society evaluates it”

An assessment of chemical risk to humans should be based on the best scientific knowledge and professional judgement, and have the following elements : 1) hazard identification, 2) dose-response assessment, 3) exposure assessment, and 4) risk characterisation. **Figure IV-3-1** shows the connection and flow of each of these elements. Hazard identification is a qualification

step which ascertains qualitatively whether there is harm to health and the kind of harm. This is followed by the quantification steps of dose-response and exposure assessment. Finally, the risk characterisation process compares the results of quantification assessments. Environmental monitoring of chemicals should consider the processes of "hazard identification" and "exposure assessment" when research plans are being made. For example, the selection and prioritisation of target compounds : that is, that making a priority list requires information about toxicity, production volumes, and use etc., and when the research site, time, and sampling frequency have been decided, exposure prediction will use environmental behaviour model.

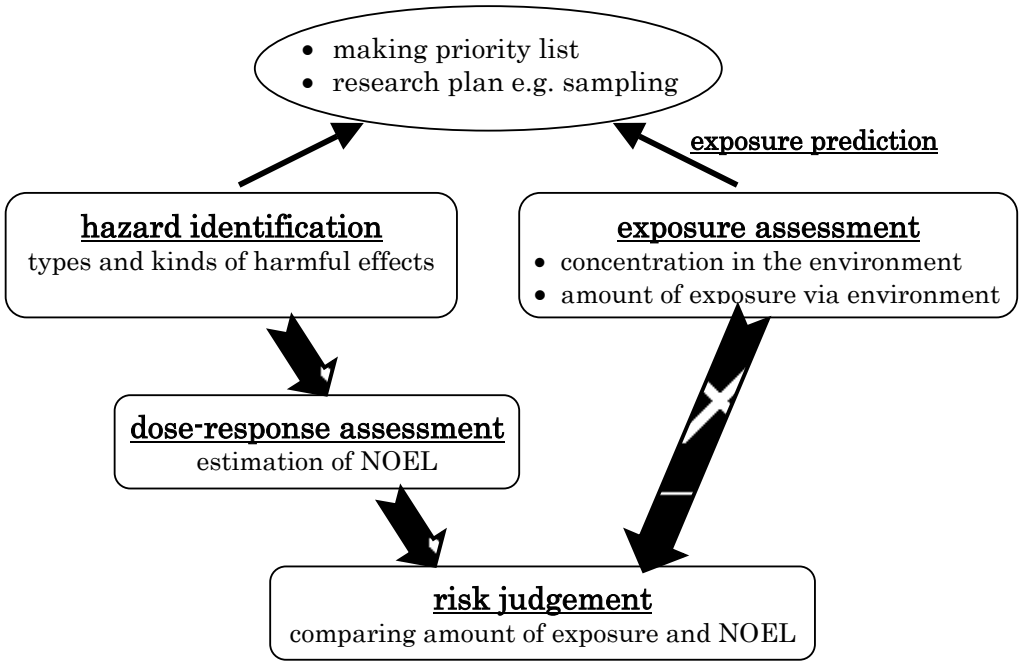


Figure IV-3-1 Factors and the flow of risk assessment

IV.3.1.1 Hazard identification

This step is used to qualitatively identify chemical hazards, in other words to clarify all of the main potential hazards which can happen with human activities. If human epidemiological information can be utilised, hazard identification becomes more efficient. However, one must not stray too far from analysing cause and effect relationships, or mistake or mix up such effects with other causes. But, unfortunately, it is a fact that for most chemicals such hazard information is not known. Therefore, we must predict health hazards based on experimental results using experimental animals.

To predict health hazards, first of all outline the potential hazards using data collected from

fact sheets and data bases. Then detail the hazards by checking the toxicity of each chemical or process by using original or review articles. Review documents published by international organisation or national organisation, groups are useful. For example, RTECS (Registry of Toxic Effects of Chemical Substances) contains acute toxicity, mutagenicity data etc. edited and published by US NIOSH (National Institute for Occupational Safety and Health), IARC Monographs on Carcinogenic Risks to Humans by IARC (International Agency for Research on Cancer), WHO (World Health Organisation), and ICPS (International Programme on Chemical Safety) which at present has published review documents for 170 compounds as EHC (Environmental Health Criteria). Also, the US Department of Health and Human Services has been making review documents (Toxicological Profiles) of 20 or so compounds every year. Analyse and organise obtained information using the following criteria.

A. Human exposure data

Human exposure data is obtained from epidemiological studies of accidental exposure in the workplace or exposure experiments using volunteers. Data obtained from exposure experiments using volunteers can provide quantitative information about dose-response relationships from which TDI (Tolerable Daily Intake) or ADI (Acceptable Daily Intake) criteria can be created, and if there is enough proof, a low safety coefficient. Occupational and accidental exposure can provide useful data to confirm the relationship between apparent harmful effects and dose if it is possible to specify causative agents and estimate the amount of exposure.

B. Toxicity test data using animals

Toxicity tests using animals are used to predict relationships between health effects and chemical characteristics, chemical form, reaction and exposure routes. When information for chemicals of similar structure is available, it is possible to investigate the possibility of toxicity based on the chemical's structure alone.

The purity (or impurity) of the compound used in the animal experiments must be known before the true cause of apparent harmful effects can be elucidated. In addition, the stability and reactivity of the compound itself and its stability in food or water is essential to guarantee the amount of exposure to animals. It is desirable to use animal species of known lineage and which are commonly used in toxicity tests, using sufficient numbers of animals per treatment group to provide statistically significant results. Ideally, use equal numbers of both sexes, rather than either just males or just female. Ensure that both exposure and observation time are appropriate for the experiments. Ideally, dose and general toxicity or toxicity effect on target organs is the

result of a linear dose-response relationship, and NOAEL (No Observed Adverse Effect Level) can be confirmed.

Toxicity testing must consider influences on drug metabolism, the immune system, and internal secretion functions. A knowledge of the target compound's pharmcodynamics, that is, absorption, distribution, accumulation, metabolism, secretion, and also species and sex differences is very useful. Information on pharmacokinetics helps improvement the accuracy of quantitative assessments. Mutagenicity tests, mutation induction tests, chromosome aberration induction test, and micro nucleus test have become common toxicity screening methods for the prediction of carcinogenesis. Results of long term carcinogenicity tests provide the most direct information for confirmation of harmfulness. When the rate of carcinogenicity in the test group administered the chemical is higher than the control group, and the time taken for cancer to develop is short, this is judged a positive carcinogenesis. And when animals of both sex or multiple organs develop cancer, or many kinds of tumour appear, or cancer develops within different species, carcinogenicity is regarded as being confirmed.

The identification or risk assessment of toxicity hazards follows several steps, first collecting information, then evaluating the reliability of the information, and then confirming the data. Generally, the procedures followed are to confirm statistically or biologically the difference between control groups and treated groups, and the correlation between dose and apparent hazard based on the results of many different toxicity tests, such as repeated treatment toxicity tests, teratogenesis / reproduction test, carcinogenesis tests, hereditary toxicity test, etc., all the while checking the effect of target organs and other harmful effects from changes in each test procedure. Then the relationship between response severity and exposure is quantified by scientific methods. Following quantification, a dose-response assessment applies animal data to the human case. The dose-response assessment is often undertaken at the same time as an exposure assessment because they are related to each other.

IV.3.1.2 Quantitative risk assessment

Risk, "P", is a function of the amount of exposure, "D", that is,

$$P = f(D).$$

A dose-response assessment determines either the function "f", the exposure assessment, D, and/or the risk assessment, P. The term quantitative risk assessment is conventionally used to cover all of dose-response assessment, exposure assessment, and risk assessment, but it would be generally better to use the three terms to show the three steps clearly.

A. Dose-response assessment

Dose-response assessment is the second step in conducting chemical risk assessment. Dose-response assessment is used to determine the LOAEL etc. by considering the correlation between chemical intake, the appearance of toxicity and the mechanism of appearance. This step is used to calculate the amount of chemical which does not cause an effect on health when a human takes or is exposed to chemicals. Generally, low dose or environmental exposure dose-response relationships are estimated by extrapolating in the direction of low concentrations data obtained from dose-response relationships produced by high doses in animal experiments or observed under relatively high exposure conditions in epidemiological research. As mentioned later, several extrapolation methods are available, but it is important to choose the most appropriate one.

Dose and amount of exposure are often treated as having almost the same meaning. Sometimes, the terms are synonymous with the amount of toxic agent administered in animal experiments, and sometimes the amount of toxic agent taken into the body calculated from the concentration of the chemical in environmental samples or food. However, the real concentration of chemical at the target organ(s) in the body generally decides the kinds and size of health effects. If the real concentration in the target compartment or organ in the body is understood as the dose (D), the accuracy of the dose-response assessment increases significantly, and a plot of the logarithm of dose against response more often than not shows a linear relationship.

Real concentrations in the target compartment or organ in the body are not only influenced by intake, but also by toxicodynamic conditions, such as chemical absorption rate, distribution, antidotal action, excretion, metabolism activation, connection rate with target, and the fixation rate etc. Understanding the details of these factors is the key to conducting accurate dose-response assessments, and then getting risk assessments right.

Non-linearity of exposure (intake) and response proved by non-linearity of antidotal action or activation becomes influential evidence for the judgement of threshold values. There are two categories of threshold toxicity evaluations which are conducted because of the appearance of toxicity mechanisms assuming that all appearances of toxicity are applicable to humans, except for specialised toxicities to experimental animals.

a) Evaluations in the case where threshold values are assumed to exist

In this first case, threshold values are assumed to exist. In other words, the dose-response curve is not linear. There is a minimum dose that must be absorbed before toxic effects are caused. This minimum dose is the threshold value. Included in this category is carcinogenesis not linked to general toxicity, teratogenesis / reproductive toxicity, and hereditary toxicity. In particular, carcinogenesis by means of chemicals causing cancer indirectly, or secondarily through hormone or

activated oxygen radicals are included in this category. Since it is considered that toxicity does not appear below a certain dose, the threshold levels are usually indicated by the NOAEL. If the NOAEL cannot be determined by toxicity tests or epidemiological research, i.e. only a LOAEL can be determined, the appearance of minute amounts of toxicity can be estimated by applying a safety coefficient (safety factor) (usually 10) to the NOAEL. However, if toxic effects are apparent even at 1/10 of the dose, the LOAEL cannot be used for evaluation. The Benchmark Dose Method (BDM) can be applied to calculations of the NOAEL of general toxicity and teratogenesis / reproduction toxicity. The BDM fits ideal curves to the results of experiments. This allows the determination to 95% confidence limits of a limit on the dose that causes the appearance of 5 to 10 % toxicity within the range of experimental doses. The 5 % toxicity appearance rate for teratogenesis / reproductive toxicity, or 10 % for general toxicity are empirically equal to the NOAEL. The BMD is also being applied for carcinogenesis evaluation.

Values obtained from the NOAEL, LOAEL or BDM can be used to determine the ADI or TDI for humans by dividing such values by a SF (safety factor) and UF (uncertainty factor). Both SF and UF are factors which apply to intake amounts which are assumed to cause no harmful effects. It is therefore OK to treat the ADI or TDI as having the same meaning. In addition, the ADI and TDI can be described as being "the level of harmful compound which it is assumed will cause no harmful effects on human health even if a human being were to take it everyday for its whole life", and are expressed as the intake amount per kg of human body weight per day.

Generally, the terms TF and TDI are used for environmental chemicals to which people are not exposed intentionally, and the terms SF and ADI are used for food additives which are intentionally added to food. The US Environmental Protection Agency (US EPA) uses a Reference Dose (RfD) for ADI, and Reference Exposure Concentration (RfC) to calculate allowed amounts per day.

The terms UF and TDI are used as factors to correlate general human epidemiological research and animal experiments containing the following uncertain factors:

(1) interspecies differences - apply conversion factors from animal to human
(2) interspecies or individual differences - differences between human
(3) different kinds of toxicity information with different reliability used to estimate human effects, such as experimental exposure period and design, the existence of supportive or nonsupportive data etc.

Point (2) is called the "distribution uncertainty." Points (1) and (3) are called the "true uncertainty". The US EPA sometimes calls point (3) the modifying factor (MF). Generally, the MF is 10 for interspecies differences assuming humans are more sensitive than experimental animals, 10 for interspecies differences taking into account the difference in groups of humans. The default value is the product of these two points i.e. UF = 100. The UF may be subdivided

when a knowledge of toxicokinetics or dynamics reflecting interspecies and individual differences in the experimental data is known. In the following cases, a maximum of 10 is added.

- when toxicity observed near the NOAEL is serious, such as liver cell death
- when the quality of the toxicity test is not good. For example, animal numbers are small, experimental conditions are insufficient, reliability of data is low, etc.
- when only an NOAEL is obtained. However, additional UF are not necessary if the BMD can be used.
- short term repeat administration toxicity tests. In general, a factor of 10 is applied for toxicity test of 3 months to 2 years, or, for example, when data from important toxicity tests such as teratogenesis / reproducibility toxicity test are not available.

For evaluation of carcinogenesis not linked to hereditary toxicity, a UF10 is added when toxicity is associated with tumours, but no addition of a UF is required for a non-tumour associated disease. On the other hand, for NOAELs obtained from occupational exposures equal to a 90 day inhalation exposure experiment, the TDI is usually calculated as UF3 - 10. This is because highly sensitive groups such as old people, children, and sick people are not included in the group of workers, and length and concentration of exposure are accurately understood.

Thus, the UF is determined by considering the kinds of toxicity and experimental design, and the TDI is determined by dividing the NOAEL, LOAEL and BMD by the UF value. Recently, efforts have been made to make the UF as a small value as possible, i.e. to make the TDI more reliable by considering information such as toxicity appearance mechanisms, physicochemical character and structural activity correlations etc. In general, the UF is not supposed to exceed 10000, and if does exceed this value, it cannot be applied to humans.

b) Evaluation in the case assuming threshold values don't exist

When threshold values are assumed not to exist, for instance, in the evaluation of carcinogenesis linked to hereditary toxicity, a Virtual Safety Dose (VSD) is calculated by applying to low dose using mathematical models. The VSD is the dose which is regarded as probably being substantially safe compared with everyday risks, and the values adopted are usually of the order 10^{-6} - 10^{-5} at present. In Japan, 10^{-5} is the current end point following WHO guidelines. In other words, the life time risk that one out of 100,000 people will suffer cancer because of exposure to a particular risk with a statistical probability of 99% is regarded as being practically safe.

The method used to calculate the VSD is to determine a dose which is equal to 10^{-5} or 10^{-6} risk after inserting the relationship between dose and carcinogenic rate (the results of carcinogenesis test which is conducted by several doses) into a mathematical model. Generally, the VSD is estimated by determining a dose which is equal to a certain risk from the reverse function $D = f^{-1}(P)$

of the dose-response function P = f(D) : where, P is carcinogenic rate, and D is the dose.

There is another way to estimated the VSD's 99%, 95% and lower confidence limits. The Linearised Multi-stage Model mentioned later is most widely used at present for the evaluation of carcinogenesis risk. When this model is used, the VSD is calculated from experimental results obtained computer simulations, determining the biggest value, q*, of the slope at the low dose range, and then dividing a certain risk level, for example 10^{-5}, by q*.

There are also mathematical models such as Probit and Logit which are based on probability distribution, One-Hit, Multi-Hit, Weibull, Multi-Stage Model, and Linearised Multi-Stage Model which are based on carcinogenicity mechanisms.

- Probit Model : In this model, the logarithm of acceptable intake, or of toxic response, of each chemical follows normal distribution whose parameters are the average, μ, and the standard deviation, σ. In this model, the dose-response curves becomes sigmoid when D becomes close to 0 and P becomes almost 0, and when D becomes larger and P becomes close to 1.

$$P = \varphi[(\log D - \mu)/\sigma] = \varphi(\alpha + \beta \log D)$$

φ : standard normal distribution function (accumulation something distribution function),

$\alpha = -\mu/\sigma$, $\beta = 1/\sigma$

- Logit Model. Although, like the Probit Model, this model gives sigmoid dose-response curve when D becomes close to 0, P becomes 0 more slowly than Probit Model.

$$P = 1/[1 + \exp\{-(\alpha + \beta \log D)\}]$$

- One-Hit Model. This model assumes that one hit by a toxic agent during a certain time period causes cell defects which cause tumours. At low doses, the slope shows linearity of λ[I - f(D)].

$$P = 1 - \exp(\lambda D)$$

λD : expectation of hit numbers

- Multi-Hit Model. This is the generalised version of the One-Hit Model, and assumes that cells becomes cancerous after being hit more than n times during a certain period. At low doses, the formula can resemble $P = \lambda D^n$, and when n = 1, this model gives linear dose-response curve, n > 1, curved downwards, and n < 1, curved upwards.

$$P = 1 - \sum_{k=0}^{n-1}\{\exp(-\lambda D)(\lambda D)^k / k!\} = \int [\prod_{0}^{D}(n)]^{-1}\lambda^n t^{n-1}\exp(-\lambda t)dt$$

- Weibull Model. Another generalised version of the One-hit Model. At low doses, when n = 1, this model gives a linear dose-response curve, n > 1, curved downwards, and n < 1, curved upwards.

$$P = 1 - \exp(-\beta D^n)$$

- Multi-Stage Model. Generalised version of Multi-Hit Model. In this model, the effects of target compounds at several stages are associated with other stimulations occurring at each stage.

$$P = 1 - \exp[-\prod_{i=1}^{\infty}(\alpha_i + \beta_i D)]$$

$$(r_i \geq 0)$$

- Linearised Multi-Stage Model. This model was developed from the Multi-Stage Model and shows linearity in the low dose range. When slope of the line is q*[(mg/kg/day)$^{-1}$], it becomes the following formula.

$$P = q^*D$$

where q* is the maximum value of the slope at the low dose range, and is equals to the 95% upper confidence limits of this model. This value is widely used as an index of the intensity of carcinogenesis of carcinogens.

