CHAPTER 2: 
DATA GATHERING

2.1 INTRODUCTION

This section describes the Screening Information Data Set (SIDS), which represents the standard set of information to be gathered for a regular SIDS Initial Assessment. For sponsors that intend to prepare a full SIDS Initial Assessment, a procedure for initial gathering of all available data and determining the need for any additional testing is discussed. This procedure can be outlined in the SIDS Plan, a document which outlines the Sponsor’s course of action with respect to the use of existing, surrogate or new data.

For a targeted assessment, the need for any additional testing is limited to the targeted endpoints, or any properties that allow the hazard assessment for the targeted endpoints.

2.2 THE SCREENING INFORMATION DATA SET (SIDS)

This section presents the information and data needed for a full Screening Information Data Set (SIDS). It also provides guidance for determining adequacy of the existing data and guidance for the collection of additional data. Finally, it describes how to prepare a SIDS Plan and distribute it among member countries for comment and approval.

2.2.1 SIDS Content

The content of the Screening Information Data Set (SIDS) was adopted in November 1989 and revised in February 2000. The SIDS content is organised under five headings: Substance Information, Physical Chemical Properties, Environmental Fate, Environmental Toxicology, and Mammalian Toxicology. Detailed information in the content is presented below. Comments on the need for specific data are found at appropriate locations in the outline below. For physical-chemical properties, environmental fate and environmental toxicity, a cautionary statement should be added whenever modelled data on inorganic substances are provided, as the model used may have limitations (e.g. outside the applicability domain) for inorganic chemicals.

For the purpose of gathering data for compiling a SIDS Dossier for either a full SIDS assessment or a targeted assessment, robust study summaries for each entry of the Dossier should be prepared. Robust studies summaries should be elaborated using OECD Templates. These templates exist for all – SIDS and non SIDS- hazard endpoints, and are located at the following URL: http://www.oecd.org/ehs/templates.
Substance Information

- Chemical Identity
  - CAS Number(s)
  - Name (OECD name(s))
  - CAS Descriptor (Only required for inorganic chemicals)
  - Structural Formula
  - Composition of the chemical(s) being assessed (Composition is, strictly speaking, not a SIDS element. However, the information allows for a comparison with the test substance which was used in the different tests. This can influence the reliability of certain studies. It is therefore strongly recommended that information on the composition (including impurities) of the produced and marketed substance is made available. In cases were confidentiality issues are involved, the values can be reported in ranges.):
    - For a single chemical: degree of purity, known impurities or additives, difference of impurities among products, details of stereo-isomers if relevant;
    - For mixtures: percentages or range of percentages of mixture components, known impurities or additives, differences among products;
    - For Class 2¹ compounds: typical composition and molecular weights, known impurities or additives, differences among products;
    - For streams²: typical descriptors, known impurities or additives, differences among products, basic elements of physical-chemical properties (e.g. water solubility, boiling point range, Log Kow, vapour pressure, etc.).

- Quantity (estimated production and/or import volume). Quantity is a SIDS element. The following information should be given in the SIDS Dossier. Information on annual production and import levels (in metric tonnes) should be provided in figures or ranges (e.g. 1,000-5,000, 5,000-10,000 tonnes per year, etc.) as well as the date and country for which those ranges apply. At a minimum the annual production and import volume in the Sponsor country or, for assessments prepared under voluntary industry programmes, the country where the lead company is located must be provided. If information on import volume is provided, these should clearly be distinguished from the production volume. Recent production volume data from public sources or recent published nameplate capacity is acceptable. If such information is restricted for competitive or antitrust reasons, then volumes should be given in ranges. Further supporting information – if available - on production volumes can also be reported in this section. Information which would be most relevant for the initial assessment would be:
  - the OECD and global annual production quantity or an estimation thereof;
  - number of producers in the Sponsor country or, for assessments prepared under voluntary industry programmes, in the country where the lead company is located;

¹ Class 2 denotes a chemical that occurs as a complex mixture of different individual substances rather than existing as a single chemical species with a well-defined molecular structure (e.g., a paraffin wax). Class 2 compounds also include unknown or variable composition complex reaction products, biological materials (UVCB). UVCB substances can for example be described by structural features (e.g. acid chlorides, alkaline earth compounds, polyoxyalkylenes), a significant precursor (e.g. Castor Oil or Tallow) or by a more general description (e.g. Resins or Waxes.)

² A stream is defined as a material that is created in a chemical process and exists as a process stream that is a complex mixture of individual substances. The stream may be isolated and treated as a product without separating out its many individual components as pure chemicals. The stream may be defined by the process conditions that created it.
 number and production quantities of producers in other countries.

For all data elements reported in this section, the source of information should also be given in the references.

- Exposure information through use pattern

(see also Monograph ENV/JM/MONO(2012)5, No 167 in the OECD Series on Testing and Assessment, Crosswalk of harmonized U.S. - Canada Industrial Function and Consumer and Commercial Product Categories with EU Chemical Product and Article Categories)

The OECD Monograph [ENV/JM/MONO(2012)5] outlines a crosswalk between the function and product categorization of chemicals used by the United States and Canada with the function, product and article categories used in the European Union in the context of the implementation of the REACH regulation. The purpose of the crosswalk is to identify the categories which are common to both sets of codes and to note the categories that are contained in one but not both listings of categories for chemical inventory reporting. It provides a system for describing the uses of chemicals for the purpose of an exposure assessment. The system comprises harmonised categories for reporting 1) industrial functions of chemicals and 2) consumer and commercial products containing chemical substances. This system facilitates exchange of information among member countries. About 35 harmonised industrial function codes and about 32 harmonised consumer and commercial product codes have been developed. The codes also describe the technical function and the final use (end-use) of a substance by industrial or non-industrial workers and consumers. Detailed description of sources of exposure (worker, consumer, environmental) is not mandatory. Readily available information on exposure to the chemical could be summarised to provide some more understanding of sources of exposure. However, the present Manual does not provide guidance on the collection of exposure information. Guidance on on initial assessment of exposure to workers and consumers and on final assessment of exposure to the environment are available as additional information to the Manual.

Exposure information at least from the Sponsor country, or, for assessments prepared under voluntary industry programmes, from the country where the lead company is located, should be included. When quantity, use pattern or sources of exposure data are provided by a non-sponsor country to the sponsor country, the data should be included in the SIDS Documents to report available exposure information (worker, consumer, environmental) for the purposes of SIDS initial assessment or targeted assessment but available overview information in this regard may be useful to present. While reporting the available exposure information, the scope of the available information should always be explicitly outlined.