The risk of carcinogenicity at low doses is obtained from animal experiments, the data from which must be applied to human doses, and the many interspecies differences considered. In general, comparisons based on body weight or body surface area are common, but it is not clear which is most appropriate. The US EPA thought it appropriate to consider body surface area (proportional to body weight_raised to 2/3rd power) when the doses used in animal experiments were applied to humans. This decision was based on the experimental results that the dose at which toxicity appeared becomes equal in both animals and human when the dose is not indicated 'per unit of body weight' but by 'per unit of body surface area. However, later the US EPA suggested that body weight raised to 3/4th power was more appropriate than body surface area ratio.

For the evaluation of carcinogenic risk, when the dose causing tumour appearance is not clear, a UF is sometimes used. For example, the maximum dose which doesn't cause cancer is divided by 5,000, adding a UF50 for carcinogenesis linked to hereditary toxicity. Also , there is another way to compare amounts of exposure which cause 5% tumour appearance rates in animal experiments or epidemiological research and amount of human exposure.

B. Exposure assessment

Chemical exposure is defined as chemical contact with the internal and/or external surfaces of a human or other organism. Exposure assessment aims to estimate the total amount of exposure by clarifying the structures and sizes of exposed groups, and by considering exposure routes, the frequency, and the periods during which chemicals in the media directly expose the environment and human beings. By comparing the levels obtained from dose-response assessments, the safety (or danger) of the present state of pollution is assessed. Knowledge about the reality of pollution and exposure obtained from exposure assessment is also useful for strategies such as risk management with end points of the efficient reduction of chemical risks. In this section the processes by which data obtained from environmental monitoring are introduced into exposure assessment are described.

a) Chance and routes of exposure

Chemicals discharged into the environment (**Figure IV-3-2**) are distributed in the atmosphere, water, soil and the biosphere by way of transfer and diffusion. In addition, there are some compounds which are bioconcentrated through the food chain in the biosphere. Human beings take in chemicals from the various environmental media such as food and drinking water, via the inhalation, oral, and dermal routes. In order to determine the amount of human exposure, calculate the amount exposure from chemical concentrations in the exposing media and the intake via each route, and finally add up these values to obtain the total amount of exposure from all routes. Finally, conduct an assessment of amount the exposure by considering the continuance of exposure, i.e. period, frequency, and timing. Chemicals are generally reported for environmental monitoring purposes as concentrations in environmental media such as the atmosphere, lake water, river water, sea water, underground water, sediment, soil, seaweed, mussels, fish, birds, etc.. One must pay attention to differences between environmental media, and media which expose humans, when such data is combined for exposure assessment.

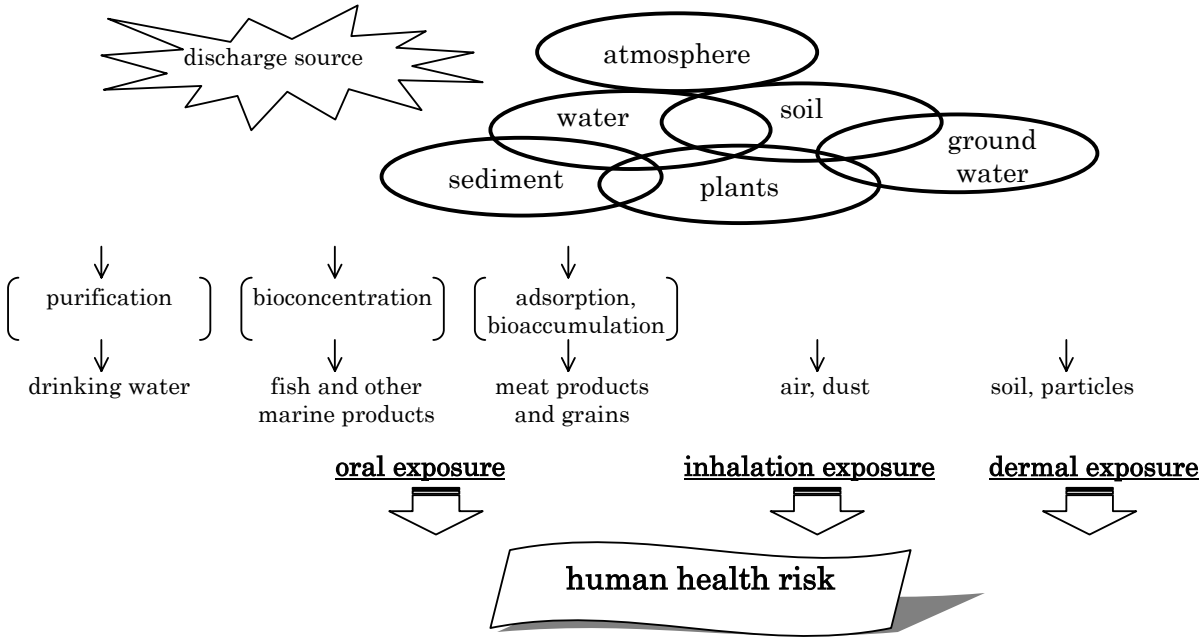


Figure IV-3-2 Exposure route of environmental chemicals to human

(1)Oral exposure

Sources of oral exposure to humans are drinking water, food and dust. The primary source of drinking water in developed nations is tap water, which is supplied after river, lake, and ground water have been purified by such treatments as aggregation, precipitation, filtration, and sterilisation etc. Most raw food raw materials, such as fish, sea products, vegetables and grains, meat, dairy products are treated by washing, processing, and cooking. Environmental monitoring data cannot be used directly for exposure assessment because some chemicals are concentrated, diluted, or decomposed during such treatments. Therefore, analysis of actual exposure media is desirable, since the accuracy of assessment becomes higher, but limitation of time or budget also happens.

Concentrations of chemical compounds in tap water can be estimated with a knowledge of their behaviour in the water purification process. For example, chemicals whose water solubility exceeds 10 μg/mL are difficult to remove by aggregation / precipitation or sand filtration, sulphated compounds are easily oxidised and decomposed, low molecular weight halogenated compounds such as trihalomethane can be produced in treatment processes, etc. For chemicals where such information is not known, it is necessary to analyse actual drinking water. Generally, analytical methods for river and lake water can be applied to drinking water.

Table IV-3-1 Average intake by food category in Japan (g/day/person) 1975～1995.

food category	1975	1980	1985	1990	1993	1994	1995
grain, rice	248.3	225.8	216.1	197.9	195.4	192.4	167.9
Wheat	90.2	91.8	91.3	84.8	86.9	86.4	93.7
Potatoes	60.9	63.4	63.2	65.3	62.5	62.2	68.9
Oil	15.8	16.9	17.7	17.6	17.9	17.6	17.3
Beans	70.0	65.4	66.6	68.5	65.9	66.8	70.0
green vegetables	48.2	51.0	73.9	77.2	81.6	81.8	94.0
other vegetables	198.5	200.4	187.8	173.1	180.6	171.7	196.2
Fruits	193.5	155.2	140.6	124.8	114.9	117.2	133.0
Seaweed	4.9	5.1	5.6	6.1	5.5	5.8	5.3
Sugar	14.6	12.0	11.2	10.6	10.2	10.0	9.9
soft drink	119.7	109.4	113.4	137.4	143.3	147.7	190.2
Sweets	29.0	25.0	22.8	20.3	20.3	19.6	26.8
Fish, sea products	94.0	92.5	90.0	95.3	96.2	97.0	96.9
Meat	64.2	67.9	71.7	71.2	73.7	74.5	82.3
Eggs	41.5	37.7	40.3	42.3	42.7	43.0	42.1
milk, dairy products	103.5	115.2	116.7	130.1	130.8	132.4	144.4

Human beings eat about 90 different kinds of foods, and for many chemicals these are the main exposure routes. Foods originate from other living things, and these living things end up on the table after adsorbing or concentrating chemicals discharged into the environment. In order to understand the amount of exposure from food accurately, it is necessary to know the amount of chemical in all foods prepared for eating. There are only a limited number of foods or food groups which have high concentrations of chemicals (**Table IV-3-1**). Therefore, after choosing the food or food group which has high concentrations of chemicals, the origin and amount of exposure through food can be determined from chemical concentrations in the food and the daily intake (**Table IV-3-1**). Although the range of environmental monitoring results becomes ever wider and additional analysis is still needed, this method has the advantage of being able to obtain accurate analytical values relatively easily because sample matrices are often homogeneous.

The amount of chemical exposure from foods in which the level and distribution of contamination is unknown has to be determined by investigations of whole foods. Commonly used methods are market basket method and the indirectly table method. The former is often used because sample collection is easier. Put simply, the method is to purchase everyday foods from every food group of **Table IV-3-1** based on national average food intakes, cook them using ordinary cooking methods, and homogenise. The homogenised food samples are the direct exposure media, and the average amount of chemical exposure can obtained from chemical analytical data. The indirectly method takes a single meal and homogenises it. This homogeneous mixture is then analysed. Both methods can provide data for accurate and convincing exposure assessments.

However, these methods analyse the whole food from which the meal is prepared, and it is often very difficult to deal with materials such as grains, vegetables, fish and sea products, meat, dairy products, etc.

Dust originates from particles or smoke discharged from factories and motor vehicles, soil particles, particles from the sea, chemicals themselves or chemicals attached to the surface of clay particles or salts. Humans inhale these dusts through the mouth and nasal cavity. Dusts in the air are also attached to food or hands, and get into human bodies by such motions as putting hands in the mouth or eating a meal. Dusts entering the nasal cavity can reach lung alveoli through the airways of the throat (the larynx and pharynx), trachea, and bronchus, but most of the dust sticks to airway mucous membranes, and are moved back to mouth as sputum, or reach the digestive organs via the gullet. In general, dusts with a diameter of more than 0.1 - 1.0 μm are assumed to stick to the upper or lower airways, and can be regarded as oral exposure media. Thus, oral exposure by dusts is through every day, unconscious motions, meals and breathing. Of these, exposure through meals is difficult to calculate because of many of indeterminate factors. Therefore, although there is possibility of overestimation, it is most practical to determine the amount of oral exposure through dusts from the Total Suspended Particulates (TSPs) in the atmosphere, chemical concentrations and aspiration rate. The TSP can be replaced by a measure of Suspended Particulate Materials (SPM). SPMs are particles with a diameter less than 10 μm. Exposure through actions such as putting soil in the mouth is also of concern, particularly for small children, therefore data detailing soil chemical concentration are also useful.

(2) Inhalation exposure

Humans may be exposed to chemicals in the atmosphere via inhalation of both gases and particles depending on such physicochemical characters as vapour pressure, adsorption isotherms to organic matters. Gaseous chemicals are assumed to reach lung alveoli via nasal cavity or mouth, but atmospheric particles form all or a part of the SPM. The diameter of the particles is as much a problem for inhalation exposure as it is for oral exposure from dusts, and the SPM which reaches alveoli without sticking to the mucous membranes of the nasal cavity, throat, or airways can be defined as the inhalation exposure media. In general, they are micro particles with a diameter of less than 1.0 - 0.1 μm.

Human behaviour, particularly living and working patterns must be considered when assessing atmospheric exposure. In general, humans spend only 1 - 3 hours outdoors, but more than 10 hours working and relaxing in the indoor environment. Therefore, the amount of inhalation of indoor environmental air is the overwhelming majority. In addition, some chemical concentrations are higher in indoor air than in the general atmosphere, so an understanding of the amount of exposure to indoor air is indispensable for calculating the true amount of exposure

and evaluating health effects. Basically, the amount of exposure is determined by measuring chemical concentrations in indoor air and the atmosphere outdoors and allocating residence times At this time, the contribution of the general environment and the indoor environment to total risk has to be clarified in order to estimate heath effects brought by environmental pollution.

(3) Dermal exposure

Soil is the main source of dermal exposure. In general, the results of soil analyses as part of environmental monitoring can be used as the exposure concentration.

b) Duration of exposure

Risk assessment of environmental pollutants targets health effects which can be caused by intermittent exposure to wide range of people for the whole of their life span, i.e. 24 hours per day for 70 years is one standard. However, when exposure from some daily patterns of activity are significantly different, such as indoor exposure, and cannot be ignored, the amount of exposure for each environment has to be calculated and added together. In addition, the timing of exposure can be an issue, so compounds which give produce effects in a certain age group have to have the amount of exposure in that period estimated separately. Thus, when a certain group has specified exposure and sensitivity, it is necessary to determine distributions depending on region, occupation, age, or sex. The results of exposure assessment should be reported in the same dose units are used for dose-response assessment because judgements on risk are conducted by combining exposure assessments with results of dose-response assessments. Many of them use intake per unit body weight (kg).

IV.3.2 Application of environmental monitoring data to exposure assessment

Data obtained from environmental monitoring would have big change as timewise and spacewise. It is, therefore, a problem which exposure concentration - mode, mean, geometric mean, or median - should be used, and how to treat values which are less than detection limits.

The results of environmental monitoring are used to assess health risks due to continuous and long term exposures at low concentrations. Thus, it is the most appropriate to use values such as the mean or median. However, some evaluations using the mode or confidence limits of the data are also necessary when, for example, a population is partially exposed to high concentrations. In addition, if multiple peaks appear in the histogram of data, the reason has to be investigated and division of the exposed group has to be considered. Furthermore, if there is a difference in

exposure status as a result of the source of an outbreak, regionally or dietary differences etc., or groups of different sensitivity are found, it is necessary to select the most appropriate data or look at reorganising the groups.

There is no problem in abandoning detection limits at the data analysis stage, or if detection limits are within the acceptable risk range, but there is the possibility that exposure at the detection limit cannot be ignored depending on the behaviour of the target chemicals. In this case, one way to evaluate the amount of exposure is to set temporary detection limits at 1/10th concentration. On the other hand, it is always desirable to improve analytical detection limits since both analytical methods and quality control techniques are very important and should sufficiently robust to facilitate representative or full data comparison when the data is the basis of risk evaluation.

When exposure assessment procedures based on environmental monitoring results start, the necessary data is often unavailable and estimates of environmental concentrations are required. Such estimates are, as mentioned in the previous section on behavioural analysis, based on regularity or connection between other appropriate environmental concentration data and physicochemical characteristics such as water solubility, vapour pressure, octanol-water partition coefficient, etc., information on hydrolysis, photodegradation, biodegradation, bioconcentration etc., and environmental conditions such as geography, weather, etc. However, in general estimated values are inferior to experimental data in terms of accuracy, and it is necessary to include this uncertainty.

IV.3.2.1 Quantification of amount of exposure

The amount of exposure is determined by using environmental monitoring data, data from direct human exposure data, or estimated values based on compound behaviour. Chemical concentrations at the contact points in the mouth, nasal cavity and skin is deemed to be the exposure concentration, and the amount of exposure within a certain time E_{total} can be determined by the following formula：

$$E_{total} = \sum_{m=1}^{n} \int_{0}^{t} C_m(t) I_m(t) dt$$

where, E_{total} is the amount of exposure between voluntary time 0 - t, $C_m(t)$ is the chemical concentration in the media , m, is the inhaled, ingested, or absorbed per time t, $L_m(t)$ is the amount of inhalation, ingestion, or contact surface area in the media, m, per time t. Environmental monitoring data can be used directly or indirectly to determine chemical concentration, but in such a case would be the potential concentration which may be absorbed directly if the compound's

adsorption rate (bioavailability) is 100 %. A chemical compound has to be adsorbed through the skin, lungs, or digestive organs in order to produce a toxic effect, and to estimate a compound's inherent adsorption function, information for each exposure route is necessary. In addition, toxicity can be the result of a specific interaction between absorbed chemicals and a biological receptor. If part of the absorbed dose is transferred to each organ, tissue, and bodily fluids, then very little chemical actually reaches the target cell, receptor, or membrane, and little disease develops. If the true amount of exposure or true concentration is estimated by explicitly considering information about chemical movement in the body, highly accurate evaluations becomes possible, but such data is not readily available.

A. Oral exposure

The media responsible for oral exposure, drinking water, food and dust, are considered to produce an amount of exposure determined by the following formula :

$$E_{ingestion}\ (\mu g/\ day) = \alpha \cdot C_{water} \cdot I_{water} + \beta \cdot \sum_{i}^{n} Ci_{diet} \cdot Ii_{diet} + \gamma \cdot C_{dust} \cdot I_{dust}$$

where, $E_{ingestion}$ = oral exposure amount per day (μg/day)

C_{water} = target compound concentration in drinking water (μg/L)

I_{water} = drinking water intake per day (L/day)

Ci_{diet} = target compound concentration in food i (μg/g)

Ii_{diet} = food i intake per day (g/day)

C_{dust} = target compound concentration in dust in the environment (μg/g)

I_{dust} = orally taken dust amount per day (g/day)

α, β, γ = absorption rate in digestive organs of target compounds in drinking water, food, and dust

In general, the amount of drinking water required per person per day is 0.5 L for infants and 1.2 - 1.5 L for adults, and often exceeds 2.0 L depending on a particular occupation or sports regime. The WHO, EPA, and Japan calculate that the amount exposure for an adult from drinking water as being from a standard 2 L of water. In addition, the EPA considers the amount exposure for an child as being from a standard 1 L of drinking water for a child weighing 10 kg. The amount of exposure from food is determined as the sum of the product of the concentration of each target chemical in each food and the amount of intake, after selecting foods which are predicted to have the highest contamination levels and greatest amount of intake. If data on the amount of

exposure through market basket methods are available, then it is OK to multiply the amount of exposure by absorption rate. Although the amount of dust taken orally per day changes a lot, from the average human daily inhaled volume (15 m^3/day, proportional to the2/3 rd power of body weight, the US sets inhaled volumes at 20 m^3/day for a standard 70 kg body weight), it can resemble the chemical concentration in TSP (or SPM), and TSP (or SPM). In addition, intake of dust or soil is estimated to be 0.0001 g/day in the relatively clean, enclosed environment, 0.05 g/day for workers in general industries, 0.48 g/day for workers on construction sites, and 10 g/day when in contact with dusty ground all the time. The intake of dust or soil in the general living environment is estimated to be 0.001 - 0.01 g/day, and by taking into account chemical concentrations in soil, exposure can be predicted. Digestive absorption rates, α, β, and γ, are compound dependent values, and they, even for the same compounds, are different depending on the nature of each medium. However, details are generally unknown. If sufficient scientific knowledge is available, the WHO adopts it, and if nothing is available, treats absorption as being 100 %, and gives an absorption rate of 1.

B. Inhalation exposure

The media responsible for inhalation exposure, air and suspended particulate materials, are considered to produce an amount of exposure determined by the following formula :

$$E_{inhalation}(\mu g/day) = \delta C_{air} I_{air} = (\varepsilon C_{gas} + \xi C_{fine} SPM_{fine} 10^{-3}) I_{air}$$

where, $E_{inhalation}$ = inhalation exposure amount per day (μg/day)

C_{air} = target compound concentration in air (μg/m^3)

C_{gas} = target compound (gas state) concentration in air (convert ppb to μg/m^3)

C_{fine} = target compound concentration in suspended particulate materials (μg/g)

SPM_{fine} = suspended particulate material amount in air (mg/m^3)

I_{air} = breathing amount per day (m^3/day)

δ, ε, ξ = alveoli absorption rate of target compounds

10^{-3} = correction factor (g/mg)

Chemical concentrations in the atmosphere are expressed using the weight-capacity unit, μg/m^3, when chemicals exist in the particulate state, and the capacity-capacity unit, ppb (part per billion), when the chemicals exist in the gaseous state. When risk assessment is conducted together with dose-response assessment, the weight-capacity unit is convenient for the results of exposure assessment, and conversion is done using the following formula :

$$\mu g / m^3 = ppb \frac{g-mol}{22.4L} \frac{MW}{g-mol} \frac{273.16K}{T} \frac{P}{hPa} \frac{10^3 L}{m^3} \frac{10^3 mg}{g}$$

where, ppb = target compound concentration (L/10^9L), MW = weight (g) of 1 g mol of target compound, 22.4 L = occupied by 1 g mol compound at 0 °C, and 1 atm (1,013 hPa), T = temperature (Kelvin), P = atmospheric pressure (hPa).

Under standard conditions, for example, 25 °C, 1 atm, the volume of perfect air 1 g mol becomes 24.45 L, and the above can be simplified to the following formula：

$$\mu g/m^3 = ppb \cdot \frac{MW}{24.45}$$

Generally the amount of inhalation exposure ($E_{inhalation}$) can be determined from the product of chemical concentration in air (C_{air}), the amount inhaled (I_{air}), and the absorption rate (δ). There is only limited analytical data in which chemicals in the air are divided into gaseous and particulate states, and where C_{air} is the total concentration. If such data can be used, the amount of exposure would be sum of both. Then, if particle size is limited to the less than 0.1 - 1.0 μm SPM fraction, and in the formula chemical concentration in suspended particulate materials is expressed as C_{fine}, the amount of suspended particulate material is SPM_{fine}. The amount inhaled per person per day is calculated as 150 m^3/day (standard body weight 50 kg) in Japan, with a range of 10 - 20 m^3 depending on body weight or the amount of exercise taken. This inhalation volume is based on a breathing rate of 20 L/min for 16 hours a day, and 7.5 L/min for 8 hours a day. The alveoli absorption rates, δ, ε, and ξ depend on compounds and the matrix, but if a value is not available, 100 % is used as the default value supplying a worst case scenario. The correction factor 10^{-3} is a unit adjustment value.

C. Dermal exposure

The amount of exposure through skin contact with ground surface deposits such as soil particles can be calculated by the following formula：

$$E_{contact}\ (\mu g / day) = \eta C_{deposit} SA \cdot SAF \cdot 10^{-3}$$

where, $E_{contact}$ = dermal exposure amount per day (μg/day)

$C_{deposit}$ = target compound concentration in ground surface deposit (μg/g)

SA = exposed skin area per day (cm^2/day)

SAF = skin adhesion factor (mg/cm^2)

η = skin absorption rate

10^{-3} = correction factor (g/mg)

The amount of dermal exposure ($E_{contact}$) is calculated from the product of chemical concentration in the ground surface deposit particles ($C_{deposit}$), attaching surface area per day (SA), skin adhesive factor of particles (mg/cm^2), and adsorption rate through the skin (η). Chemical concentration from environmental monitoring is used. The EPA uses a standard human body surface area, i.e. skin area, of 18,000 cm^2 for a 70 kg person, and because it is proportional to 2/3rd power of body weight, it becomes 14,000 cm^2 for body weight of 50 kg, or 16,000 cm^2 for a body weight of 60 kg. It is not known how much skin is exposed during everyday life, but it is assumed to be 1/3 of the total surface area for exposure assessment. Therefore, the area of skin to which ground surface deposits, such as soil can be attached daily is calculated as 4,8000 cm^2 for a 50 kg body weight, or 5,400 cm^2 for a 60 kg person, and 6,000 cm^2 for a 70 kg person. The skin adhesive factor is the amount of particles that attach per unit area of skin. If no data available, a value of 1 mg/cm^2 can be used. If no data is available on chemical adsorption rates through the skin, the amount of exposure can be calculated by using values of 1 % for organic compounds, and 0.1 % for inorganic compounds. A correction factor of 10^{-3} is a unit adjustment value.

D. Total exposure amount

The amount of total exposure is the sum of oral, inhalation, and dermal exposures.

$$E_{total}\ (\mu g / day) = E_{ingestion} + E_{inhalation} + E_{contact}$$

The value obtained is the amount of exposure per day, and is converted into a value for daily exposure per body weight in order to compare with TDI etc. for risk characterisation. In Japan,

$$E(\ \mu g / kg / day) = \frac{E_{total}\ (\mu g / day)}{BW(kg)}$$

where the standard body weight is 50 kg.

IV.3.2.2 Risk characterisation

Risk characterisation is the last step in the risk assessment process, i.e. the process of assessing the results of hazard identification, dose-response assessment, and exposure assessment, and estimating the extent of risk to humans. Risk manager communicate based on this information. Risk assessment takes place using the whole range scientific knowledge at the time of assessment,

but it is also clear that it is made up of many uncertain factors. Therefore, the results obtained are not absolute and don't guarantee safety. Assumptions in risk assessment include the following :

- Toxic effects in animals appear in human as well.
- Absorption, distribution, metabolism, and excretion are the same in humans as in animal models.
- Carcinogenesis linked to hereditary toxicity does not have a threshold value, but the appearance other toxic effects has threshold values.
- The difference in sensitivity between experimental animals and human is about 10 times.

Usually such data cannot actually be obtained, so the concepts have to be assumed. Therefore, it is necessary to obtain higher reliability by using data for similar chemical compounds where possible, and the premises upon which evaluation is based have to be written into the risk characterisation process. On the other hand, usually risk assessment assumes life time continuous exposure, so risk managers have to understand this point and take social needs into account during regulation preparation, risk diminishment policy etc.

A. Evaluation in the case that threshold values exist

For evaluations where threshold values exist, human risk is judged by comparing the determined TDI and actual exposure. Generally, if daily intake is less than the TDI, it is assumed that there will be no health hazard even if a human takes that dose for life. The International Programme on Chemical Safety (ICPS) distributes TDI for each exposure route based either on actually determined or estimated rates of exposure from air, food, and water, determines concentrations in the various media, and uses such concentrations as Guidance Values for assessment. In addition, tap water quality guidelines of the WHO makes a general chemical contribution from drinking water of 10 %.

Because TDI has uncertainty factors, assessment is sometimes done using a range of values of 1/10 to 10 times. This method is useful when deciding the order of priority of risk characterisation or risk diminishment treatment, or to try to adjust international values. However, when TDI is regarded as a range, it becomes difficult to interpret and obtain consensus recognition for the application.

Another method of evaluation in cases where threshold values exist is the Margin of Safety (MOS) or Margin of Exposure (MOE). The MOS has been used for safety evaluation of medicines, and it is determined by dividing the lowest toxic dose by the effective dose. A chemical is judged safer when the larger the value obtained. When this concept is applied to environmental

chemicals, the NOAEL obtained from toxicity tests or epidemiologic research is divided by the amount of human exposure. The EC uses MOS, the USA uses MOE, and the use of the methods are not the same. The MOS used by the EC is applied to evaluation of high production chemicals by the Organisation for Economic Cooperation and Development (OECD). That is, the NOAEL is indispensable for MOS calculation, and addition of an toxicity test itself is required when the kinds and quality of toxicity tests are not sufficient. Also, when MOS becomes, for example, less than 100, the reliability of exposure data has to be re-evaluated and if necessary re-investigation of the real exposure situation has to be conducted. If it can be confirmed that MOS is small, eventually, risk diminishment treatment is conducted. On the other hand, the US EPA suggests use of MOE for evaluation of carcinogens not linked to hereditary toxicity. The MOE is determined by dividing the amount of exposure by the LED (confidence limits lower value of dose which increase abnormality at 1 % or 10 %) obtained by Benchmark Dose method or the median. When MOE is evaluated, use the way of thinking of UF.

B. Evaluation in the case that threshold values don't exist

For evaluation of carcinogens which cause toxicity but without threshold values, i.e. have hereditary toxicity, the amount of exposure risk is usually evaluated by determining intake and VSD at the risk level of 10^{-5} - 10^{-6}, then comparing the values obtained with a control. In principle, VSD is determined by selecting an appropriate mathematical model based on the mechanism by which cancer develops, and inserting a low dose into the experiment of less than 1/10,000. However, since vital investigation of the mechanisms of cancer development have not been undertaken, VSD has extremely large uncertainty. Incidentally, values of VSD may be separated by up to two orders of magnitude depending on mathematical models. Because of these large uncertainties, the risk of carcinogenesis does not consider individual differences in sensitivity and the rate of contribution of each exposure route. VSD has to be understood as a value which indicates the intensity of carcinogenesis.

IV.3.3 An example of risk assessment - Dioxins

IV.3.3.1 Hazard identification

A. Outline of dioxins

Dioxin is the general name given to the polychlorodibenzo-p-dioxin (PCDD) family of

compounds, and often the context in which this descriptor is used includes the polychlorodibenzofurans (PCDFs). Dioxins are unintentionally produced by-products of certain chemical synthetic processes, and incineration processes. There are 75 PCDD isomers (c0ngeners) and PCDF 135 isomers (**Table IV-3-2**) The aqueous solubility, vapour pressure, degradation character (photodegradation, photooxidation, hydrolysis) of dioxins decreases as the number of substituted chlorine atoms on the rings increases. Dioxins with more than four substituted chlorines are bioconcentrated, global pollutants because of their high lipid solubility (lipophilicity) and stability.

Table IV-3-2 Isomer numbers of PCDD/Fs

Substituted chlorine numbers	PCDDs			PCDFs		
	molecular formula	M.W.	number of isomers	molecular formula	M.W.	number of isomers
1 (Mono)	$C_{12}H_7O_2Cl$	218.64	2	$C_{12}H_7OCl$	202.64	4
2 (Di)	$C_{12}H_6O_2Cl_2$	253.08	10	$C_{12}H_6OCl_2$	237.08	16
3 (Tri)	$C_{12}H_5O_2Cl_3$	287.53	14	$C_{12}H_5OCl_3$	271.53	28
4 (Tetra)	$C_{12}H_4O_2Cl_4$	321.97	22	$C_{12}H_4OCl_4$	305.97	38
5 (Penta)	$C_{12}H_3O_2Cl_5$	356.42	14	$C_{12}H_3OCl_5$	340.42	28
6 (Hexa)	$C_{12}H_2O_2Cl_6$	390.86	10	$C_{12}H_2OCl_6$	374.87	16
7 (Hepta)	$C_{12}HO_2Cl_7$	425.31	2	$C_{12}HOCl_7$	425.31	4
8 (Octa)	$C_{12}O_2Cl_8$	459.75	1	$C_{12}OCl_8$	443.75	1

The main absorption routes of dioxins are through the digestive organs, the skin, and the lungs. Regardless of the absorption route, in general the greater the chlorine substitution of a dioxin isomer, the lower the rate of absorption rate. Absorbed dioxins reach the tissues by means of the blood stream, and are accumulated in the liver and fat stores.

Dioxins stimulate the production of metabolic enzymes, e.g. the cytochrome P450, produced by the liver etc. such as CYP1A1 or CYP1A2 etc. through the aromatic hydrocarbon (Ah) receptor. The enzyme CYP1A1 is especially efficient at combining with dioxins. Cytochrome P450 is not only involved in chemical metabolism, but is also implicated in metabolic processes that promote carcinogenicity and the development of true cancer sources. The mechanism of action of these enzymes and dioxins is related to mechanisms of dioxins accumulation in the liver and the appearance of toxicity. Factors which determine movement of 2,3,7,8-TCDD in the body are solubility and diffusion velocity to fatty tissues, combination with CYP1A2 in the liver, excretion, and metabolism.

The results of animal experiments have shown that dioxins have manifold toxicities, such as acute toxicity, chronic toxicity, carcinogenesis, reproduction toxicity, teratogenesis, immune system

toxicity etc. All these toxicities are not restricted to a single species, but are different depending on animal species, lineage, age, sex etc.

According to current information, the promotion of cancer by dioxins is generally accepted, but since dioxins don't cause breaks in DNA strands directly, and various mutagenesis and hereditary toxicity test are negative, the cancer developing mechanism of dioxins is judged to have threshold values.

The effects of dioxin on humans include serious chloracne caused by excessive occupational or accidental exposure, liver damage, nervous symptoms, effects on respiratory organs etc. Long-term (continuous) health effects include chloracne, but there is no proof that dioxins cause reproductive toxicity in humans. However, the IARC reclassified 2,3,7.8-TeCDD up from a Group 2B carcinogen (possible cancer causing agent in humans) to a Group 1 (human carcinogen) at the working committee in February 1997. Other dioxins are classified as Group 3 (not categorised at present).

B. Examination of NOAEL by animal experiments

Table IV-3-3 summarises the results of a detailed search of all animal experiments conducted using dioxins, which observed effects at the lowest dose and were able to evaluate the NOAEL or LOAEL. Teratogenesis and immune toxicity can be observed at higher dose levels.

Table IV-3-3 Summary of results of animal experiments about 2,3,7,8-TeCDD

Toxicity	animal species	observed health effects	NOAEL (pg/kgBW/day)
Chronic toxicity	Swiss strand mouse	amyloidosis, dermatitis	1,000 (LOAEL)
Carcinogenesis	SD mouse	liver hyperplasia nodule (benign tumour)	1,000
		liver cancer	10,000
Reproductive toxicity	SD rat	fall of conception rate, low body weigh to new born	1,000
	red haired monkey	endometriosis	126 (100-180) (LOAEL)

Experiments using three different kind of animals give the same NOAEL or LOAEL. Within these, oral dose tests using the Swiss strand mouse for one year caused male amyloidosis (starch like degenerative high molecular compounds attach to tissues such as kidney) and dermatitis. The lowest dose 7 ng/kgBW/week (equivalent to 1 ng/kgBW/day) is regarded as the LOAEL.

Long term tests using the SD rat (mixed feed, 105 weeks) gave almost the same results, "liver cancer development at 70-100ng/kgBW/day", as the long term administration tests (forced administration, 104 weeks) using the OM rat by the NTP (US National Toxicity Evaluation Plan).

The results were significant, giving clear dose-response relationships between tested and control groups, and were highly reliable.

The results of a three generation reproduction test using the SD rat were an extreme fall in rates of conception at 100 ng/kgBW/day, inter-uterine death at 10 ng/kgBW/day, and growth defects in the new born, etc. The effects appear at 10 ng/kgBW/day for the F1 and F2 generations. Putting these together, the NOAEL is given as 1 ng/kgBW/day.

Reproductive toxicity tests using the red haired monkey suggested that the control group, and test groups given 5 ng/kg feed (equivalent to 126 pg/kgBW/day dose) and 25 ng/kg feed, show endometriosis at 22, 71, and 86 %, respectively. Classifying by the degree of seriousness, middle level endometriosis didn't appear in the control group, but 43 % and 71 % appeared in the groups given doses of 5 ng/kg and 15 ng/kg - a significantly high result. From these results, 126 (100 - 180) pg/kgBW/day is regarded as the LOAEL, with effects appearing at the lowest level. Other tests using series of red haired monkey support these results. When females were raised with a diet containing 50 ng/kg 2,3,7,8-TeCDD for seven months (equivalent to a dose of 1.26 ng/kgBW/day), two out of eight didn't conceive, four out of six pregnant monkeys had miscarriages, one out of two newborns was immature, and only one was normal.

Another report suggests that there is no significant difference in fecundity between control groups and groups fed a diet containing 5 ng/kg 2,3,7,8-TeCDD (equivalent to 126 pg/kgBW/day dose) for seven months, but after raising the dietary concentrations to 25 ng/kg (equivalent to 630 pg/kgBW/day dose) three out of eight animals didn't conceive, three out of five pregnant animals had miscarriages, one died during pregnancy, and there was only one normal birth.

These results prove that endometriosis observed in red haired monkeys fed a diet containing 5 ng/kg 2,3,7,8-TeCDD is one of the causes of miscarriage and sterility. Understanding the appearance of endometriosis is important and cannot be ignored because there is a dose-response relationship apparent in the results of these experiments, and this test is conducted using primates which have the closest half life and body burden of dioxins to that of humans.