Physical-Chemical Properties

This section includes the reporting requirements for the physical-chemical elements required for a SIDS Dossier, both for SIDS elements and for non-SIDS elements. The latter should be included when this information is available because it may be relevant and applicable to the assessment of the hazard of the chemical. If more than one value is reported, the recommended value should be identified.

Tests for physical/chemical properties should be conducted in principle on the pure substance or the substance as defined by the manufacturing process.

Physical-chemical data for any of the SIDS elements, like boiling point and melting point, when taken from reliable references rather than from actual test reports may be accepted. For example, numerical values from standard references like the CRC Handbook of Chemistry may act as a reference to characterise the physical state and basic chemical properties of an HPV chemical. The MedChem database
is also a good source of data. It may be appropriate to support physical-chemical data obtained from standard handbooks with a valid QSAR prediction, within the limitations of the QSAR model.

In the OECD review of SIDS data greater scrutiny is frequently given to the reliability of vapour pressure, octanol/water partition coefficients ($K_{ow}$) and water solubility studies. Such data are more critical to the initial assessment of potential hazards, e.g. bioaccumulation. Critical information such as temperature and methods used, which affects the value of physical-chemical properties, must be provided in all cases for all testing results and, when available, for data acquired from the literature.

- **Melting Point**: Melting Point is a SIDS element. The relevant Test Guideline for Melting Point is OECD Test Guideline 102, ‘Melting Point/Melting Range’. If more than one melting point value is available, the recommended value should be identified (along with a rationale as to why it is most appropriate value) and the mean of at least 2 measurements reported along with the range of accuracy. Melting points should always be stated for substances other than gases (and liquids, whose melting point is lower than approximately 0°C.) Temperature of decomposition is acceptable. For viscous liquids, “pour point” is an acceptable alternative to report.

- **Boiling Point**: Boiling point is a SIDS element. The relevant Test Guideline for Boiling Point is OECD Test Guideline 103, ‘Boiling Point’. If more than one boiling point value is available, the recommended value should be identified and the mean of at least 2 measurements reported along with the range of accuracy as $^\circ$C at a given pressure (kPa). Boiling points should always be stated for substances other than gases or solids and liquids which either boil above 300 $^\circ$C or decompose before boiling (in which cases estimates based on vapour pressure or the boiling point under reduced pressure are necessary). For substances which have an obviously high boiling point (e.g. some inorganic or organic salts), an estimation could be sufficient. For certain process streams, such as refinery streams or Class 2 mixtures, the data are often best expressed as boiling point ranges. Temperature of decomposition is acceptable.

- **Relative Density** (required for inorganic chemicals, and should be provided if readily available for organic chemicals): Density (Relative Density) is a SIDS element only for inorganic chemicals. The relevant Test Guideline for Density (Relative density) is OECD Test Guideline 109, ‘Density of Liquids and Solids’. Information on relative density should be provided for organic chemicals, when it is available.

- **Vapour Pressure**: Vapour Pressure is a SIDS element. The relevant Test Guideline for Vapour Pressure is OECD Test Guideline 104, ‘Vapour Pressure’. A value for this parameter should always be provided. If a boiling point cannot be quoted due to decomposition or the melting point is above 360$^\circ$C, it may not be necessary to conduct the test for vapour pressure. If a melting point is $< 360^\circ$C but $> 200^\circ$C, a limit value based on measurement or a recognised calculation method is acceptable. Calculations that indicate that the vapour pressure is probably less than $10^{-5}$ Pa at 25$^\circ$C, could preclude the need for testing. For substances which have an obviously low vapour pressure (e.g. some inorganic or organic salts), an estimation could be sufficient. This test is not essential for chemicals with a boiling point of $< 30^\circ$C. The vapour pressure should be determined for at least 3 temperatures in the range of 0 – 50$^\circ$C, with the mean vapour pressure expressed as Pascal units (N/m$\text{^2}$) at 20 – 25$^\circ$C. An experimental value would be preferred, but there may be interpolation or extrapolation where necessary. If a transition (change of state, decomposition) is observed, the following information should be noted: nature of the change, temperature at which the change occurs at atmospheric pressure, vapour pressure at 10 and 20$^\circ$C below the transition temperature and 10 and 20$^\circ$C above this temperature (unless the transition is from solid to gas).
Partition Co-efficient: n-Octanol/Water\(^3\); Partition Coefficient is a SIDS element. The relevant Test Guidelines for Partition Coefficient are OECD Test Guidelines 107 and 117. For OECD Test Guideline 107, ‘Partition Coefficient (n-octanol/water): Shake Flash Method’, the measurement concentrations (12 concentrations are optimal) for each determination of concentrations in n-octanol and in water, under 3 different conditions, should be included in the free text field for Results. For OECD Test Guideline 117, ‘Partition Coefficient (n-octanol/water), High Performance Liquid Chromatography (HPLC) Method’, the average retention data should be reported as a mean of at least 2 measurements and should be included in the free text field for Results. Details on fitted regression line, calibration methods, etc. should also be reported. OECD Test Guideline 122, ‘Partition Coefficient (n-octanol/water) pH-Metric Method for Ionisable Substances’ might also be considered to be relevant for this element. If more than one value is reported, the recommended value should be identified (along with a rationale as to why it is the most appropriate value). Even for those substances which are extremely soluble/insoluble in either phase, an attempt should be made to provide a limit value (if necessary based on the individual solubilities in n-octanol and water). If the test cannot be performed, an estimated value for Log K\(_{ow}\) should be provided. However it should be noted that estimated values which are higher than 6 are, in general, not reliable.

The following references may be useful for the calculation of Log K\(_{ow}\):

Water Solubility: Water Solubility is a SIDS element. The relevant Test Guideline for Water Solubility is OECD Test Guideline 105, ‘Water Solubility’. A value for this parameter should always be stated, including gases if necessary, excluding substances unstable in water. Determinations should be made at or near 20°C. If solubility/temperature dependence is > 3% per °C, further measurements should be made at 10°C above and below the initially chosen temperature. If the substance is "insoluble" in water, the detection limit of the analytical method should be indicated. Two to five replicates per trial should be used and information on calibration data for the chosen methods and readings for the test solution should be included. Quantitative values are needed but not below 1 ppb (e.g., less than or equal to 1 µg/L).

Dissociation Constant (for substances normally capable of dissociation): Dissociation Constant is a SIDS element. The relevant Test Guideline is OECD Test Guideline 112, ‘Dissociation Constants in Water’ for determining pH and pKa values. Where applicable, values for the dissociation constants (pKa) and the conditions under which they were measured (pH) should be provided. Dissociation constants are particularly important for acids, bases and inorganic chemicals and are normally known, calculated or measured. Dissociation constant testing is not required for chemicals that do not possess functional groups capable of dissociation, e.g., hydrocarbons.

Oxidation-reduction Potential (required for inorganic chemicals; may be required for certain organic chemicals): Oxidation-Reduction (Redox) Potential is a SIDS element for inorganic chemicals. Oxidation-Reduction (Redox) Potential should also be required for organic chemicals when deemed necessary. At present there is no agreed Robust Study Summary template for

\(^3\) Not necessarily needed or provided for inorganic and ionic substances.
Oxidation-Reduction Potential, however the minimum information to be reported is outlined below, and a Robust Study Summary should be prepared when the template is agreed.

Any additional information that may be relevant to the initial hazard assessment should be reported using the following entries: test substance identity, method used, test conditions, results, reliability, reference. Details such as fat solubility, particle size distribution and the like, may be supplied.

**Environmental Fate**

This section contains the reporting requirements for SIDS elements and for non-SIDS elements. The latter should be included when this information is available because it may be relevant to the assessment of the hazard of the chemical. Reporting of studies should give the test method, test conditions (laboratory versus field studies), test results (e.g. percent degradation in specified time period) and references. Information on breakdown products (transient and stable) should be provided when available.

- **Photodegradation:** Photodegradation is a **SIDS element**. An OECD Test Guideline for Photodegradation is currently being developed (Phototransformation of Chemicals in Water-Direct and Indirect Photolysis; Draft New Guideline, August 2000). For photodegradation, an estimation is generally sufficient. Estimation of photodegradability (and hydrolysis) can be based on reference documents, such as:
  - OECD Environment Monograph No. 61, The rate of photochemical transformation of gaseous organic compounds in air under tropospheric conditions (OECD / GD (92)172).
  - An Assessment of Test Methods for Photodegradation of Chemicals in the Environment” (ECETOC Technical Report No.3)

- **Stability in Water** (not required for classes of chemicals whose molecular structure does not possess functional groups subject to hydrolysis, or are generally recognised to be resistant to hydrolysis. In these cases a qualitative statement can be provided.) Stability in Water is a **SIDS element**. The relevant Test Guideline for Stability in Water is OECD Test Guideline 111, ‘Hydrolysis as a Function of pH’. Testing is generally required for hydrolysis. Consideration should be given to the possible use of estimation methods. Where additional testing is required for hydrolysis, consideration should be given to the choice of test protocol. When possible, the products of hydrolysis should be identified. Testing or estimation should utilise pH 4, 7 and 9 and other pH levels likely to be found in the environment.

- **Transport and Distribution between Environmental Compartments including Distribution Pathways** [including Henry’s Law constant, aerosolisation, volatilisation, soil adsorption and desorption, either based on experimental data or if not available or appropriate, calculated using structure-activity relationships (SARs)]. Transport and Distribution Between Environmental Compartments including Distribution Pathways is a **SIDS element**. Information on transport and distribution, as may occur for example during the chemical life cycle, should indicate whether the calculation is on a global basis or is site-specific, and whether it is based on laboratory measurements or field observations. Important environmental fate pathways based on calculations

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4 Bioaccumulation is not a SIDS element. However, available data on this endpoint should always be reported or a prediction based on the properties of the substance made.
Transport:
Potential chemical partitioning and distribution in the environment can be calculated using computer models. Three such models are described by Mackay et al. (1996) and are referred to as equilibrium criterion (EQC) models:

Level I = steady-state, equilibrium, without degradation and advection
Level II = steady-state, equilibrium, with degradation and advection
Level III = steady state, non-equilibrium, with degradation, advection, and inter-media transfer

In particular, calculation of potential chemical distribution between environmental compartments using the Level I model should be provided.

The level III model can be used in two different ways:
- If the releases of a substance to different compartments in a country or a region are known, the model can be used to estimate the resulting concentrations of the substance in each compartment. Within the refocused HPV Chemicals Programme, these estimations are not required.
- The partitioning of a substance between the different compartments depending on the compartment to which the substance is released can be estimated. A fictive amount of the substance can be added alternatively to air, soil and water, and the resulting percentages partitioning to the other compartments can be obtained. When this approach is chosen, the resulting concentrations in the different compartments are fictitious and should not be reported. Only the relative distribution to the different compartments is relevant.

While a level I estimation is sufficient to fulfil the SIDS element, it is recommended to always perform a level III calculation, as it gives a better indication of the environmental fate of the substance.

Distribution
Available data on partitioning coefficients between different media should be reported here, e.g. adsorption/desorption in soil or sediment, Henry’s law constant etc.

For adsorption/desorption to soil, the conditions under which it was measured should be indicated although this is not a SIDS element. The relevant Test Guideline for Adsorption/Desorption to Soil is OECD Test Guideline 106, ‘Adsorption-Desorption Using a Batch Equilibrium Method’, or the screening method OECD Test Guideline 121, ‘Estimation of the Adsorption Coefficient (Koc) on soil and on Sewage Sludge using High Performance Liquid Chromatography (HPLC)’.

This property is particularly important for inorganic chemicals and in cases where Log Kow is not useful in view of the expected properties of the chemicals. There is no agreed Robust Study Summary template for partitioning coefficient in general, however the minimum information to be reported is outlined below.

- Aerobic biodegradability: Aerobic Biodegradation is a SIDS element. The relevant Test Guidelines for Biodegradation are OECD Test Guidelines 301, ‘Ready Biodegradability’
(sections A-F) and OECD Test Guideline 302, ‘Inherent Biodegradability’ (sections A-C). The feasibility of each OECD Test Guideline (301A-301F) frequently depends on the physical-chemical properties (e.g., stability in water), and the structure of the test substance. Testing is generally required, other than for gases, unless adequate data are already available. However, volatile substances should be tested in a closed system. For poorly soluble substances, the nature and concentration of any vehicles such as solvents and other processes that enhance the contact between the test substance and the micro-organisms should be reported. Test results on anaerobic biodegradation as well as simulation test results should also be reported in this section. The relevant test guideline for simulation tests is draft OECD Test Guidelines 308, ‘Aerobic and Anaerobic Transformation in Aquatic Sediment Systems’.

- Bioaccumulation potential: is not a SIDS element. There are various ways to inform this endpoint, either by making a prediction of the bioconcentration factor (BCF) using physical-chemical properties – the chemical should be within the applicability domain of the model used (e.g; BIOWIN for organic chemicals). Alternatively for chemicals presented a potential to bioaccumulate, experimental data may be available from tests conducted using the OECD Test Guideline 305, ‘Bioconcentration: flow-through fish test’.

**Environmental Toxicology**

This section contains reporting requirements for SIDS elements and for non-SIDS elements. Data for the latter should be included because it may be applicable to the assessment of the hazard of the chemical. Where available, templates for Robust Study Summaries have been included.