However, there has been no confirmatory evidence from supplementary experiments, and the rate of appearance of endometriosis in the control groups was also fairly high, so there are a few problems in using this information directly in human health effect evaluations.

C. Examination of results of epidemiological research

The appearance of chloracne etc. is taken as a sign of human health effects of dioxins. In addition, a range of epidemiological research has been undertaken on occupationally exposed workers, accidental sufferers, and veterans exposed to Agent Orange in the Vietnam War.

There is one record of human poisoning by dibenzofurans - that of Yusho disease in Japan and

Taiwan. Taiwanese data suggests Yusho disease caused a delay in muscle growth, bone structure and sexual development, a drop in IQ, and effects on the immune system of newborn babies who were exposed through breast milk or prior to birth through the placenta, but case numbers are small and a complete evaluation has not yet been determined.

D. Conversion to toxicity equivalent values

Much of the available toxicity information on dioxins is mainly restricted to 2,3,7,8-TCDD, and that for other dioxins is rather limited. The toxicity of dioxins is strongly influenced by the number and position of the chlorine substituents attached to the molecules' ring structures, and the ability of molecules to combine with the receptors. To assess receptor binding potentials and hence toxicity, the toxicity, or potency, of 2,3,7,8-TeCDD and other dioxins (total 17 isomers of PCDD and PCDF which have substituted chlorines at positions 2, 3, 7, and 8) is expressed as a fraction of the toxicity of 2,3,7,8-TCDD. Expressions of TEQ (Toxic Equivalent) in this section indicate values which have been converted to potencies.

IV.3.4 Dose-response assessment

In Japan, health risk assessment index values are established as the TDIs which are desirable and acceptable limits which maintain human health.

IV.3.4.1 Establishment of TDI

Because there is no appropriate human epidemiology data at present, results of cancer development test by long term administration to SD rat were judged as the most reliable, and were adopted for establishment of the TDI. This test looked for significant increases in liver cell hyperplasia nodule and liver cell cancer, and cancroid of hard palate, nasal and lung membranes, after giving a mixed feed to SD rat for 105 weeks. The NOAEL of liver cell hyperplasia nodule and cancer are 1,000 pg/kgBW/day and 10,000 pg/kgBW/day, respectively.

Table IV-3-4 Establishment ground of TDI values (pg/kgBW/day) for dioxins

	liver hyperplasia nodule	liver cancer
NOAEL (pg/kgBW/day)	1,000	10,000
Uncertainty factor	100	1,000
Details : interspecies difference between rat and human	10	10
Individual difference within human	10	10
Significance of effects	1	10
TDI : (NOAEL/uncertainty factor)	10	10

Judging that there is threshold value for dioxins' carcinogenesis, 10 pg/kgBW/day becomes the TDI calculated by dividing the NOAEL by an uncertainty factor based on the results summarised in **Table IV-3-4**. The reason for the significance difference in effects between liver hyperplasia nodules and liver cancer is that liver hyperplasia nodules are benign and reflects the seriousness of liver cancer.

IV.3.4.2 Establishment of health risk assessment index value

The aim of health risk assessment index values are to prevent health effects by conducting environmental pollution reduction policies and to evaluate the amount of human exposure at desirable, maintainable levels. Therefore, attention is paid not only to carcinogenesis but also to the appearance of related effects, and health defects, to establish a health risk assessment index value.

From this point of view, the results of studies of endometriosis in the red haired monkey also have to be considered when establishing a health risk assessment index value because endometriosis data in the red haired monkey shows a dose-response relationship, and although the mechanism of the appearance of endometriosis is not clear, and the relationship between hormones and immune actions are assumed, the Ah receptor is linked to the appearance of toxicity.

At present, no country has directly established index values for dioxin intake using data obtained from red haired monkey experiments, but the Netherlands suggested a new index value of 1 pg/kgBW/day based on those results.(**Table IV-3-5**)

Table IV-3-5 Dioxins TDI values suggested by Netherlands (pg/kgBW/day)

	endometriosis
LOAEL (pg/kgBW/day)	100
uncertainty factor	100
details : interspecies difference between rat and human	2
individual difference within human	5
significance of effects	10
TDI : (NOAEL/uncertainty factor)	1

In Japan, because there have been no supplementary experiments to back up the data obtained form red haired monkey endometriosis tests, and the symptoms appeared in the control group, health risk assessment index values are not calculated directly from such endometriosis data. However, knowing that this is an important issue and important knowledge, the value of 5 pg/kgBW/day or a double uncertainty factor added to the TDI values (10 pg/kgBW/day) became the health risk assessment index value.

At this point there is no clear scientific data available to make a judgement on whether it is necessary to establish health risk index values lower than 5 pg/kg/day. However, there are some reports of lower dose experiments with results that suggest some health risks such as change of lymphocyte, increase in rates of death caused by influenza infection, decreased learning ability, decrease in reproductive organ weight and sperm production. Therefore, it is important to make an effort to accumulate scientific knowledge about dioxins, such as the effects of internal secretion systems etc., and to conduct re-evaluations of risk assessment when necessary, as well as to strive for more risk reduction

Table IV-3-6 Ground of establishment of dioxins health risk assessment index values(pg/kgBW/day)

	liver hyperplasia nodule	liver cancer
NOAEL (pg/kgBW/day)	1,000	10,000
Uncertainty factor	200	2,000
Details : interspecies difference between rat and human	10	10
Individual difference within human	10	10
Significance of effects	1	10
Possibility of endometriosis	2	2
Health risk assessment index values : (NOAEL/uncertainty factor)	5	5

IV.3.4.3 Exposure assessment

A. Dioxin Residues in the general environment

Concentration of dioxins in sediment and living things (fish) in rivers tend to be a little lower than those of lakes and seas, according to monitoring targeting countrywide rivers, lakes, and the sea undertaken Japan's Environment Agency since 1986. Also, Japan's Environment Agency has been monitoring the atmosphere since 1986, and revealing the trend for concentrations to be highest in residential areas near by industrial factories, lower in middle size urban areas, and lowest in background areas such as mountains.

B. Dioxin exposure situation from the general living environment in Japan

a) Exposure situation from the general living environment

The main routes of dioxins exposure in the general environment in Japan are considered to be (1) food, (2) the atmosphere, (3) water, and (4) soil, and an estimation of the amount of exposure

from each route has been undertaken.

(1) Intake from food (diet)

Dietary intake of dioxins in Japan is estimated to be 163 pgTEQ/person/day (equivalent to 3.26 pgTEQ/kgBW/day) by the market basket method targeting Osaka prefecture. In addition, according dietary intake estimated by the table meal method in 9 prefectures conducted by Japan's Environment Agency, is an average 1.25 pgTEQ/kg/day (0.26 - 2.60 pgTEQ/kg/day). Combing these results these together, dietary dioxins intake in Japan is estimated to be 0.26 - 3.26 pgTEQ/kg/day (**Table IV-3-7**).

Table IV-3-7 Intake of dioxins from food

Country	intake (pgTEQ/kg/day)
Japan (1)	3.26
Japan (2)	1.25 (0.26 - 2.6)
Germany	2.2
Canada	2.3
Netherlands	2.0
USA	0.3 - 3.2
UK	2.1

note : calculated using a standard body weight of
50 kg in Japan, 60 kg in the other countries

(2) Intake form the atmosphere

The following representative atmospheric dioxin concentrations in Japan were assumed on the basis of the results of monitoring in residential areas close to industrial zones, in middle and small sized cities, and background areas from 1990 to 1994, obtained by the Environment Agency, e.g. 0.6, 0.5, and 0.06 pgTEQ/m^3 for big city areas, medium and small size city areas, and background area. Atmospheric dioxin intake of dioxins is shown in **Table IV-3-8** and was calculated by multiplying the above representative concentrations by daily inhaled volume (15 m^3/day) and using a standard body weight of 50 kg.

Table IV-3-8 Estimated intake of dioxins from the atmosphere

	representative concentration (pgTEQ/m^3)	intake (pgTEQ/kgBW/day)
big city area	0.6	0.18
Medium and small size city area	0.5	0.15
Background area	0.06	0.02

note : estimated by using daily inhaled volume of 15 m^3/day, standard body weight of 50 kg

(3) Intake from water

The estimated intake from water is 0.000036 - 0.00048 pgTEQ/kgBW/day or 0.0004 - 0.0012 pgTEQ/kgBW/day of dioxin. From these numbers, it is considered sufficient to estimate the intake of dioxins from water as around 0.001 pgTEQ/kgBW/day.

(4) Intake from soil

Intake from soil is estimated by combining an estimate of intake by this route during childhood and then an estimate of intake for the rest of a person's life time (**Table IV-3-9**)

Table IV-3-9 Intake of dioxins from soil (pgTEQ/kgBW/day)

	oral intake			skin contact intake	total of intake from soil
	Child age	the rest of life time	Total		
City area	0.023	0.060	0.083	0.0013	0.084
Background	0.002	0.006	0.008	0.0001	0.008

(5) Summary of exposure situation of dioxins from the general living environment

The average amount of exposure to dioxins in Japan from the four routes described above is estimated to be around 0.3 - 3.5 pgTEQ/kgBW/day (**Table IV-3-10**).

Table IV-3-10 Average exposure amount of dioxins in the general living environment in Japan

(pgTEQ/kgBW/day)

	Big city area	middle and small size city area	background area
Food	0.26 - 3.26	0.26 - 3.26	0.26 - 3.26
Atmosphere	0.18	0.15	0.02
Water	0.001	0.001	0.001
Soil	0.084	0.084	0.008
Total	0.52 - 3.53	0.53 - 3.50	0.29 - 3.29

b) Exposure situation in 'biased environments'

In order to understand dioxin exposure in Japan in its entirety, in addition to estimating the exposure levels in the general living environment, it is necessary to assume a special, 'biased environment' with higher exposure levels than seen in the general living environment and estimate the difference between these exposure levels. The following two cases were chosen as examples of such biased environments :

- the case assuming that intake from fish is large because of Japanese eating customs
- the case assuming the environment surrounding an incinerator is one of the main sources of

dioxins in Japan

Actual, personal intake of dioxins is considered to have a fairly wide range depending on regional preferences and styles of cuisine. In addition, it is necessary to pay attention that estimation here is based on a certain premises:

(1) Exposure estimation in the case that intake from fish is large

i) Intake of fish

According to a national nutrition survey (1995), Japanese intake of fish and fish products is on average 95.2 g per day, standard deviation 52.0 g. If it is assumed that intake follows a normal distribution, then :

$$\mu + 1.64\sigma = 95.2 + 1.64 \times 52.0 = 180.5 \quad g$$

and about 5 % of people have a fish intake of 180 g per day, i.e. two times the average dietary intake of fish.

ii) Concentration of dioxins in fish

Research results suggest that there are differences in the concentration of dioxins in coastal and inshore fish, deep-water fish and imported fish found for sale in the market place and destined for human consumption, so it is necessary to distinguish both fish species and the source of the fish.

iii) Dioxin intake from fish

Representitive concentrations of dioxins in coastal and inshore fish are 0.90 pgTEQ/g. Representitive concentrations in deep-sea fish are 0.1 pgTEQ/g and 0.08 pgTEQ/g for imported fish.

(2) Intake of dioxins in the case that intake from fish is large

This estimation is performed by using the two assumptions shown below. However, whether such intake is continuous is dependent on the dining habits of the individual, and actual personal intake can be smaller than this evaluation.

i) in the case that fish intake is two times of average

It is assumed that there are 5 % of people who eat twice the average intake of fish, and in this case the estimate also assumes that these people don't eat meat or eggs as animal protein.

- Based on exposure research in Osaka using the market basket method, intake from fish is assumed to be 105 pgTEQ/day, or 4.2 pgTEQ/kgBW/day (2 x 105 pgTEQ/day ÷ 50 kg).
- It is assumed that the average intake of dioxins from food found in a survey conducted by the Environment Agency (1.25 pgTEQ/kgBW/day) originates in fish. Based on this, the average intake of dioxins from food is 1.27 pgTEQ/kgBW/day (2 x 1.25 pgTEQ/kgBW/day x 0.508).

- By using the above averages, dioxin intake from fish is 2.74 pgTEQ/kgBW/day [2 x (2.1 + 0.64) ÷ 2].

ii) in the case of intake of average amount fish from mainly coastal area

In this case, dioxin concentration in fish is 0.9 pgTEQ/g, and the average intake of fish is 95.2 g, then the average intake of dioxins from fish is 1.71 pgTEQ/kgBW/day (0.9 pgTEQ/g x 95.2 g/day ÷ 50 kg). There has been little data on dioxin intake from fish in Japan, and the few estimates of intake from fish have a wide range, but putting them together, the average intake of dioxins from food becomes 2.74 pgTEQ/kgBW/day, and possibility of dioxins intake from fish is estimated as around 1.28 - 4.2 pgTEQ/kgBW/day. In addition, including dioxin intake from other routes, dioxin intake is estimated as 3.59 pgTEQ/kgBW/day (1.90 - 5.28 pgTEQ/kgBW/day) in the large urban area (**Table IV-3-11**).

Table IV-3-11 Dioxins intake when the intake from fish is large (pgTEQ/kgBW/day)

	large urban areas (big cities)	medium and small cities	background (rural) areas
Food	3.32 (1.63 - 5.01)	3.32 (1.63 - 5.01)	3.32 (1.63 - 5.01)
Atmosphere	0.18	0.15	0.02
Water	0.001	0.001	0.001
Soil	0.0084	0.084	0.008
Total	3.59 (1.90 - 5.28)	3.56 (1.87 - 5.25)	3.35 (1.66 - 5.04)

Assumption : dietary intake of fish is twice the average amount of fish from inland sea and bay

(3) Exposure around incinerators

In this section, in order to understand exposure around incinerators, the largest yearly average concentration of dioxins which reaches the is predicted by calculating the diffusion of gas fumes from incinerator chimneys using modelling.

i) classification of incinerators and prediction of diffusion concentration

In order to characterise incinerators, incinerators are classified using 47 criteria, such as furnace type, cooling method, dioxin strategies, methods for treating gas fumes, height of chimneys etc. The maximum yearly average landed concentrations of dioxins originated in gas fumes from chimneys were predicted by atmosphere diffusion model for each classification. Estimates were conducted by assuming discharge of dioxins at concentrations two standard deviations higher than the average, according to the discharge concentration distribution current incinerators and the average discharge concentrations of dioxins. In these cases, incinerators were assumed to represent an average facility, and a composite of a mechanised batch system and independent chimney.

ii) Results of prediction of diffusion concentrations

For facilities which have average discharge concentrations, the maximum, yearly average landed concentrations of dioxins were predicted as 0.01 - 0.8 pgTEQ/kgBW/day incorporating measurements of dioxins in gas fumes, and 0.2 - 1.9 pgTEQ/kgBW/day without. For facilities which have higher than average discharge concentrations, the maximum yearly average landed concentration was predicted as about 3 pgTEQ/kgBW/day.

iii) Establishment of environmental concentration around incinerators

Dioxins concentrations in the atmosphere around incinerators were established as 3 - 4 pgTEQ/m^3 from the results of predictions of diffusion concentrations, and concentrations in the atmosphere in large cities. Atmospheric fall out was determined by the amount of deposition at the point of the maximum landed concentration. Concentrations in soil were obtained from actual data obtained from samples taken around incinerators used for industrial wastes.

iv) Total intake of dioxins around incinerators

Total intake of dioxins around incinerators was predicted by combining the amount of atmospheric deposition (100 ngTEQ/m^3/year), concentrations in the atmosphere (3 - 4 pgTEQ/$m)^3$, and concentration in soil (150 pgTEQ/g) s shown as **Table IV-3-12**.

In this section, the above two cases of special 'biased environments' were chosen as examples, but there is considered to be a wide range of actual personal exposures depending on differences in regional conditions and eating habits etc. These predictions are made using incomplete data for dioxins in the general environment and food etc. available from exposure assessment, and accumulation of data in future is necessary.

Table IV-3-12 Dioxins intake around incinerators

	intake (pgTEQ/kgBW/day)
food	0.26 - 3.26
atmosphere	0.9 - 1.2
water	0.001
soil	0.63
total	1.79 - 5.09

IV.3.4.4 Risk judgement

In Japan, 10 pgTEQ/kgBW/day was used as the TDI for dioxins, and 5 pgTEQ/kgBW/day as the health risk assessment index value. Then, from exposure assessment, an exposure of 0.3 - 3.5 pgTEQ/kgBW/day in the general living environment was estimated. The average amount of

exposure in groups which have twice the average intake of fish was assumed to be 3.6 pgTEQ/kgBW/day (1.0 - 5.3 pgTEQ/kgBW/day). The average amount of exposure in groups living around incinerators was estimated as 1.8 - 5.1 pgTEQ/kgBW/day. Putting all this together, the following can be concluded about the risk posed by dioxins in Japan:

- The possibility of health effects from general environmental exposure is considered to be very small at this point in time, because estimated exposure values are lower that health risk assessment index values. However, it is thought desirable to attempt to reduce environmental concentration of dioxins from this point forward in order to secure higher long term safety, because present exposure levels cannot be said to be low enough when compared to assessment index values.
- In order to decrease health risks in the future, there must be an attempt to reduce environmental concentrations of dioxins, because it is possible that estimated values of the amount of exposure will be the same as, or more than, the health risk assessment index values under conditions of especially high exposure..

The following views were not mentioned in this section's risk assessment of dioxins : A. mother - child transfer of dioxins through breast milk, and B. coplanar PCBs.

A. Intake from breast milk

Dioxins are secreted into milk. Dioxin concentrations in breast milk are approximately the same in the developed countries, including Japan. However, the WHO and many other nutrition experts keep promoting breast milk for infant nutrition because mother's milk has been shown to have clear advantages for infant health and growth. Since continued breast feeding is appropriate, proper measures to find the sources of contamination should be undertaken to secure the safety of mother's milk now and in the future.

B. Coplanar PCBs

It is difficult to conduct accurate exposure assessments of coplanar PCB because there is not enough data about environmental concentration etc., and dioxin toxicity equivalent factors have not evaluated. The toxicity of coplanar PCB has a similar mechanism to that of dioxins, so the human health risk through exposure to these compounds must be assessed, and to do this there must be more research and more accumulated knowledge of the toxicity of coplanar PCBs.

IV.3.5 Revision of the Tolerable Daily Intake (TDI) for dioxins

In 1996, the Japanese government set the TDI (Tolerable Daily Intake) of dioxins (PCDD/Fs : polychlorinated dibenzo-p-dioxins and polychlorinated dibenzofurans) at 10 pg / kg BW / day 2,3,7,8-TeCDD after the above mentioned procedure (**IV.3.3**). At the same time, "risk evaluation index values", which are defined as "the level which is desirable to maintain positively", were set at 5 pg/kgBW/day. Thereafter, in May 1998, the WHO European Centre of Environment and Health and IPCS (the International Programme on Chemical Safety) investigated published information on the toxicity of dioxins, and suggested that the TDI of PCDD/Fs should be 1 - 4 pg/kgBW/day, including 12 kinds of coplanar PCB (Co-PCBs). In response to this, in June 1999, the Japanese Government began to revise the TDI for dioxins (PCDD/FS and Co-PCBs), and decided on a value of less than 4 pg/kgBW/day. This change basically followed the WHO's suggestion. However, one feature of this process is that TDIs are determined not NOAEL or LOAEL which are obtained by animal toxicity tests, but body burdens. Therefore, the process of TDI calculation described in this section.

IV.3.5.1 Basic concept

The tolerable daily intake (TDI) is the amount of chemicals ingested per day which it is judged will not cause harmful health effects to appear even when humans ingest that amount for life.

After considering the movement of dioxins in the body, toxicity mechanisms etc., it is appropriate to base the calculation of TDI on the following concepts (**A.** to **D.**) based on the same criteria as the ones the WHO meeting adopted.

A. Judgment that there is no genetic harm

Dioxins are considered not to cause any direct genetic harm, and, therefore, the threshold level becomes the boundary of suspected harmful health effects. Therefore, the method applies an uncertainty coefficient into the NOAEL or LOAEL for calculation of the TDI.

B. Aiming at a body burden

For substances which have a high accumulation character but show big differences in the degree of accumulation between species, such as dioxins, it is appropriate to aim at a body burden rather than an amount of intake per day in order to investigate relations between the substances and the effects.

When small amounts of substances which have a high accumulation character have been taken continuously for long time, at first the accumulated amount of material increases because more is absorbed than is metabolised and discharged. However, as the amount accumulated increases, the amount of metabolism and discharge also increases, and the amount of material which exists in the body (the body load) reaches an equilibrium at a definite level corresponding to the amount of intake.

In general, the appearance of toxicity attributable to the chemical substance is related to the amount of material which exists in the body. However, it is important to know how much chemical substance is continuously ingested or absorbed by humans when the body load reaches the level which causes toxicity, in order to evaluate the toxicity of substances which have high accumulation characteristics.

Dioxins also show big differences in the rate of disappearance (half life) between species. Therefore, when applying results gained from toxicity tests to human beings, it is appropriate to aim not at dose, but body load, to determine the body load which causes health effects in test animals, and to determine how much amount is continuously ingested to reach the body load for human beings.

C. Evaluation of test data

For each toxicity test in which the toxic response at the lowest body load, after considering the toxicological significance of the reaction, is aimed at an evaluation index, dose dependency, reliability and repeatability of the test etc. becomes a TDI calculation object.

For dioxins, there are many reports of toxicity test results. Some of them judge that the responses which appear in animals has no toxicological significance, and some are tests whose reliability and repeatability are not good enough, even if the response itself has toxicity significance. These test results are not appropriate for use a baseline data from which to conduct quantitative evaluation of toxicity. Therefore, it is necessary to discuss carefully which test results should be chosen in order to adopted as the basis of a TDI calculation.

D. Set up of uncertainty coefficient

When the TDI of humans is calculated from the results of toxicity tests, factors such as species differences between animals and humans, individual differences in sensitivity to test substances between humans, and the reliability and propriety of toxicity tests etc. carry much uncertainty and have big effects on the calculated values. Therefore, during calculation, each factor must be carefully discussed, an appropriate coefficient (the uncertainty coefficient) set up, and methods

which compensate for the uncertainty chosen.

In the case of substances with extremely varied effects on living organisms, and where the appearance of such effects shows big difference between species and lineage, such as dioxins, the significance of the uncertainty coefficient is very important for toxicity evaluation.

In general, the uncertainty coefficient for species differences and individual differences are set up based on knowledge about the movement in the body, and the mechanisms of action. Test conditions, dose dependency and the toxicological significance of the effects which are used for evaluation etc. are also important factors for the reliability and propriety of toxicity tests.

IV.3.5.2 Body load in each toxicity test

Body burdens have been determined from 2,3,7,8-TCDD toxicity tests by collecting data from those extremely low doses which cause toxic reaction. Since such toxicity test data barely have appropriate NOAELs, LOAEL data were used instead. Also, when reliable values are available for body burden, such information was adopted, but otherwise calculated values based on estimates from literature knowledge were adopted.

IV.3.5.3 Animal body load which becomes calculation basis of TDI

Factors such as the adequacy of the results of toxicity tests which investigated the effects on derivatisation of drug metabolic enzyme (CYP1A1), the composition of lymphocyte, chlordane, immune toxicity, sex organ system (spermatozoon production, endometritis, sex organ form), and learning ability were discussed as the basis for TDI calculation by considering toxicological significance, dose dependency, reliability and reproducibility of tests.

IV.3.5.4 Human body load

There are no reports of systematic research into the relationship between species difference and body burden upon appearance of the effects of dioxin of toxicity. However, generalising the results of existing toxicity tests and epidemiological research, it is judged that there is no big difference between the body load which causes toxic effects in human and animals.

IV.3.5.5 Calculation of daily human intake

The same calculation and formula as that adopted by the WHO specialist meeting is used to estimate the average daily intake required for humans to reach their lifetime exposure body load.

IV.3.5.6 Determination of uncertainty coefficient

It is necessary to apply an uncertainty coefficient to calculate human TDI based on LOAEL for human which have been estimated from toxicity data in order to compensate for the inherent uncertainty of the data. The following factors, some of which are the same as those used by the WHO specialist meeting, were considered for the coefficient :

1. Use LOAEL instead of NOAEL as the baseline values for TDI calculation.
2. It is not necessary to consider species differences originating from transport in the body (see IV.3.5.4) because body burden is used at the time of calculation of the least toxic amount for humans.
3. There is no clear knowledge that human are more sensitive to dioxins than animals. Rather there is data which show that human are less sensitive. For example, Ah receptor affinity research.
4. Lack of knowledge about individual differences in the rate of appearance of toxic effects in humans.
5. Lack of knowledge about the half-life of each dioxin congener in humans.

IV.3.5.7 Determination of TDI

A. Selection of body load on which TDI calculation is based

According to tests which have clearly evaluated toxicity effects, the relationship between body load and the appearance of toxic effects in each toxicity test suggest that the value of the lowest appearance body load will be around 86 ng/kg.

B. Report of WHO (European Region Secretariat) specialist meeting

A specialist meeting of the WHO European Centre suggested TDI values within 1-4 pg TEQ/kg/day, but did not think that some reported tiny effects were obviously bad effects even when these tiny effects happened in residents of developed countries. Also, they considered 4 pg TEQ/kg/day as a tolerable daily intake at present, because confirmed effects can be related to other compounds than dioxins. However, they did suggest it appropriate to have a final goal of decreasing human intake levels to less than 1 pgTEQ/kg/day. Japan accepted this concept.

C. Conclusion

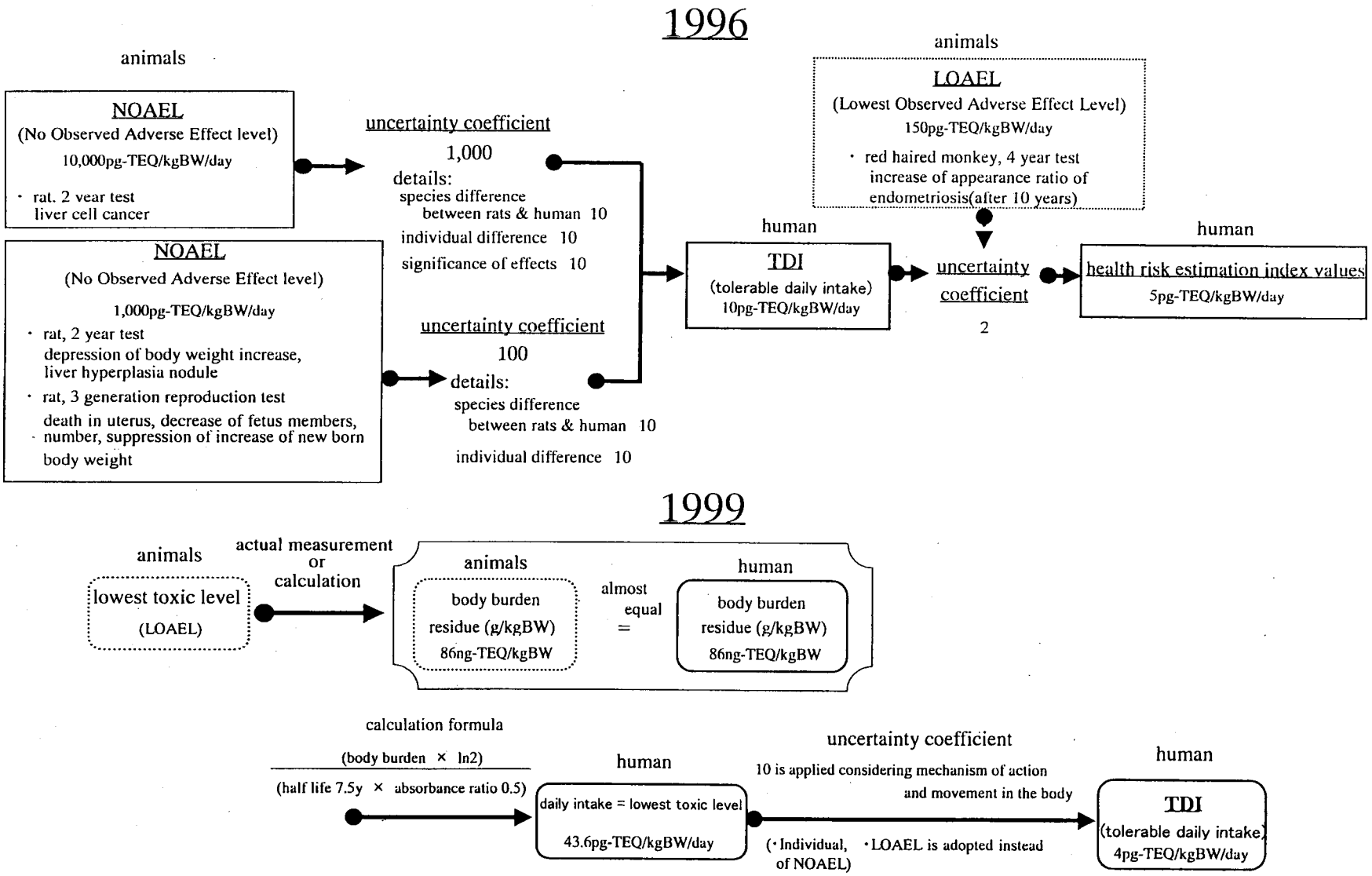
Although there are some unresolved aspects concerning the human health effects of dioxins, at present the TDI for dioxins had been set at 4 pgTEQ/kg/day (including coplanar PCB) based on calculations incorporating an uncertainty coefficient, a human daily intake of 10 to 43.6 pg/kg/day which corresponds to body load value, and 86 ng/kg as 2,3,7,8-TCDD. However, there are some known small negative effects at body loads less than 86 ng/kg, and, therefore, it is important to further toxicity investigations to determine the significance of these toxicological observations.

IV.3.5.8 Difference from former TDI calculation methods

Comparison between the 1996 and 1999 TDI calculation methods is shown in **Figure IV-3-3**. Although the 1996 version determines human TDI directly by applying an uncertainty coefficient to the non-toxic concentrations determined in toxicity tests, the 1999 version does not use the amounts administered in toxicity tests, but actual body loads as the basis of TDI calculations.

Usually, when a human TDI is determined from the results of toxicity tests, a standard uncertainty coefficient of 100 has been applied. During a recent risk assessment risk, scientific knowledge of the transport and mechanisms of action of dioxins in the body were introduced in order to set uncertainty coefficients based on species and individual differences, and these methods of estimating values appropriate for human application have come to be used. At that time, an uncertainty coefficient of 10 was set.

Again, usually TDI evaluation targeted results of long-term, continuous administration toxicity tests. However, such evaluation is based on the premise that dioxin toxicity is mainly manifested through combination with the Ah receptor, and it thus became possible to apply the results of single and short term administrations to animals to long term human exposure to trace amounts by using the concept of body loads. Therefore, highly sensitive, multiple health effect indexes, such as reproductive toxicity tests etc., can be considered.



FigureIV-3-3 Comparison of TDI calculation methods for dioxins

IV.3.5.9 Significance and notes on TDI

The general significance of TDIs is that TDIs are values calculated with the intention of aiming for a maximum daily intake without manifestation of negative health effects in the case of continuous intake for life. Therefore, there is no suggestion of harm to health if the long term average intake is within the TDI, even if intake temporally exceeds the TDI by a small amount.

The new TDI aims to minimise effects of exposure in early life stages (embryo / fetus) which are thought the most sensitive to dioxin toxicity tests. Therefore, for evaluation of human beings as a whole, the new TDI can be regarded as being on the safe side. In this respect, effects such as carcinogenicity appear as a result of higher exposure. Sensitivity differences between humans and animals, and individual differences are included by applying an uncertainty coefficients to the results of toxicity tests.

Exposure to dioxins is mostly from food. Individual contamination will vary depending on the type of food consumed. However, nutritionally it is important to eat a balanced diet. In addition, the benefits of breast feeding for infants are such that breast feeding should be encouraged, while scientists continue to research the effects of dioxin exposure through breast feeding on infants. Such conclusions were also reached by the WHO specialist meeting.

At present, the average Japanese daily intake is about 2.6 pgTEQ/kg/day. Exposure seems to be decreasing as dioxin concentration in breast milk is decreasing.

The current human exposure to dioxins in Japan cannot be said to be low enough when compared to the new TDI. Therefore, environmental discharges must be reduced in order to reduce concentrations of dioxins in food chains, and reduce human body loads. Since dioxins are not valuable chemicals produced commercially for the good of humanity, and at the very least they are non-beneficial, and possibly harmful, to all living things, it is obvious that reducing intake as much as possible is desirable for the benefit of all in the future.

IV.4 Ecological risk assessment

In the nature there are many, diverse living things and in adapting themselves to survive in their environment, they form ecosystems made up of many interdependent relationships which in turn contribute towards keeping an active balance of material and energy circulation. When chemicals invade in such systems, they may cause direct toxic effects on living things or cause indirect toxicity by changing the environment. When the effect on an organism exceeds its natural range of tolerance, interdependent relationships between organisms become irregular, at which point the ecological effects of the chemical begins to be observed . Ecological risk assessment of chemicals is an operation used to estimate the likelihood at which more than one chemical in the environment produces adverse effects on organisms and ecosystems. The results of ecological risk assessment are used as a standard for chemical management.

Ecological risk assessment is still in the process of being developed compared with human health risk assessment because of the many difficulties faced, such as species diversity, diversity of effects, differences in sensitivity, and differences in perceived value e.g. about which living things should be protected. The US EPA provided some general principles for ecological risk assessment in its "Guide to Ecological Risk Assessment" in 1996, and the EU describes methods of ecological risk assessment in the "environmental assessment " section of its "manual of new and present chemical risk assessment technique" published in 1997. In addition, the OECD strengthened the scientific technology basis of ecological risk assessment in the safety assessment program of high production volume chemicals (HPVC) and established ways for its active use. In this section, ecological risk assessment methods based on the methods of the OECD HPVC project are described since they have the most satisfactory results.

IV.4.1 Outline of ecological risk assessment of OECD HPVC project

The HPVC of OECD are a group of chemicals which produced in volumes greater than 1,000 ton in more than two countries, or more than 10,000 ton in one country. The project is based on the judgement that, in order to assess the environmental effects caused by current HPVC chemicals, it is most efficient to co-operate internationally to collect and evaluate data. This project has established a screening information data set (SIDS) for early risk assessment, supplementing patchy HPVC data, and then judges the necessity of additional investigation and tests based on each chemical's SIDS (**Table IV-4-1**).

Table IV-4-1 SIDS items necessary for early assessment

General information	Chemical Abstract registry No. (CAS No.), compound name, chemical structure
Source	production volume, use
Physicochemical characters	melting point, boiling point, density (specific gravity), vapour pressure, octanol-water partition coefficient (P_{ow}), water solubility, pH and pKa values, oxidation reduction potential
Environmental movement	photodegradation, degradation in water, biodegradation, Henry's law constant, environmental monitoring data
Ecological toxicity	fish acute toxicity, daphnia acute toxicity, algal growth inhibition, daphnia reproduction inhibition*, other toxicity (soil organisms, plants, birds)* →* : the necessity of the test depends on the judged degree of exposure
Toxicity	acute oral, inhalation, dermal toxicity, 28 days repeat administration toxicity, hereditary toxicity (in vitro, in vivo), reproduction toxicity, teratogenesis

This evaluation of early stage ecological effects of HPVCs on the hydrosphere by SIDS is used to clarify the risk to ecosystems by comparing the maximum tolerable concentration (MTC) and predicted environmental concentration (PEC). Ecological risk assessment based on results of environmental monitoring becomes possible by substituting the PEC with actual measurement data.