It should always be clearly noted where aquatic tests were performed at measured or nominal concentration above the solubility limit in the test medium. If no mortality or other effects are observed, then the LC$_{50}$, EC$_{50}$ and NOEC should be indicated as being above the stated solubility limit in the test medium. If solvents are used to enhance the solubility of poorly water-soluble substances, then this should be clearly stated. However, testing at the solubility limit, without solvents, is preferred.

For substances that decompose in water, the LC$_{50}$, EC$_{50}$ and NOEC values should be expressed in terms of the measured concentration or loading of the parent substance realising that any substantial amount of breakdown product needs to be identified, quantified, or possibly tested separately.

In general, more weight should be given to studies performed in closed systems where care was taken to minimise material loss.

Specific guidance on the testing and interpretation of the results for difficult substances, e.g. poorly water-soluble substances, volatile substances, substances that degrade in the test system etc., can be found in the **OECD Guidance Document on Aquatic Toxicity Testing of Difficult Substance and Mixtures** (Series on Testing and Assessment No 23, ENV/JM/MONO(2000)6) as well as in the OECD Guidance Document on the use of the Harmonised system for the Classification of Chemicals which are Hazardous to the Aquatic Environment (Annex 2, Section 3.5 of the Harmonised Integrated Hazard Classification System for Chemical Substances and Mixtures).

- Acute Toxicity to Fish: Acute Toxicity to Fish is a SIDS element. The relevant Test Guideline for Acute Toxicity to Fish is OECD Test Guideline 203, ‘Fish, Acute Toxicity Test’.

- Acute Toxicity to Daphnia: Acute Toxicity to Aquatic Invertebrates (e.g. Daphnia) is a SIDS element. The relevant Test Guideline for Acute Toxicity to Aquatic Invertebrates (e.g. Daphnia) is OECD Test Guideline 202, Part 1, ‘Daphnia sp., Acute Immobilisation Test’.
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- Toxicity to Algae: Toxicity to Aquatic Plants (e.g. Algae) is a SIDS element. The relevant Test Guideline for Toxicity to Aquatic Plants (e.g. Algae) is OECD Test Guideline 201, ‘Alga, Growth Inhibition Test’.

- Chronic Toxicity. This is a SIDS element, in some circumstances. Necessity determined based on physical chemical properties of the chemical. Any new data required should be collected using the most sensitive species (fish, daphnia or algae) within limitations of the chemical properties (see section 2.3.2 for further guidance on test selection).
  - Chronic toxicity to fish: where data are available they should be reported. The relevant Test Guideline is OECD Test Guideline 210: ‘Fish, Early –Life Stage Toxicity Test’.
  - Chronic toxicity to aquatic invertebrates: the relevant Test Guideline for Chronic Toxicity to Aquatic Invertebrates (e.g. Daphnia Reproduction) is OECD Test Guideline 211, ‘Daphnia magna Reproduction Test’.

- Toxicity to microorganisms, e.g.; bacteria: This is not a SIDS element. Available data should be reported. The relevant Test Guideline for toxicity to aquatic microorganisms is OECD Test Guideline 209, ‘Activated Sludge, Respiration Inhibition Test’. Single species tests and tests on overall processes such as nitrification or soil respiration are also included in this element. The relevant Test Guideline for toxicity to soil microorganisms is OECD Test Guideline 216, ‘Soil Micro-organisms: Nitrogen Transformation test’ as well as 217, ‘Soil Micro-organisms: Carbon Transformation Test’. There is no agreed Robust Study Summary template for Toxicity to Bacteria, however the minimum information to be reported is outlined below.

- Terrestrial Toxicity. If significant exposure is expected or identified in the terrestrial environment (soil), appropriate terrestrial toxicity tests could be considered (see section 2.3.2. below). However, if testing is not to be conducted, then language can be added to note whether the substance(s) might result in exposure and hazard in terrestrial species. The relevant Test Guideline for toxicity to terrestrial plants is OECD Test Guideline 208: Terrestrial Plants, Growth Test; the relevant Test Guideline for toxicity to soil swelling organisms is OECD Test Guideline 207: ‘Earthworms, Acute Toxicity Test’. Other toxicity tests may be available on non-mammalian species such as avian and should be reported whenever they are available.

- Toxicity to Sediment Dwelling Organisms: this is not a SIDS element. Available data should be reported. Test Guidelines for toxicity to sediment dwelling organisms are under development: OECD Test Guideline Proposal 218 ‘Sediment-Water Chironomid Toxicity Test Using Spiked Sediment’ and OECD Test Guideline Proposal 219 ‘Sediment-Water Chironomid Toxicity Test Using Spiked Water’.

Mammalian Toxicology

This section includes the reporting requirements for SIDS elements and for non-SIDS elements. The latter data should be included when available because they may be applicable to the assessment of the hazard of the chemical. With the exception of data on irritation and sensitisation, observations on humans should be reported under Experience with Human Exposure. Observations on humans regarding irritation and sensitisation can be reported in sections on irritation and sensitisation.

- Toxicokinetics: this is not a required SIDS element. Available data should be reported, since they may be valuable in the design for filling required SIDS elements and in the interpretation of other test data. The relevant Test Guideline is OECD Test Guideline 417: ‘Toxicokinetics’.

5 Skin irritation, eye irritation, respiratory irritation, sensitization and carcinogenicity are not SIDS elements. Available data, if adequate, on these endpoints should always be reported.
Acute Toxicity (either by oral, dermal or inhalation routes; required only on the most relevant route of exposure): is a SIDS element. Testing is generally required if adequate data are not available, but only on the most relevant route of exposure. With a few exceptions, all substances should be tested by the oral route. Gases and vapours should be tested only by the inhalation route. Dependent upon the most important route of human exposure and physical-chemical properties of the substance, the dermal or the inhalation route could also be considered.

The relevant Test Guidelines for Acute Toxicity testing are:

- OECD Test Guideline 423: Acute Oral Toxicity - Acute Toxic Class Method
- OECD Test Guideline 425: Acute Oral Toxicity - Up-and-Down Procedure
- OECD Test Guideline 425: Acute Inhalation Toxicity
- OECD Test Guideline 403: Acute Dermal Toxicity

OECD Test Guideline 401, ‘Acute Oral Toxicity’ has been replaced with the above listed Test Guidelines and is not to be used anymore. Data generated with this guideline after 17 December 2002 cannot be accepted to fulfil the SIDS element.

Corrosion/irritation

Skin irritation/corrosion:
This is not a required SIDS element. When available, data should be reported. OECD Test Guideline 404, ‘Acute Dermal Irritation/Corrosion’ might be considered relevant for the endpoint of Skin Irritation/Corrosion.

Eye irritation/corrosion
This is not a SIDS element. When available test data should be reported. OECD Test Guideline 405, ‘Acute Eye Irritation/Corrosion’ might be considered relevant for the endpoint of Eye Irritation/Corrosion.

Skin sensitisation: is not a required SIDS element. When data are available they should be reported. OECD Test Guideline 406, ‘Skin Sensitisation’ and 429, ‘Skin Sensitisation: Local Lymph Node Assay’ might be considered relevant for the endpoint of Skin Sensitisation.

Repeated Dose Toxicity. is a SIDS element. The protocol for new studies should specify the use of the most relevant route of exposure.

The relevant Test Guidelines for Repeated Dose Toxicity are:

- OECD Test Guideline 407: Repeated Dose 28-day Oral Toxicity Study in Rodents.
- OECD Test Guideline 410: Repeated Dose Dermal Toxicity: 21/28-day Study
- OECD Test Guideline 412: Repeated Dose Inhalation Toxicity: 28-day or 14-day Study

OECD Test Guideline 422, ‘Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test’ is also acceptable. Guidance on test selection can be found in Chapter 2 (section 2.3.2).

If data on repeated dose toxicity over longer durations or even chronic toxicity is available, they can also be reported in this section.
When determining adequacy of existing data, the duration of exposure is a key consideration in addition to details about the test species, the route of exposure and the quality of data.

- Genetic Toxicity. Genetic Toxicity *in vitro* is a SIDS element. Two end points required, generally gene mutations and chromosomal aberrations. These endpoints may be evaluated by using the following tests:
  - Gene mutation in prokaryotic cells, should be performed preferably in *Salmonella typhimurium* (e.g. OECD Test Guideline 471, ‘Bacterial Reverse Mutation Test’). The chemical class of the test substance may determine which test organism and whether modified procedures may be needed. The test should be carried out with and without metabolic activation. OECD Test Guideline 476, ‘*In vitro Mammalian Cell Gene Mutation Test*’ is also relevant for the evaluation of Genetic Toxicity.
  - Chromosomal aberration may be evaluated in mammalian cells grown *in vitro* (e.g. OECD Test Guideline 473, ‘*In vitro Mammalian Chromosomal Aberration Test*’) or by *in vivo* methods (see Item 5.7)

When determining if additional testing is required, the quality of data, the nature of the test organism, strain and/or cell system and information on whether metabolic activation was addressed are important considerations.

Genotoxicity *in vivo*: if one of the test results on genetic toxicity *in vitro* is positive, it is necessary to perform a test on genetic toxicity *in vivo* such as the micronucleus test or metaphase analysis of bone marrow cells. The relevant test guidelines are:

- OECD Test Guideline 474 Mammalian Erythrocyte Micronucleus Test
- OECD Test Guideline 475 Mammalian Bone Marrow Chromosomal Aberration Test
- OECD Test Guideline 483, ‘Mammalian Spermatogonial Chromosome Aberration Test’ might also be applicable to this endpoint, as well as OECD Test Guideline 486, ‘Unscheduled DNA Synthesis (UDS) Test with Mammalian Liver Cells in vivo’.

When determining if additional testing is required, the quality of data, the nature of the test organism, strain and/or cell system and information on whether metabolic activation was addressed are important considerations.

- Carcinogenicity: is not a SIDS element. When data are available they should be reported. The relevant test guidelines are:
  - OECD Test Guideline 451 Carcinogenicity studies
  - OECD Test Guideline 453 Combined chronic toxicity/carcinogenicity studies

- Reproductive Toxicity: is a SIDS endpoint and requires data to assess fertility. Requirements for fertility data can be met through use of OECD Test Guideline 415: One-Generation Reproduction Toxicity Study or OECD Test Guideline 416: Two-Generation Reproduction Toxicity Study. In addition, OECD Test Guideline 421, ‘Reproduction/Developmental Toxicity Screening Test’ or OECD Test Guideline 422, ‘Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test’ can also be used as discussed in Section 2.3.2.

- Developmental toxicity: is a SIDS endpoint and required to assess pre- and post-natal developmental toxicity. The relevant Test Guideline is OECD Test Guideline 414, ‘Prenatal Developmental Toxicity Study’. OECD Test Guideline 421, ‘Reproduction/Developmental Toxicity Screening Test’ or OECD Test Guideline 422, ‘Combined Repeated Dose Toxicity
Study with the Reproduction/Developmental Toxicity Screening Test can also be used in certain circumstances as discussed in Section 2.3.2.


- Experience with Human Exposure (if available). Experience with Human Exposure, if available, is a SIDS element. Information on workplace exposure such as concentration of chemicals in the workplace (manufacturing, maintenance and professional use) and indoor environment should be described. Information related to the number of workers (in ranges for each situation including manufacturing, maintenance and professional use), the frequency, duration and level of exposure should also be mentioned if available. In addition, details of effects of accidental or occupational exposure, epidemiological and clinical studies, case reports and the like can also be described. If data on experience with human exposure is available, it should be presented in the same order as data with laboratory animals in the previous sections.

2.2.2 Existing SIDS Data

The existing SIDS data may come from various sources and be available in a variety of formats. This section provides guidance for retrieving existing information.

**Data gathering**

There is a need to identify, assemble and review data relevant to the SIDS elements. The data gathering process described below may differ depending on whether the hazard assessment covers the full range of SIDS or only targeted endpoints, and also whether the hazard assessment is sponsored by industry or by a member country. A three-stage data gathering approach has been found effective for locating all relevant data for review, based on past experience with the HPV chemicals.

**Stage 1**

Firstly, industry should search their files for privately held data on the chemical. All available information should be noted since refinement of the data search will take place at stage 3.

**Stage 2**

Stage 2 involves a broad search of databases and the published literature to obtain all available data on the chemical. As far as possible, original publications should be retrieved. The data sources listed below are not an exhaustive list but provide a useful starting point.

- Search of published scientific literature through the use of e.g. ACToR. Health effects data are available online through the National Library of Medicine network. Other broad-based databases that may be of use include the following: STN easy online, Poltox CD-ROM 1966-2000, ECOTOX, Medline, Enviroline, Embase, Aqualine, ASFA 3 (same as Aquatic Pollution and Environmental Quality), Chemical
Abstracts, SciSearch, BIOSIS, Pesticide Fact Sheets, Chemtox TOXLINE, OSH-UPDATE, HSELINE.