The MTC of ecosystem of the hydrosphere is considered to be the maximum chemical concentrations which don't appear to produce intolerable harmful effects by exposure, and the OECD supposes that when 95% of organisms are protected, hydrosphere ecosystems are preserved, i.e. safe. However effects on endangered species and precious species are considered individually.

The MTC of chemicals in a hydrosphere ecosystem is assessed by a three-stage process: initial stage, refined stage and comprehensive stage depending on available information type and quantity. **Figure IV-4-1** shows the flow chart.

At first, the data available for ecological risk assessment has to be checked and evaluated. At this point ,important factors are a chemical's octanol-water partition coefficient (P_{ow}), bioconcentration character, and effects on aquatic organisms.

P_{ow} should be evaluated carefully because it is very important to the initial stage of risk assessment. For example, P_{ow} obtained by the shaking flask method is not appropriate for measurement of non-polar chemicals ($P_{ow} > 5$), so the slow stirring method or generator column method should be used. Also, P_{ow} is not appropriate for surfactants, polymers, inorganics, and organometallic compounds.

Bioconcentration character is an index of indirect effects, obtained by experiments or

quantitative structure activity relationships (QSAR). However, QSARs often cannot predict concentrations of chemicals which are non-polar under outdoor conditions. When there are more than one bioconcentration factor (BCF) for some species, the geometric mean for the species should be used, but experimental conditions should be considered as well. When there is a BCF for more than two species, use the one for the most nutrient intensive lifestage. BCFs for algae, daphnia, and fish should be treated separately.

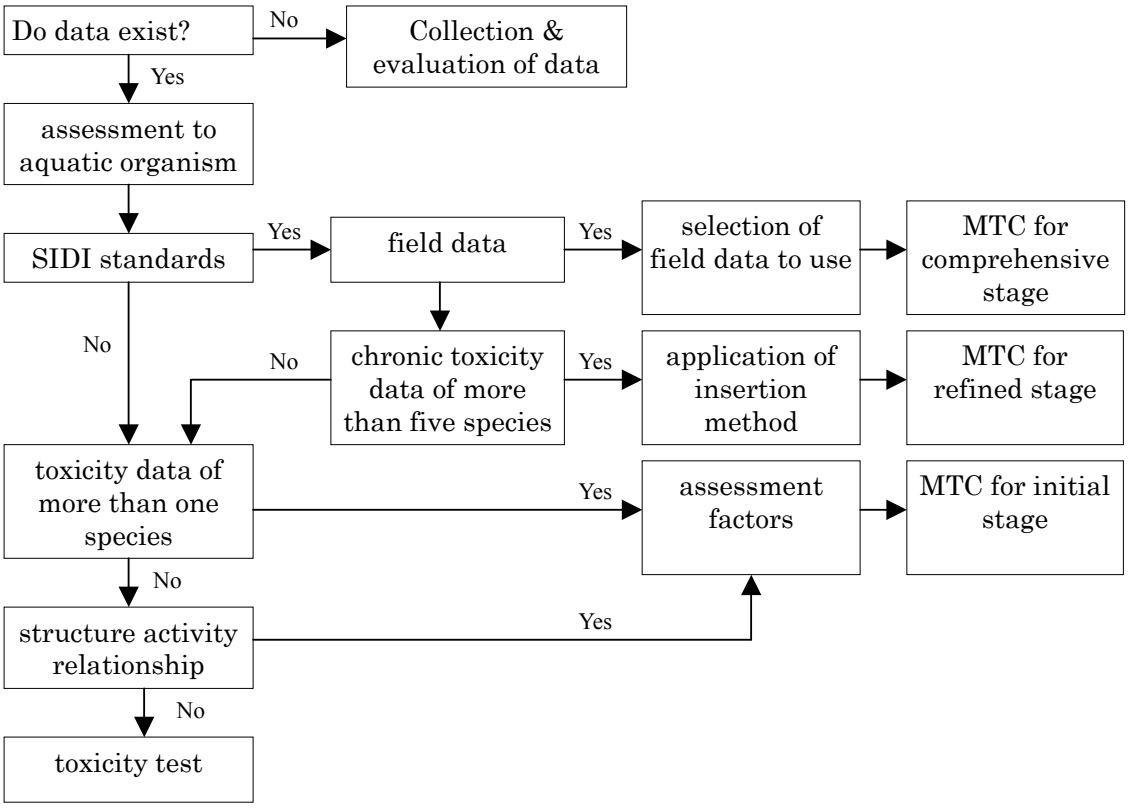


Figure IV-4-1 Flow chart for calculation of maximum tolerable capacity (MTC)

The results of chronic toxicity tests are needed for chemicals which have a high BCF. A 96 hr acute toxicity test is not long enough for these compounds. Know the solubility of the target compounds in water, solubility limits and effective concentrations.

Interpretation of toxicity data is important, for example, measurement / set-up concentration, response of control group, use of high sensitivity species, and water quality values. Endpoints such as survival, growth, reproduction should be paid more attention than other endpoints such as biochemical parameters. If a chronic toxicity test wasn't conducted for most sensitive species determined by acute toxicity testing, it is necessary to pay attention to the kinds of experimental animals used.

When there is a range of toxicity data for one species, the following points should be considered.

- If toxicity data is collected over the same period as the effect parameter (endpoint), use geometric parameter.
- When effect parameter and exposure period are different for one species, use the lowest values from the longest experiments after considering the importance of both endpoint and exposure period.
- Data used for insertion method are limited only for NOEC values and geometric mean MATC values [MATC = (NOEC x LOEC)$^{1/2}$]. For a chronic toxicity test which reports only the lowest effect concentration (LOEC), if the values are converted to estimated NOEC values properly, they can be adopted. For example, NOEC = LOEC / 2 for one particular case can be used. Also regression formula for estimation can be used.

At the initial stage, generally short term (acute) toxicity test for primary producers (algae), primary consumer (daphnia), and predators (fish) is needed. At more refined stages, long term (chronic) toxicity, semichronic toxicity tests, and at the comprehensive stage, diverse species mixture test and data from field observations. The initial evaluation based on SIDS applies an evaluation factor. If there is no toxicity data, or only data from one species, or the data is unreliable, predicted values by QSAR can be used if the situation warrants it.

For compounds where data is available which exceeds the range of SIDS, higher level evaluation can be conducted. If chronic NOEC for more than five different species is available, the insertion method which considers sensitivity of other species can be applied. Also, if data from short term multi species tests and (semi) field tests, including long term ecosystem observations, are available, comprehensive evaluation becomes possible by combination with chronic toxicity data. Evaluation factors in this case are judged depending on the situation. Indirect effects on birds and mammals and effects on benthic organisms can be considered depending on the use and characters of chemicals.

Thus, ecological risk assessment becomes possible by comparing “estimated non-effective concentration” which are basically expressed as PNEC and MTC etc. and “data from environmental monitoring”. Therefore, according to the above mentioned processes, the kinds and meaning of ecological toxicity tests which are necessary for the calculation of estimated non-effective concentration, the use of toxicity data and risk assessment method are described as follows:

IV.4.2 Ecological effect tests

IV.4.2.1 Representative values of toxicity

The results of ecological effect tests are eventually collated statistically as representative values such as LC_{50} (lethal concentration 50 %), LD_{50} (lethal dose 50 %), EC_{50} (effect concentration 50 %), ED_{50} (effect dose 50 %), TC_{50} (tumour concentration 50 %), TD_{50} (tumour dose 50 %). These representitive values become important indexes for ecological risk assessment. The capital letters, L, E, and T, of these description indicate a toxicity endpoint : L is short for the lethal of lethal toxicity, E, observed effects (endpoints) such as abnormality in appearance, behavioural change, biochemical pathological change, growth inhibition, reproductive inhibition, increase in rate of deformity, etc; T is used for appearance of tumours as the endpoint. The second capital letter indicates the exposure routes : C means concentration in air or water, D an oral or dermal dose. Since ecological effect tests have been mainly conducted for aquatic organisms, more data is available on concentrations than direct doses. The letters of the end indicate ratio of the observed number of endpoints against a given sample number, shown as a percentage. Therefore, LC_{50} means half of a given sample will die at the stated concentration, and LC_{10} indicates an exposure concentration which causes mortality in 10 % of the sample. By the way, E often means not only hazardous effects, but also harmless or useful effects, for example ED_{50} is frequently used for judging the effects of animal medicines.

In ecological effect tests, the greatest concentration of a chemical which doesn't cause an effect with a significant difference from the control group is called the no observed effect concentration(NOEC). The NOEC is an important risk assessment index, and is calculated from experimental data statistically (multiple comparison test at 5% risk rate). The no observed effect level (NOEL) is the maximum amount of toxicant that does not produce an effect, and may be calculated by converting the NOEC to a level, and is used for both exposure concentration and intake. The lowest concentration which causes an effect is the lowest observed effect concentration (LOEC).

IV.4.2.2 OECD ecological effect test methods

The OECD recommends 11 test methods in its ecological effect test guidelines, revising and adding to them as required, and ecological risk is assessed from the results of such tests either comprehensively or step by step. Of the tests, the algal growth inhibition test, the daphnia acute toxicity test, and the fish acute toxicity test are designated as 'minimum premarketing sets of data'

(MPD), and the minimum toxicity data necessary for initial stage screening. The Japanese Environment Agency conducts five tests - algal growth inhibition test, daphnia reproduction test, fish acute toxicity test, plant growth test, and earthworms acute toxicity test.

A. Algal growth inhibition test (201)

a) Purpose and meaning

Algae are the primary producers in the hydrosphere's food network. Plants which produce food and oxygen are the most basic requirements for consumers. Extreme increase and decrease in algal growth caused by chemicals will affect organisms at higher trophic levels in natural ecosystems. This test can investigate the effects of chemicals on growth and reproduction of single celled green algae for several generations under standard experimental conditions. However, it is often not appropriate to extrapolate the results of this test to effects on other primary producers.

b) Experimental method and results

Algae species used in this test are *Selenastrum capricornutum*, *Scenedesmus subspicatus*, and *Chlerella vulgaris*. Standard culture techniques are used. Under continuous lighting, the algae are exposed to the target compound for 96 hours at 21 - 25 ± 2 °C, and the growth of the algae is measured (total organism or cell numbers) at 24, 48, 72, and 96 hours after the beginning of the experiment. By drawing a growth curve from the data obtained, and comparing the area underneath the growth curve, or the growth rate, with that of the control, inhibition rates such as the EC_{50} and NOEC can be calculated.

B. Daphnia acute toxicity test (202 Part I)

a) Purpose and meaning

Daphnia are important primary consumers in the hydrosphere ecosystem, and useful for initial stage risk assessment because they are sensitive to many toxic substances, and because their response is similar to other aquatic invertebrates. This test also plays a role as a preliminary, or concentration range-finding test for the next step (reproduction test : Part II). The daphnia test is an economical method which gives useful information for risk assessment or planning of supplementary test.

b) Experimental method and results

The daphnia species used in this test is *Daphnia magma* or other daphnia, cultured in the standard culture medium within 24 hours after birth. The daphnia are exposed to target

compounds for 24 hours (48 hours is also OK) without feeding (at 18 - 22 ± 1 °C). After 24 or 48 hours observation, the number of mobile / immobile daphnia is counted Swimming inhibition is defined as being when daphnia doesn't move after mechanical stimulation or gentle shaking. The inhibition rate for each concentration is calculated, and the EC_{50} and the lowest concentration which inhibits swimming in 100 % of daphnia is calculated

C. Daphnia reproduction test (202 Part II)

a) Purpose and meaning

Daphnia are important primary consumers in the hydrosphere ecosystem, and useful for initial stage risk assessment because they are sensitive to many toxic substances, and because their response is similar to other aquatic invertebrates. This test uses the results of the daphnia acute toxicity test (Part I), and is considered to belong to the category of long-term (chronic) toxicity tests because it covers the life cycle of daphnia, the and the standard effects assessed, i.e. endpoints, give useful information economically for risk assessment or the planning of supplementary experiments.

b) Experimental method and results

The daphnia species used this test are the same as used in daphnia acute toxicity tests (Part I). Lighting cycle, hours light, and 8 hours dark. The daphnia are exposed to the chemical for at least 14 days at 18 - 22 ± °C. The experiment is conducted in flow-through systems, and total exchange of water and observation are done at least every 48 hours. Observations with the naked eye include such things as life/death of parent, existence of eggs in the incubator male, dormant eggs, parent size, number of babies, etc. The rate of inhibition of reproduction for each concentration is calculated, and the EC_{50} and LC_{50} calculated, The NOEC is obtained by statistically comparing the number of babies in the treatments against those in the control.

D. Fish acute toxicity test (203 revised)

a) Purpose and meaning

Fish are high level consumers in hydrosphere ecosystems. Fish acute toxicity tests can give index of concentration-response relationships, but cannot give information about target organ toxicity mechanism because pathological dissection is not conducted.

b) Experimental method and results

Fish typically used are Zebra fish, *Brachydanio rerio*, Flathead minnow, *Pimephales promelas*,

Carp, *Cyprinus carpio*, Red killifish, *Oryzias latipes*, Guppy, *Poecillia reticulata*, Bluegill, *Lepomis macrochirus*, and Rainbow trout. Tests may be conducted in static or flow-through systems. Lighting is 12 - 16 hours/day, water temperature is appropriate for the test species ± 2 °C, and exposure to target chemical is for 96 hours without feeding. Mortality is observed at 24, 48, 72, and 96 hours after the test begins. The mortality rate for each concentration is calculated, and LC_{50}, the lowest concentration that causes 100% mortality, and NOEC calculated

E. Fish prolonged toxicity test (204)

a) Purpose and meaning

This test is used when longer observation than are possible with acute tests are more appropriate to gather the information needed.

b) Experimental method and results

The same fish species used in acute toxicity tests may also be used for longer term tests, i.e. Zebra fish, Flathead minnow, Carp, Red killifish, Guppy, Bluegill, and Rainbow trout. Aqueous concentrations of the test chemical are set such that lethal and other sub-lethal effects can be determined, and NOEC values calculated. Tests may be conducted in static or flow-through systems. Lighting is 12 - 16 hours/day, water temperature is appropriate for the test species ± 2 °C, and exposure to target chemical is for 14 days. Mortality is observed every day, and other effects as appropriate e.g. appearance, abnormal swimming behaviour, response against stimulation, and feeding may be checked daily, body length and body weight changes checked at the end of the exposure period. If necessary, the observation period can be extended for a further 1 - 2 weeks. The NOEC is determine after calculating the mortality rate for each concentration.

F. Bird acute toxicity test (205)

a) Purpose and meaning

After feeding the birds the target compound for five days, determine the chemical concentration in the food causes 50 % death within three or more recovery terms.

b) Experimental method and results

Use juveniles of Mallard, Quail (Korin-uzura), Pigeon, Common Quail, Pheasant (Korai-kiji), and Partridge. Feeding conditions depends on the bird species, but in general enclosures (bird cages), temperature, humidity, and lighting should be suitable for keeping them. Feed the test groups food containing target chemical by for five days,. Allow the birds to feed as much, or as

little, as they want. Then feed chemical-free for at least three days. If effects continue, extend the period, and observe toxic symptoms, abnormal behaviour, death, body weight, and feeding amount. The mortality rate for each concentration and LC_{50} calculated.

G. Avian reproduction test (206)

a) Purpose and meaning

To investigate the concentrations of target chemical which affects avian reproduction by comparing with control.

b) Experimental method and results

Adult birds of Mallard, Quail (Korin-uzura), Common Quail etc. Enclosures depend on the species and age of the birds, and the temperature (22 ± 2 °C), humidity, and lighting should be suitable for keeping them. Raise either a pair of birds, or one male and two females as a group in the enclosures. Experiments start when the birds are first given food containing the target chemical. Allow the birds to feed freely throughout the experimental period. When egg laying begins, collect the eggs every day and store them in an incubator to hatch them. Don't incubate obviously damaged eggs. Measure the thickness of the egg shell for a number of eggs from each treatment. Compare mortality rates, body weight, amount of feeding, pathological observation, number of eggs laid, number of damaged eggs, thickness of egg shell, survival ability, incubation rate of parent birds, and survival rate, body weight, feeding amount of juvenile birds, with the control groups, then determine the statistically significant NOEC and effective concentrations.

H. Earthworm acute toxicity test(207)

a) Purpose and meaning

This basic, short term exposure test using terrestrial organisms uses soil as the transport medium for pollutants. There are two tests, one uses an artificial soil, the other simplified test is a filter paper feeding toxicity test.

b) Experimental method and results

Use *Eisenia foetida* which are at least 2 months old. For the filter paper feeding toxicity test, expose the worms to the target chemical in the dark at 20 ± 2 °C for 48 hours (or 72 hours) without feeding, and observe mortality rate after the exposure ceases. For the artificial soil test, expose the worms to the target chemical under continuous lighting at 20 ± 2 °C for 14 days without feeding, and observe fate of earthworms on days 7 and 14. Calculate the rate of inhibition for each

concentration, and determine the LC_{50}, the lowest concentration which causes 100 % mortality, and the lowest concentration in which 100 % survive.