- In the event that original study reports may not be obtained, standard references known to publish “peer reviewed” data should be searched. Examples of useful references are as follows:
  - **ACToR** ([http://actor.epa.gov](http://actor.epa.gov)): searches many data collections for toxicity and other information
  - **Merck Index** – For physical-chemical properties and use information. Available as a book and online in the STN network.
  - **Condensed Chemical Dictionary** – For physical-chemical properties and chemical use information. Book.
  - **Kirk-Othmer Encyclopedia** – For chemical use information. Book.
  - **Patty’s Industrial Hygiene and Toxicology** – For health hazard data. Book.
  - **USEPA IRIS** – For toxicity data, NOAELs, RfDs, RfCs and cancer slope factors. Available online and as downloadable files.
  - **ATSDR Toxicological Profiles** – For health effects, use and exposure data. Available online, as published reports and CD-ROM.
  - **NTP (National Toxicology Program)** – For health effects, use and exposure data. Published reports and on-line (by subscription or free.)
  - **IARC (International Agency for Research on Cancer)** – For health effects, use and exposure data. Available online, as published reports.
  - **OSHA (Occupational Safety and Health Administration)** – For workplace exposure standards and their basis. Federal Register, other publications and online at [http://www.osha.gov/](http://www.osha.gov/).
  - **ACGIH (American Conference of Governmental Industrial Hygienists)** Recommended workplace standards and their basis. Publications and CD-ROM.
  - **AIHA (American Industrial Hygiene Association)** Recommended workplace standards and their basis. Publications and available on-line. Subscription service.

- Physical-chemical properties can also be obtained from standard reference works such as:
  - *Hawley’s Condensed Chemical Dictionary*, Richard J. Lewis, author of editions 14 and 15. Other editions by Hawley;
  - *The Beilstein Handbook of Organic Chemistry*;
• *Sax's Dangerous Properties of Industrial Materials*, Richard J. Lewis, author of editions 8 – 11;
• *Bretherick’s Handbook of Chemical Reactive Hazards*, Peter Urben, editor of 7th Edition;
• *Lange’s Handbook of Chemistry*, James Speight, author of 16th Edition. Previous editions with different authors;

International reviews such as Concise International Chemical Assessment Documents (CICADs) and Environmental Health Criteria Monographs should be consulted where available. The Environmental Health Criteria (EHC) documents contain data on use, exposure, human toxicology and environmental toxicology. The more recent EHCs also include a proposal for maximum permissible risk levels. CICADs are either based on EHCs or on selected national or regional evaluation documents. Searches for both CICADs and EHCs may be conducted at http://www.inchem.org/pages/search.html. Sponsors should search multiple databases to ensure that all existing data have been obtained. Some of the data may not have been peer reviewed; however, the information may provide supporting data for a SIDS element. These may consist of some of the following resources:

• **IUCLID** (International Uniform Chemical Information Database) – For chemical use, exposure, environmental fate, ecotoxicity and mammalian toxicity. IUCLID files generated under the Existing Substance Regulation are also often available in the European chemical substances information system (ESIS) (http://ecb.jrc.ec.europa.eu/esis/).

• **AQUIRE** (Aquatic Information Retrieval) – For aquatic toxicity data. Available online in the CIS network.

• **TOXNET** by the National Library of Medicine (NLM) offers links to Toxline, TRI, HSDB and others at www.toxnet.nlm.nih.gov. Further, EPA’s ECOTOX database covers Aquire, phytotox, terretox at www.epa.gov/ecotox/.

• **RTECS** (Registry of Toxic Effects of Chemical Substances) – For health effects data. (Note: mainly positive findings are reported here, other results might be available in other databases.) Available online in the TOXNET and STN networks.

• **TSCATS** (Toxics Substances Control Act Test Submission) Database – For unpublished chemical hazard data submitted under TSCA Section 4, 8(d), 8(e) and FYI. Available online in the CIS network or in the NLM network as a subset of TOXLINE.

• **TRI** (Toxics Release Inventory) – For environmental release data in the US. Available online (http://www.epa.gov/tri/).
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- HSDB (Hazardous Substance Data Bank) – For chemical use, fate and health effects data. Online in the TOXNET network.

- Verschueren, K. *Handbook on Environmental Data on Organic Chemicals*. Book


- There may be other national reviews available, for example from the UK Health and Safety Executive (HSE), German MAK commission (DFG Herausgeber, List of MAK and BAT values, Wiley, VCH), German Advisory Committee on Existing Chemicals (BUA reports, S. Hirzel Wissenschafrliche Verlagsgesellschaft), Nordic Expert Group, the Netherlands DECOS. HSE publishes comprehensive reviews for Occupational Exposure standard setting, toxicity reviews and other more focussed documents such as their compendium of asthmagens. These are searchable on HSELINE, details of which are available at [http://www.hse.gov.uk](http://www.hse.gov.uk).


Appropriate search strategies should be adopted and search terms should be stated in the SIDS Dossier.

Stage 3

The third stage in the process involves selection of the most appropriate data collected during stages 1 and 2. Peer-reviewed data sources such as those listed above may prove useful in deciding which data is valid and the most relevant. However, when compiling the data for the Dossier, sponsors should be careful not to leave out studies, as the real selection takes place for the elaboration of the assessment report.

Information from the data search should be organised and formatted in a SIDS Dossier as described in further detail in this Chapter 2; the format of the SIDS Dossier generally follows the format of IUCLID files. Robust Study Summaries should be prepared for the key studies and included within the Dossier (see section 2.4.2. regarding robust study summaries). Furthermore, the *Guidance for Determining the Quality of Data for the SIDS Dossiers: Reliability, Relevance and Adequacy (Chapter 3)* should be used for determining whether information is satisfactory for use in the initial assessment of a chemical, be it a full or a targeted hazard assessment. Since it is not feasible to give guidance to cover every situation it is essential that suitably-qualified personnel evaluate all data. The results of the evaluation will influence the decision on further testing.
Use of existing datasets already presented in the format of SIDS Dossier

For many chemicals sponsored within the OECD HPV Chemicals Programme, datasets following the format of the SIDS Dossier already exist, following submissions to national/regional programmes (e.g. Robust Study Summaries elaborated for the US HPV Challenge Programme or IUCLID files submitted in the context of the EU Existing Substances Regulation). Sponsor countries have often used existing datasets in the past as a basis for developing SIDS Dossiers.

General Procedure

Merging pre-existing dossiers into the SIDS Dossier can help save resources. Nevertheless, the general philosophy regarding transparency and quality of entries in the SIDS Dossier should apply to all entries in the Dossier, independent of the origin of the record. The following procedure should therefore be respected to maintain a high level of quality in the SIDS Dossier:

- In chapters 2-5, for existing entries for studies which are published in the literature or for which the original study report is available to the author, the publication or report should be reviewed and its reliability should be determined, similarly to newly-created entries. If it is judged to be a key study, a complete Robust Study Summary needs to be developed.