I. Plants growth test (208)

a) Purpose and meaning

This test is used to assess the effects of solid or liquid target chemicals on germination and early stage growth of various land plants in soil which has been treated once with the target chemical.

b) Experimental method and results

Plants used for the test are divided into the following three categories, i) rice plant, wheat, etc. ii) rape, radish, turnip, etc. iii) pea, lettuce, koroha, etc. Choose at least one species from each category. Use soil which has been sifted through a 0.5 mm sieve, has a carbon content of less than 1.5 % (organic matter content 3 %), contains 10 - 20 % of particles less than 20 μm, and whose pH is adjusted between 5.0 - 7.5. Within 24 hours of the target chemical being mixed into the soil, plant more than five seeds of the same size, and raise under appropriate conditions of temperature, humidity, and lighting, and watering. Harvest the plants no earlier than 14 days after 50 % of control group has germinated, and calculate the rate of germination for each concentration and the average weight per plant. Calculate the rate of inhibition for each concentration, and determine the EC_{50} (growth) and LC_{50} (germination).

J. Activated sludge respiration inhibition test (209)

a) Purpose and meaning

This tests monitors the effect of activated sludge on decomposers in the environment. It is a useful test to monitor the effects on sewage treatment facilities because it is not sensitive to even highly toxic chemicals. This test determines chemicals which cause harmful effects to aerobic microorganisms in sewage treatment facilities, and provides a quick screening method to determine chemical concentrations which do not inhibit biodegradation tests.

b) Experimental method and results

Use 3,5-dichlorophenol as a standard compound. The EC_{50} (3 hours) of this compound is 5 - 30 mg/L. The activated sludge used for the test is collected from a sewage treatment facility which mainly treats domestic sewage, and made up to 4 g MLSS/L after washing. Control1 : add 16 mL of artificial sewage before start of the test, add 200 mL of activated sludge and aerate by Pasteur

pipette (0.5 - 1.0 L/min). Prepare test concentrations every 15 minutes, and finally, make Control 2 in the same way as Control 1. After three hours, measure the respiration rate of Control 1 by using a dissolved oxygen meter for 10 minutes (Rc_1). Measure the respiration rate of each test concentration every 15 minutes (Rs), make each feeding time 3 hours. Finally, measure Control 2 (Rc_2). Feeding time can be 30 minutes. Calculate respiration rates from a locus of linear part within about 6.5 - 2.5 mg/L of dissolved oxygen, and determine inhibition rate from the formula [(1 - (2Rs) / (Rc_1 + Rc_2)].

K. Fish early life stage test (210)

a) Purpose and meaning

This test clarifies lethal and sub-lethal chemical effects on fish during different growth stages.

b) Experimental method and results

For freshwater species, use Zebra fish, Fathead minnow, Killifish, Rainbow trout; for seawater fish use the Sharphead minnow. Use 3,5-dichlorophenol as a standard compound. The EC_{50} (3 hours) of this compound is 5 - 30 mg/L. Use adult fish, baby fish and fry as samples. The test is conducted in static or flow-through exposure systems, and expose just fertilised eggs to the target chemical at least until all control fish feed freely. During exposure, keep dissolved oxygen at more than 60 % of saturation without aerating. Observe incubation, survival, behaviour, and appearance abnormality every day, and measure body weight and body length at the end of the test. Determine the NOEC and LOEC for each endpoint, such as death rate, survival rate of embryos, baby fish, and fry, and incubation time, body length and body weight, abnormal behaviour / shape, etc.

IV.4.2.3 Multi species mixture ecological toxicity test

Most of the OECD's ecotoxicology tests observe adverse effects on specified single species, except for the test using activated sludge, and the principal viewpoint is distinction of reproduction and other effects to the organisms. It is, however, important to evaluate effects on ecological structure or function in order to evaluate chemical effects on ecosystems. One cannot neglect to understand effects on ecologically important parameters such as energy flow, reciprocal relation, material circulation, change of respiration, self fixation ability, or bioconcentration. Investigation of ecological effects use microcosms or mesocosms consisting of a diverse mixture of species including ecological producers, predators, and decomposers.

A microcosm is a small, model hydrosphere ecosystem, and individuals or groups of organisms are raised in a container environment where it is possible to control nutrition, day-night cycles, temperature, light intensity etc. Several test systems of different size and group composition have been used for ecological effect assessment. There are scene-set-up type, pilot plant type, and flask type systems in which the composition of species is known exactly, and in which it is possible to measure the numbers of individuals, and analyse the character of each species. The system can be maintained under specific conditions and develop after natural selection for one particular group of organisms.

A mesocosm is an isolated field experimental system, isolated from the rest of the hydrospheric environment. There are static types e.g. small lakes and ponds, and flow through systems, such as streams and small rivers.

These chemical ecotoxicology tests using diverse species generally determine ecosystem non-effect concentration, fixable concentration, species co-existence possibility concentration, and ecosystem destruction concentration etc., by observing changes in numbers of individual and groups, ATP (adenosine triphosphatase) activity, and respiration activity etc. However, multi species mixture tests need multi-variate analyses to investigate and assess effects and it is often difficult to report the results as one numeric value, compared to single species tests the results of which are easy to quantify. Therefore, there are many problems in the use of the results of mesocosm and microcosm tests, such as the development of appropriate analytical evaluation methods and clarification of methods for mathematical analyses, and ecological effect tests using mixtures of diverse species are still under research, and haven't yet reached the stage where they are able to be used for regular evaluation of chemical ecological risk.

IV.4.2.4 Cultured cell toxicity test

Instead of *in vivo* toxicity test using individual organism, investigations using *in vitro* test with cultured cell systems have become popular. Test using cultured cells can give results easily and quickly, and it is expected to become a useful method for toxicity assessment by finding correlations with the results of *in vivo* tests.

Fish cells originating from Rainbow trout, Bluegill, Carp, and Killifish etc. can be used. Chemical toxicity in cultured cells are evaluated by measurement and observation of life and death of cells and cell numbers, amount of protein, colony formation, reproduction rate using amounts of DNA, RNA as an index, enzyme activity, form change, DNA damage, chromosome abnormality, and mutagenesis etc.

IV.4.3 QSAR

It is not true to say that ecotoxicology tests have been conducted on all currently used and produced chemicals, nor that toxicity information for risk assessment is available for all such chemicals. Therefore, because of the experience that "chemicals which have similar structure or similar physiochemical characters have similar biological activity, such as toxicity", quantitative structure activity relationships (QSAR) have been developed, and used for prediction of toxicity where data is not available for ecological risk assessment and the confirmation of results of toxicity tests.

In order to estimate toxicity from chemical structures, a value of toxicity to organisms for at least one chemical, chemical structure and reactivity parameters, and statistical tests are needed. Chemical toxicity is caused by a chemical reaction with a target organ after being transferred into the general area of the target organ in the body, so QSAR is expressed by the following empirical formula :

$$\log (1/C) = \text{transport effect} + \text{electron effect} + \text{steric effect} + \text{constant}$$

where C is the molar concentration of chemical causing toxicity. For chemicals which have a fair degree of similarity in their core and active structural components transport, electron, and steric effects are often expressed as substituent parameters. Famous ones are hydrophilicity (π), Hammett constant (σ), and Traft steric substituent constant (Es), respectively. π is expressed as the octanol-water partition coefficient of a substituent, σ is benzoic acid ester, Es is a substituent constant which is determined from hydrolysis reaction rate constant of the aliphatic ester. In order to apply this empirical formula to chemicals which don't have structural similarity, establishment of parameters which can explain the behaviour of not just substituents, but the whole molecule is required. For example, octanol-water partition coefficients, parachor, water solubility, molecular volume, molecular surface area etc. for the transport term; dissociation constant (pKa), molecular orbit index, dipole moment, electron polarity etc. for the electron term; and molecular weight, van der Waals force, molecular volume, molecular shape, molecular surface area, Traft steric substituent constant (Es), molecular refractive index, topological parameter etc..

There are cases where the assumption of similarity is difficult because of the diversity of chemicals to be estimated. Therefore, a QSAR which ignores the similarity assumption is conducted. In general, the accuracy of estimation becomes poor, but practicality increases. That is the method which determines regression formulae for toxicity values and parameters, and each

value and devices of parameter relate to accuracy.

For example, the following relationships between fish acute toxicity (LC_{50}) and MCI (molecular connectivity index, $^3\chi_p$) or octanol-water partition coefficient ($\log P_{ow}$) :

i) molecular connectivity index

$\log (1/LC_{50}) = 3.581 + 0.539\ ^3\chi_p$ (r = 0.769, n = 581)

$\log (1/LC_{50}) = 30.142 + 0.419\ ^3\chi_P - 2.636$ (IP/atom) (r = 0.838, n = 581)

ii) $\log P_{ow}$

$\log (1/LC_{50}) = -3.732 + 0.7351 \log P_{ow}$ (r = 0.783, n = 571)

$\log (1/LC_{50}) = -4.027 + 0.4581 \log P_{ow} + 0.316\ ^3\chi_P$ (r = 0.854, n=571)

where unit of LC_{50} is μmol/L, IP/atom is ionisation potential and determined from the following formula :

IP/atom = (fist ionisation potential of each atom, eV) / Σ atomic numbers

The above regression formulae are obtained without limiting the species of fish, experimental period, and kinds of chemical, and if only compounds which are the same structure series are used, regression formulae with a higher correlation can be obtained.

The OECD puts QSAR application range together as follows : QSAR can only apply to a compound which has normal toxicity, such as anaesthetic compound, and which depends on chemical polarity (e.g. $\log P_{ow}$), liquid compounds at room temperature and a solid compound whose water solubility data is known. The OECD classified chemicals into two categories shown in **Table IV-4-2**. Class I compounds can be used for fish, daphnia, and algae, Class II compounds can be estimated by QSAR of fish acute toxicity.

Table IV-4-2 Categorisation of chemicals for QSAR

classification	structure	applicable QSAR	reliability
Class I	aliphatic alcohols, aliphatic ketones, aliphatic ethers, alkoxy ethers, halogenated aliphatic hydrocarbon, saturated alkanes, halogenated benzenes (containing C, H, N, O, G, Cl)	fish and daphnia acute, chronic toxicity, algal chronic toxicity (non-polar anaesthetic compound)	concentration can be predicted
Class II	non or weak acidic phenol, aromatic amine, aniline, aliphatic primary amine, weak basic pyridine	fish acute toxicity (phenol and aromatic primary amine)	range can be predicted

The following regression formulae can be used:

i) class I

- Fathead minnow (*Pimephales promelas*) 96 hours 50 % lethal concentration (96h-LC_{50})
  $\log LC_{50}$ (mmol/L) = -0.94 $\log P_{ow}$ + 0.94 $\log (0.000068 P_{ow} + 1)$ + 1.75 (r^2 = 0.98, n=65)
- Guppy (*Poecilica reticulata*) 7 and 14 days 50 % lethal concentration (7,14d-LC_{50})
  $\log LC_{50}$ (mmol/L) = -0.87 $\log P_{ow}$ + 1.87 (r^2 = 0.98, n = 60, S = 0.24)
- Fathead minnow (*Pimephales promelas*) and Zebra fish (*Brachydanio rerio*) 28 days no effect concentration (28d-NOEC) and no effect concentration of early life stage test (ELS)
  $\log$ NOEC (mmol/L) = -0.90 $\log P_{ow}$ + 0.8 (r^2 = 0.91, n = 30, S = 0.33)
- Water flea (*Daphnia magna*) 48 hours 50 % free swimming inhibition concentration (48h-EC50)
  $\log EC_{50}$ (mmol/L) = -0.91 $\log P_{ow}$ + 1.72 (r^2 = 0.98, n = 19, S = 0.33)
- Water flea (*Daphnia magna*) 18 - 21 days reproduction inhibition no effect concentration (18-48h-NOEC)
  $\log EC_{50}$ (mmol/L) = -1.04 $\log P_{ow}$ + 1.30 (r^2 = 0.98, n = 17, S = 0.25)
- Water flea (*Daphnia magna*) 18 - 21 days growth inhibition no effect concentration (18-48h-NOEC)
  $\log EC_{50}$ (mmol/L) = -1.07 $\log P_{ow}$ + 1.25 (r^2 = 0.97, n = 10, S = 0.40)
- algae (*Selenastrium capricornutum*) 72 - 96 hours 50 % growth inhibition concentration (72-96h-EC_{50})
  $\log EC_{50}$ (mmol/L) = -1.00 $\log P_{ow}$ + 1.77 (r^2 = 0.93, n = 10, S = 0.17)

ii) Class II

- Fathead minnow (*Pimephales promelas*) 96 hours 50 % lethal concentration (96h-LC_{50})
  $\log LC_{50}$ (mmol/L) = -0.65 $\log P_{ow}$ + 0.7 (r^2 = 0.95, n = 40) phenols, anilines (polar anaesthetic action)
- Fathead minnow (*Pimephales promelas*) 96 hours 50 % lethal concentration (96h-LC_{50})
  $\log LC_{50}$ (mmol/L) = -0.60 $\log P_{ow}$ + 0.6 (r^2 = 0.97, n = 21) phenols (polar anaesthetic action of non-coupling agent)
- Fathead minnow (*Pimephales promelas*) 96 hours 50 % lethal concentration (96h-LC_{50})
  $\log LC_{50}$ (mmol/L) = -0.59 $\log P_{ow}$ + 0.2 (r^2 = 0.98, n = 6) phenols (non-coupling action of oxidising phosphorisation?)
- Fathead minnow (*Pimephales promelas*) 96 hours 50 % lethal concentration (96h-LC_{50})

$\log LC_{50}$ (mmol/L) = -0.67 $\log P_{ow}$ + 0.05 (r^2 = 0.91, n = 11) phenols, anilines (non-coupling agent)

IV.4.4 Use of toxicity data

IV.4.4.1 Prediction of no effect concentration

Methods which predict the no effect concentrations of chemical are complex and not easily understood, and still under research. Thus it is necessary to establish evaluation systems as open systems which always reflect research results and adopt temporary evaluation methods.

Data added with application of chemical registration are generally results of acute toxicity tests. However, ecological risk assessment requires predicted no effect concentrations (PNEC). The PNEC is the concentration which cannot predict some intolerable harmful effects on an ecosystem, and the target actually analysed is a conceptual calculated value. The HPVC project of the OECD expresses it as a maximum tolerable capacity (MTC), but generally the term PNEC is used for the hydrosphere environment,.

For example, ecotoxicology tests using fish include 96h fish acute toxicity tests, prolonged toxicity tests (14 - 21 days), and early life stage tests. However, toxicity data obtained from these tests have different meanings. Therefore, for PNEC prediction it is necessary to put them together in a standardised manner which absorbs the differences in the toxicity data. In addition, predicted PNEC also considers other variables, such as difference between individuals within the same species, species differences, combination of experimental methods, unknown factors etc. Thus factors used for simplification of prediction are called assessment factors (Afs), which have the same meaning as uncertainty factors and safety factors. There is no firm scientific ground to calculate Afs, and countries or international organisations decide them individually.

At the process of refined stage as shown in **Figure IV-4-1**, the insertion method considering different sensitivity between species can be used for PNEC prediction. The insertion method relies on methods of statistical probability, and three methods based on computer programs can be used. In practice, chemicals for which satisfactory toxicity data is available are extremely limited and such application cannot be used in a lot of cases.

By combining the test results using complex systems such as laboratory system using diverse species, microcosm, experimental ponds, field experiments etc., a comprehensive evaluation can be considered. At present, there is no internationally agreed protocol concerning ecosystem experiments, but the US EPA has been developing multispecies test methods, and guidelines have be made by the Society of Environmental Toxicology and Chemistry (SETAC). The OECD recommends criteria in order to judge the usefulness of the results from PNEC prediction by

comprehensive evaluation.

IV.4.4.2 Assessment factors

The OECD's early stage assessment of ecological risk of HPVC which have SIDS against aquatic organisms applies the assessment factors in **Table IV-4-3**, where the environmental concern level (ECL) is the chemical concentrations which can badly affect an ecosystem, and is equivalent to the PNEC and MTC at an early stage. Recommended assessment factors are 10 for the prediction of sensitivity between species, 10 for the prediction of NOEC from acute toxicity, and 10 for the prediction of field conditions from the NOEC giving the lowest chronic toxicity. However, assessment factors are empirical, and there are no scientific grounds for these numbers.

Ecotoxicology test data for aquatic organisms are available from SIDS as basic toxicity data, such as fish acute toxicity, daphnia acute swimming inhibition, and algal growth inhibition (normally acute), and for compounds where there is concern about long term effects, daphnia chronic test data is also available.

If only acute toxicity data is available, factors of 100 - 1,000 are applied to the lowest LC_{50} or EC_{50}. A factor of 1,000 applies as ECL = LC_{50} / (10 x 10 x 10) if only a fish toxicity LC_{50} is available of the three basic acute toxicity tests. This value errs on the side of safety and environmental protection.

Table IV-4-3 OECD's assessment factors for prediction of environmental concern level (ECL)

A. elements of assessment factors to predict ECL from toxicity data of aquatic organisms	assessment factor
1. general application (information applied at the lowest values)	
a. values predicted from chronic toxicity values, NOEC or QSAR from data sets including algae, Crustacea, and fish	10[a)]
b. values predicted from acute toxicity values (LC_{50}, EC_{50}) or QSAR from data sets including algae, Crustacea, and fish at least	100[b)]
c. values predicted from acute toxicity values (LC_{50}, EC_{50}) or QSAR	1,000
2. practical assessment factors from screening information data set (SIDS)	
a. daphnia NOEC, algal NOEC	10[a)]
b. algal EC_{50}, daphnia EC_{50}, fish LC_{50}	100[b)]
B. setting up conditions of assessment factors in order to predict ELC for groups of birds and mammals which live on fish from data of birds and mammals (information applied at the lowest values)	assessment factor
a. at least three NOEC	10
b. less than three NOEC	10[a)]
c. at least three LC50	100[b)]
d. less than three LC_{50}	1,000[c)]

A factor of 100 can be used if there is any of the following evidence：

i) toxicity data covering a wide variety of species can be used if the data includes the most sensitive species
ii) if the structural similarity or QSAR, the ratio of acute vs. chronic toxicity is low compared to many other compounds
iii) if the difference in toxicity between species is small, and chemicals react non-specifically, or like anaesthetics.
iv) chemical discharge into the environment is short term or intermittent, and there is no environmental residues.