- Existing entries for studies which cannot be retrieved should remain in the Dossier for completeness’ sake. A comment should be added that the reliability of these results cannot be assessed (reliability 4).

- Existing entries which have no reference (i.e. expert judgements) should be deleted from the SIDS Dossier as these discussions should be in the SIAR.

- Existing entries of (Q)SAR results generated with old versions of models should be deleted and replaced with estimations from the latest versions of the models.

Whenever pre-existing datasets are used for the purpose of a submission to the OECD HPV Chemicals Programme, issues regarding data ownership should be solved in advance of the submission.

Clarification on data ownership

- Case of study results used for the preparation of an OECD assessment report: the proprietary rights related to the use of study results contained in existing published or unpublished Dossiers or the scientific literature for use in an assessment report for the purpose of the OECD Programme is not governed by any OECD Council Decision, and only national regulations apply. Good practice should guide the user of study results not published in the open literature to request permission from the data owner prior to submitting the assessment report to the OECD.

- Case of study results available in an OECD assessment report that are used to fulfil national/regional regulatory requirements or for use in another assessment submitted to the OECD Cooperative Chemicals Assessment Programme: the use of study results published in SIDS Initial Assessment Reports to fulfil data requirements under national/regional assessment schemes or to prepare another assessment submitted to the OECD is subject to the proprietary rights protection as defined in the legislation of those national/regional schemes (i.e. normally request permission from the data owner). In other words, the use of a company-owned study result in a SIDS Initial Assessment does not mean that the proprietary rights of that company are forfeited.
Specific issues with IUCLID files

For many substances, a IUCLID report has been submitted by European producers and importers to the European Commission in the context of the European Existing Substances Regulation. These reports have been published by the European Commission, both as a PDF file and as a IUCLID export file (http://ecb.jrc.ec.europa.eu/esis/). These files might be used as a starting point for developing a SIDS Dossier.

In addition to the general considerations outlined above, wherever possible, the SIDS Dossier should be elaborated with the IUCLID software, which is the most commonly used software and mandatory for REACH registration dossiers.

2.3 THE SIDS PLAN

Once the existing data have been collected and reviewed, it is necessary to decide the need for additional adequate data. The Sponsor decides, for each endpoint, as to: the adequacy of existing data (through test data, surrogate data, or SAR), or the need to gather additional information through the performance of additional tests, or (Q)SAR predictions or read-across from analogues. All existing information should be gathered and described in an initial version of the chemical’s SIDS Dossier.

2.3.1 Determining the Need for Additional Data

To avoid unnecessary duplication of work and possible needless use of animals for testing, it is important that all existing available relevant data be located and reviewed. The requirement to complete any individual data element of the SIDS by further testing will depend upon the reliability and quantity of data available. In analysing the adequacy of existing data, Sponsors shall conduct a thoughtful, qualitative analysis rather than use a rote checklist approach. Sponsors shall maximise the use of existing and scientifically adequate data to minimise further testing.

When existing data are determined to be inadequate to support the requirements for a SIDS element it should not be automatically assumed that additional tests are required. There are a variety of circumstances in which a SIDS element could be waived or met through other approaches. These include:

Animal Welfare Considerations. The statement on animal welfare adopted by the Second High Level Meeting of the Chemicals Group should be taken into account when determining the need for new SIDS testing. To facilitate its consideration it is reproduced here.

"The welfare of laboratory animals is important. It will continue to be an important factor influencing the work in the OECD Chemicals Programme. The progress in OECD on the harmonization of chemicals control, in particular the agreement on Mutual Acceptance of Data, by reducing duplicative testing, will do much to reduce the number of animals used in testing. Such testing cannot be eliminated at present, but every effort should be made to discover, develop and validate alternative testing systems.

“The High Level Meeting invites the Chemicals Group, the Management Committee, the Updating Panel, Lead countries and the Secretariat, to ensure that the spirit of this Declaration is an integral part of their work.” [ENV/CHEM/HLM/M/82.1, para. 95]

6 The general content of this section is based on a document discussed at the 20th Joint Meeting of the Chemicals Group and Management Committee of the Special Programme on the Control of Chemicals (May 1993).
**The Use of (Q)SAR.** Appropriate information derived from (Quantitative) Structure Activity Relationships can be of assistance in determining the need for new testing. The OECD (Q)SAR Toolbox for Grouping Chemicals into Categories is a useful tool to help filling data gaps and forming chemical categories. It is a software application intended to be used by governments, chemical industry and other stakeholders in filling gaps in (eco)toxicity data needed for assessing the hazards of chemicals. The Toolbox incorporates information and tools from various sources into a logical workflow. Crucial to this workflow is grouping chemicals into chemical categories. When reporting (Q)SAR predictions in the SIDS Dossier, there are essential elements to report in support of the prediction (see section 2.4.2 on Template Prediction Reporting Format below). Also, the *Guidance on the Use of Structure-Activity Relationships (SAR) in the HPV Chemicals Programme* (Chapter 3) should be consulted.

**The Use of Chemical Categories or test data on analog(s).** One approach is to consider closely related chemicals as a group, or category, rather than test them as individual chemicals. In the category approach, not every chemical needs to be tested for every SIDS endpoint. However, the test data finally compiled for the category must prove adequate to support a screening-level hazard assessment of the category and its members. That is, the final data set must allow one to assess the untested or weakly documented endpoint(s), ideally by interpolation between and among the category members. In certain cases, such as where toxicity does not change among tested category members, extrapolation to the untested category members may be acceptable. See also *Guidance on the Development and Use of Chemical Categories in the HPV Chemicals Programme* in Chapter 3.

**Practical Considerations.** Practical reasons for completing less than the SIDS for an individual chemical include the availability of information concerning isomers that have a similar structure-activity profile; closely-related homologues; relevant precursors and breakdown products along with information on metabolism and degradation (see section 2.3.3 below on analogues). As a general approach, for each particular endpoint, the use of range-finding tests may be an appropriate first step to establish relative levels of toxicity between isomers.

Less than a standard SIDS testing regime may also be appropriate for chemicals that are unstable under test conditions or for reasons based on their physical/chemical properties. For example:

- It might not be appropriate to test the aquatic toxicity of gases, and QSAR estimations might be sufficient to fill the corresponding SIDS elements.
- Testing to obtain dissociation constant data is not needed for chemicals or classes of chemicals generally known not to dissociate (e.g., hydrocarbons).
- Testing for stability in water is not needed for substances generally recognised to have molecular structures or possess only functional groups (e.g., hydrocarbons) that are generally known to be resistant to hydrolysis.
- For substances which have an obviously high boiling point and low vapour pressure (e.g. some inorganic or organic salts), an estimation of these two endpoints could be sufficient.
- For strong acids, reproductive and developmental toxicity tests may be waived with proper justification.
- For highly reactive substances that release HCl, repeated-dose and reproductive and developmental toxicity might be waived with proper justification.