When chronic toxicity data is available in addition to acute toxicity data, assessment factors of 10 - 100 are applied to the lowest NOEC after considering the following :

i) If the chronic NOEC of one or two species (fish, daphnia, or algae) which represent one or two nutrition stages, an assessment factor of 50 or 100 may be applied to the lowest NOEC. Compare this PNEC to the PNEC calculated from the lowest acute toxicity data, and make the lowest value the PNEC.
ii) If the chronic NOEC of three species (fish, daphnia, and algae) which represent three nutrition stages are available, a factor of 10 may be applied to the lowest NOEC. If there is confidence that the test was conducted using species which have the highest sensitivity, a factor of 10 can be applied to the lowest NOEC within two species (fish and/or daphnia and/or algae) which represent two nutrition stages. In addition, when assessment factors are changed from basic values, the reason has to be clarified.

A similar method is used to predict safety levels for groups of birds and mammals which live on fish from ecological toxicity data using bird and mammals. In addition, effects on benthic organisms may be assessed. However, in the practical terms they cannot be assessed in many cases because available toxicity data is limited.

Table IV-4-4 compares recommended assessment factors used in the OECD, European Union (EU), and European Chemical Industry, Ecology and Toxicology Centre (ECETOC). The OECD predicts by 10 for every estimation step. Assessment factors used by the EU are different depending on chemical character and test conditions. In general, a factor of 100 can be used between the NOEC and $E(L)C_{50}$ for acute toxicity and chronic toxicity tests. The recommendations of the ECETOC rely on comparisons of toxicity data. It is suggested that ratio of acute toxicity and chronic is 40, the ratio of chronic and ecosystem toxicities, 5, and ecosystem and field, 1.

The OECD says that application of assessment factors is not suitable for metallic forms of

elements and slightly water soluble compounds. Care must be taken when using assessment factors with chemicals which have peculiar properties, such as over 3 log P_{ow}, and show high bioconcentration, and particular attention has to be paid to whether tests were conducted at concentrations which exceeded solubility, or whether test terms were long enough.

Table IV-4-4 Assessment factors for applying toxicity data to aquatic organisms to predict PNEC

information which can be applied	assessment factors which are applied to minimum values		
	OECD	EU	ECETOC
one acute toxicity $L(E)C_{50}$ from one species nutrition stage	1,000	-	-
at least one acute toxicity $L(E)C_{50}$ from each of three species nutrition stage	100	1,000	200
one chronic toxicity NOEC (fish or daphnia)	-	100	-
two chronic toxicity NOEC (fish and/or daphnia and/or algae) from species which represent two nutrition stages	-	50	5
chronic toxicity NOEC from three species (usually fish, daphnia, and algae) which represent three nutrition stages	10	10	5
field observation or diverse species mixture test (model ecosystem)	-	depends on situation	1

note) Algae is not used alone.

IV.4.5 Estimation and judgement of ecological risk

The most convenient and practical method to estimate ecological risk is the quotient method. This method simply divides the environmental concentration or the predicted environmental concentration (PEC) by the toxicological benchmark concentration (TBC). If the value is 1, it can be said that a chemical has the possibility to cause toxic effects. In general, the PNEC or MTC which have been adjusted by assessment factors are used as the TBC. In addition, the NOEC, LC_{50}, and EC_{50} can be used as the TBC.

Initial assessment by the HPVC project of the OECD is undertaken not to judge ecological risk of chemicals directly, but to decide if supplementary testing is necessary. The OECD uses the quotient method for this judgement. That is, if PEC / PNEC < 1, supplementary testing is not a high priority at this point, but if PEC / PNEC = 1, conduct test covering more than the SIDS items or an exposure analysis to assess the risk in more detail. For example, if an estimated PNEC is obtained from only acute toxicity and assessment factors, one strategy would be to conduct a chronic toxicity test using species which showed the highest sensitivity in the acute toxicity test. Also, if there is an indirect effect on birds and mammals, or hazard to benthic organisms living, these assessments have to be considered at the next stage.

Trials to assess the level of ecological effect assumed to be caused by chemicals in the

environment use the ecotoxicological risk quotient (ERQ) as an index. This index shows the level of chemical effect on ecosystem, and is the negative logarithm of the ratio of the concentration in the environment and toxicity standard concentration:

Ecotoxicological risk quotient (ERQ^C)
= -log (environmental concentration / toxicity standard concentration)

Also, an index which shows comprehensive ecotoxicological risk quotient has been proposed assuming there are various chemicals in the environment and they cause effects in a complex manner.

Comprehensive eco-toxicological risk quotient (ERQ^a)
= -log [∑(environmental concentration / toxicity standard concentration)]

The comprehensive ecotoxicological risk quotient is determined assuming that the complex effects caused by the chemicals are neither multiplicative nor suppressive but additive effects in order to simplify quantification This index can be used for regional comparison of the level of ecological risk.

The concentration of a chemical in the environment (its environmental concentration) is the object of risk assessment, and actual measurement data (or predicted values) of concentration in water for water environment, and concentration in soil for soil environment may be used. The LC_{50}, EC_{50}, NOEC, and PNEC and MTCs are being considered as assessment factors obtained from the tests using toxicity standard concentrations.

Because the ERQ differs depending on toxicity standard concentration, the species, test methods and endpoint must be specified, e.g. daphnia ERQ (14d-NOEC), red killifish ERQ (96h-LC_{50}). Also, if the PNEC and MTC being considered as assessment factors are used as standard, the values is described as ERQ (PNEC) because it absorbs species differences in the test and endpoint, and this index can be used for the comprehensive assessment. If the ERQ (PNEC) is more than 0, it indicates that no toxic effects are likely to be caused on organisms in the environment.

Recently, quotient methods like this are the only assessment methods which are often used. The advantage that this method has is that it can be used easily and quickly, and it is easy to understand because there are no complicated mathematics or statistical techniques. Also, the quotient method can multiply multiple chemical risk. The toxicity of chemical mixture is sometimes larger than the sum of the individual chemical toxicities (multiplicative effect), and sometimes smaller than the sum of the individual chemical toxicities (suppressive effect), but it is

assumed that addition of quotient method doesn't have such effects. This assumption doesn't become problem if mode of action of each constituent is the same in the mixture.

It is known that the effects of chemical mixtures whose constituents' mode of action are different are strictly additive for fish acute toxicity test using industrial chemicals, although usually slightly smaller than strict addition, and it is rare to have multiplicative and suppressive effects. However, caution must be used when each constituent in the mixture reacts independently. Also, results obtained from the observation of aquatic organisms may not be applicable to other endpoint, exposure realities, and species. When the mode of action of each chemical is not known, theoretical assumptions about chemical interactions have to be clarified.

Application of quotient method also has many restrictions, because although the quotient method is useful to judge the size of risk, it cannot conduct quantitative assessments, such as the level of effect and possibility of appearance of effects, nor distinguish kinds of effects. For example it is meaningless to predict that a risk reduction policy reduces a quotient value from 25 to 12. This is because one cannot explain clearly the effect on the endpoint caused by quotient value reduction. Also because quotient values do not reflect the intensity of effects or exposure patterns appropriately, LC_{50} values, for example, which are obtained form a continuous series of constant concentration 96 hours exposure test may not be appropriate for reproductive toxicity assessment caused by short or intermittent exposure. Furthermore, the quotient method cannot be used for assessment of secondary effects. This method cannot judge effects of interactions nor effects which exceed the range which can be measured by a simple quotient, such as bioconcentration, because effects from exposure to effect factors spread widely. In order to make good these defects, mathematical model such as the statistical exposure model must be relied upon.

IV.5 Information sources and searches useful for the evaluation of research results

As has been mentioned several times, various bits of information such as chemical substances' names, structures, physiochemical characters, production, use and existence reality, toxicity, standard levels, regulations and the ground etc., are needed during the many stages of planning, data analysis, and risk assessment etc., when environmental monitoring of chemical substances is conducted, and it is an absolute requirement to collect, arrange, analyse and utilise these information. In this section, lists of information sources and data bases which are useful for collection such information are presented. International government organisations and non-government organisations evaluate the safety of chemical substances to meet specific

requirements and officially announce the results for evaluation material. From internet sites many related pieces of information can be obtained.

IV.5.1 Information about compounds

Names of chemical substances are big issues when doing searches because names used by different databases are not always the same. In such cases, Chemical Abstract registry numbers are a useful starting point, and names, alternative names, structures, uses, physical characters, toxicity etc. can be confirmed in a number of ways from books, CD-ROMs, and on-line services e.g.

- RTECS (Registry of Toxic Effects of Chemical Substances) : NIOSH (National Institute for Occupational Safety and Health)
- CA (Chemical Abstract) and CAS On-line : CAS (Chemical Abstracts Service)
- Merck Index
- Sigma-Aldrich (the Sigma-Aldrich Library of Chemical Safety Data) : Sigma Aldrich Corp.

IV.5.2 Information about toxicity

Information about toxicity, adverse effects and methods of evaluation can be obtained from the following.

- RTECS (Registry of Toxic Effects of Chemical Substances)
- HSDB (Hazardous Substances Data Bank: NLM (CD ROM)
- IARC Monographs on the Evaluation of Carcinogenic Risks to Humans : IARC (International Agency for Research on Cancer)
- EMBASE: STN International/DIALOG (On-line Network Service)
- Pharm-Web (Internet, http://www.pharmweb.net/)

IV.5.3 General information

General information which is useful for risk assessment may be obtained from the following sources.

- WHO Technical Report Series: WHO (World Health Organization of United Nations).
  Activity report of WHO.

- Environmental Health Criteria : IPCS (International Programme on Chemical Safety)

  General evaluation of the effects on humans and the environment of pesticides, chemical industrial products, environmental pollutants, natural poisons, etc.
- Health and Safety Guide : IPCS

  Guides to the management and treatment of accidental exposure to chemical substances such as pesticides, chemical industrial products, environmental pollutants, natural poisons, etc.
- IARC Monographs

  General information useful for risk assessment centering around carcinogenic risk evaluation for humans to such things as natural materials, pharmaceutical products, chemical industrial products, pesticides, environmental pollutants etc.
- IARC Scientific Publication

  Scientific reports on carcinogenic risk (research about methodology)
- Pesticide Residues in Food, Evaluation, Report JMPR (FAO/WHO Joint Meeting on Pesticide Residues, Food and Agriculture Organization of United Nations)

  Recommendations of ADI and MRL (Maximum Residue Limit) of Pesticides.
- Joint Assessment of Commodity Chemicals : ECETOC (European Chemical Industry Ecology and Technology Centre)

  Evaluation of the effects on humans and the environment of currently existing industrial chemical products.
- Technical Report : ECETOC

  Review of scientific articles about potentially harmful industrial chemical products.
- Monograph : ECETOC

  Discussion about evaluation methods of toxicity.
- Technical Report : NTP (National Toxicology Program)

  Evaluation by toxicity tests of the carcinogenicity of chemicals to which humans are exposed and for which research value is high.
- Toxicological Profile : ATSDR (Agency for Toxic Substances and Disease Registry)

  Evaluation of the health effects of harmful wastes, such as chemicals which are buried in large quantity as harmful wastes.
- Federal Register

  US official gazette. Analytical methods, instruction of evaluation, regulation etc. are listed in detail.
- Concise International Chemical Assessment Document

  Summarising data on risk assessment of chemicals by international co-operation,

exposure indexes are introduced.

- International Chemical Safety Card

  Summarises acute effects on humans and the physical danger of chemicals.
- Toxicity of Chemicals, Carcinogenicity : EC (European Communities)
- OECD (Organization for Economic Cooperation and Development) SIDS Initial Assessment Report

IV.5.4 Internet sites or contact address

IV.5.4.1 Information of safety evaluation and data base

- Chem Finder : http://chemfinder.camsoft.com/
  (chemical structures, physical characters etc.)
- Concise International Chemical Assessment Document :
  http://www.who.ch/programmes/WHOProgrammes.html
- ECDIN : http://ulisse.etoit.eudra.org/Ecdrin/Ecdrin.html
  (environmental chemicals data base of EU)
- Environmental Health Criteria : gopher://gopher.who.ch:70/11/.pcs/.ehc
  (summary of recent EHC)
- International Chemical Safety Card : http://www.nihs.go.jp/ICSC/
- International Uniform Chemical Information Database (IUCLID): European Union
  (EU data base of currently existing compounds)
- KIS-NET : http://www.fsinet.or.jp/~k-center/k-p5.htm
  (chemical safety information system of Kanagawa prefecture)
- National Toxicology Program: http:///ntp-server.niehs.nih.gov
  (test information, publication, safety information, chemical structures information, etc. of US NTP)
- NORDBAS : Nordic Council of Ministries (Environmental Hazard
  Classification-classification of selected substances as dangerous for environment)
- SWEDEN KEMI : http://db.nihs.go.jp/dcbi/genera/KEM/
  (compounds list of KEMI Sunset Project)
- Toxicological Profile Query : http://atsdrl.atsdr.cdc.gov:8080/gsql/toxprof.script
  (Summary of Toxicological Profile of US ATSDR)
- US Federal Register : http://cos.gdb.org/repos/fr/fr-intro.html
  (US official gazette)

IV.5.4.2 International organisations

The following organisations web sites can accessed for information.

- CIS/ILO [International Labor Office (ILO) International Occupational Safety and Health Information Centre (CIS)] : http//turva.me.tut.fi/cis/home.html
- EC (European Communities) : Office for Official Publications of the European Communities, 2, Rue Mercier L-2985 Luxembourg (reference of Toxicity of Chemicals, Carcinogenicity)
- ECETOC : http://www.nihs.go.jp/guide/ingovel.html#ECETOC (reference of Technical Report, Joint Assessment of Commodity Chemicals)
- IARC : http://www.iarc.fr/ (link to information of IARC)
- OECD's Work on Environmental Health and Safety : http://www.oecd.org/ehs (OECD information of chemicals, prevention of accidents, pesticides plan etc.)
- WHO: http://www.who.ch/ (link to WHO information)

IV.5.4.3 Governments of Europe, US, and Australia, and related organisations

- Australia : http://www.erin.gov.au/portfolio/epg/epg.html (Australian Priority Existing Chemicals Program)
- Environment Canada Health Canada : Ministry of Supply and Services, Canada Communication Group, Ottawa, KIA0S9, Canada (Canada Priority Substances List Assessment Report)
- BUA GDCh-Advisary Committee on Existing Chemicals of Environmental Relevance : Gesellschaft Deutscher Chemiker E.V. BUA, Postfach 10 14 80 D-60444 Frankfurt, Germany (BUA Report)
- BG Chemie : Berufsgenossenschaft der Chmeischen Industrie, Postfach 10 14 80 D-6900, Heiderberg 1, Germany (Toxicological Evaluation)
- MAK Commission : VCH Verlagsgeselshaft, Postfach 10 11 61, D-6940 Weinheim, Germany (MAK Evaluations)
- Health Council of Netherlands (GR) : Gezondheidsraad Postbus 90517 NL-2509LM's Gravenhag, Netherlands (Basis-Document, Criteria-Document)
- RIVM : Rijksinstituut voor Volksgezondheid en Mimieuhygiene (RIVM), Postbus 1 NL-3720 BA Bilthoven, Netherlands (Integrated Criteria Document)

- Dutch Expert Committee on Occupational Standards (WGD) : WGD Werkgroep van Deskundigen (WGD), Gezondheidsraad, secretariaat WGD Postbus 90517 NL-2509 LM DenHaag, Netherlands, (Health-based Recommended Exposure Limit)
- Swedish National Chemicals Inspectorate : http://db.nihs.go.jp/genera/KEMI/contents.html (KEMI Report Series)
- BIBRA Toxicology International : BIBRA Information and Advisory Service, Woodmansterm Rd, Carshalton Surrey SM5 4DS, UK (Toxicity Profiles)
- Health and Safety Executive (HSE) : HSE Books. P.O. Box 1999 Sudbury, Suffolk CO10 6FS, UK (Criteria Document for an Occupational Exposure Limit)
- US EPA : http://www.epa.gov/ (link to all information of EPA such as HAD : Health Assessment Document, Hazard Information Profiles, IRIS : Integrated Risk Information System)
- US NIOSH (National Institute for Occupational Safety and Health) : http://www.cdc.gov/niosh/homepage (publication, explanation of data base of NIOSH)
- US FDA(Food and Drug Administration) : http://www.fda.gov/fdahomepage.html
- National Institute for Occupational Safety and Health (NIOSH): http://www.cdc.gov/niosh/homepage (Criteria Documents)
- National Toxicology Program (NTP) : http://ntp-server.niehs.nih.gov (NTP Technical Report, NTP Toxicity Report)
- American Conference of Governmental Industrial Hygienists (ACGIH) : http://www.acgih.org/ (Threshold Limit Values and Biological Exposure Indices)
- Agency for Toxic Substances an disease Registry (ATSDR) : http://atsdrl.atsdr.cdc.gov:8080/gsql/toxprof.script (Toxicological Profile)
- CIR Panel of Experts : Cosmetic Ingredients Review, 1110 Vermont Ave., N.W., Suite 810, Washington DC, 20005, USA (CIR : Cosmetic Ingredient Review)

IV.5.4.4 Japanese government and related organisations

- Environment Agency of Japan : http://www.eic.or.jp/
- Ministry of Health and Welfare : http://www.mhw.go.jp/
- National Institute for Environmental Studies : http://www.nies.go.jp/
- National Institute of Health Sciences : http://www.nihs.go.jp/
- National Institute for Resources and Environment : http://www.nire.go.jp/