For some chemicals standard tests may be irrelevant or not provide meaningful results. Testing should not be conducted, when it cannot be done safely. When testing is not practical or meaningful for reasons such as stated above, the reason for not testing should be given in the SIDS Dossier and/or the SIAR.
Limited Exposure Potential, \(^7\) (especially for intermediates which have a limited exposure potential). In the case of a full SIDS assessment, reduced testing may be appropriate for a SIDS chemical due to limited exposure potential, depending on production or use scenarios. The considerations below are specific to chemical intermediates. A chemical that is intended to undergo a further deliberate reaction to produce another industrial substance is considered an intermediate. In the context of the OECD Cooperative Chemicals Assessment Programme, reduced testing may be permissible for intermediates handled in a specific manner that results in a limited potential for exposure. Eligibility for reduced testing is possible only for chemicals whose entire production is used as an intermediate. Specific circumstances and the associated reduced data requirements are given below:

a) Non-isolated intermediates, i.e. those chemicals whose life cycle is restricted to the reaction vessel and its specific equipment. All forms of repeat-dose testing (including reproductive and developmental toxicity testing) may be waived. If the releases to the aquatic environment can be shown to be negligible, testing on acute toxicity towards fish might be waived if this endpoint can be adequately filled with \((Q)SAR\) estimations.

b) Isolated intermediates that are stored in controlled on-site facilities. If repeat dose data are available, reproductive and developmental toxicity may be waived. If repeat dose data are not available, testing using OECD Test Guideline 422 should be considered on a case-by-case basis.

c) Isolated intermediates with controlled transport, i.e. to a limited number of locations within the same company or second parties that use the chemical in a controlled way as an intermediate with a well-known technology. If repeat dose data are available, reproductive and developmental toxicity may be waived. If repeat dose data are not available, testing using OECD Test Guideline 422 should be considered on a case-by-case basis.

Data that support claims for exemptions from SIDS testing based on limited exposure must meet criteria for reliability and adequacy of SIDS data. This requirement for reliability and adequacy of data also applies to substantiated evidence of existing or potential exposure made by a member country that objects to the reduced data requirement based on limited exposure.

Specific information is required to support a claim for reduced testing. The details are set out below:

1. Information on sites
   - Number of sites
   - Basis for "closed process" conclusion at each site:
     - process described in enough detail to clarify the basis for claiming that the process is closed;
     - monitoring data, including the limits of detection;
     - if monitoring data are not available, statement that no monitoring has taken place and basis for believing, in the absence of data, that the chemical has not been released and that exposure does not occur.
   - Data on "presence in distributed product" or, in the absence of data, the basis for believing it is not present. (The basis can be an explanation from the manufacturer why it is unlikely that the chemical is not or no longer present in a distributed product.) Information on conversion rate and presence after purification should be available.

2. Information on transport. If transport occurs, then in addition to the above, provide the following:
   - Mode of transport (e.g. water, truck, rail, pipeline);
   - Volume (annual);
   - Types of consignments (e.g. bulk or drums);

\(^7\) This is with the caveat that use pattern/exposure scenarios may differ in countries other than the sponsor’s/lead country and that in such cases this should always be mentioned in the assessment profile.
Controls during transport and transfer at dispatching and receiving sites (placards, labels, etc.).

3. Supporting evidence from a data search showing that the chemical is not present in other end-products. (The basis can be an explanation from the manufacturer why it is unlikely that the chemical is present or used in a distributed product.)

For chemicals other than intermediates, the possibility of reduced SIDS testing exists based on considerations of limited potential for exposure. Adequate experience is not yet available though to develop suitable criteria to define such considerations in sufficient detail.

A proposal for reduced testing due to a limited exposure potential (including for intermediates) must be put forth to other member countries to provide an opportunity for their review and comment, preferably through the use of the community website. A member country can object to the reduced SIDS testing requirements if they provide substantiated evidence of existing or potential exposure in their country. In cases where no agreement can be reached via the community discussion group, the SIAM will decide.

The justification for reduced testing should be reflected in the dossier entry for the endpoint that was not completed, so that when data searches are performed at a later stage, the reason for not performing the test can be retrieved.

These considerations for reduced testing are not relevant for targeted assessments.

2.3.2 Notes on Test Selection

Any new SIDS testing that is required should be performed according to internationally acceptable Test Guidelines and Good Laboratory Practices. Test reports should contain suitable, signed GLP and quality assurance statements.

In cases where the SIDS Plan proposes complex or unorthodox approaches, the Sponsor is encouraged to post the SIDS Plan on the community discussion group early in the process for review and comment by other SIDS Contact Points.

Ecotoxicity testing

For aquatic effects testing, prolonged/chronic toxicity testing should be considered in addition to acute tests if there is concern for long-term effects. If there is concern for possible long-term effects, for example based on the structure and properties of the chemical such as a high Log Kow and a lack of ready biodegradability, and there is potential for significant exposure to the aquatic environment, prolonged/chronic toxicity testing may be considered. Any new data should be collected using the species that had the lowest L/EC₅₀ in the acute tests, taking into account animal welfare considerations and any practical limitations due to the chemical properties. If algae are the most sensitive species, a growth inhibition test with a different algal species or with a different aquatic plant such as Lemna should be considered.

The need for terrestrial testing may be considered if significant exposure is expected or identified in the terrestrial environment (soil). Factors to consider when determining whether terrestrial toxicity testing should be performed include:

- Potential for reaching the terrestrial environment based on use and transport patterns and disposal practices, e.g., take into account all phases of the chemical’s life cycle;
- Physical-chemical properties indicate that the compound may be persistent, has a potential to bio-accumulate, or that a major portion may partition to the soil; and/or
- Monitoring data indicate residues in soil, sewage sludge or groundwater.

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OECD Test Guidelines and GLP or equivalent Test guidelines and GLP principles of Member countries.
The terrestrial test selected at the SIDS stage should be appropriate to the receiving environmental compartment (e.g. in the case of sewage sludge, toxicity to earthworms and plants). In addition, attention should be given to the potential for cross-media distribution. Initially, a test should be performed on terrestrial invertebrates and/or plants. The artificial soil test is preferred because the paper contact test is not truly representative of the natural habitat. Taking into account animal welfare considerations, the need for avian toxicity testing should only be considered at the post-SIDS stage.

**Mammalian toxicity**

For mammalian toxicity, substances should be tested by the most relevant route, i.e. the oral route for many chemicals. Dependent upon the most important route of human exposure and physical-chemical properties of the substance, the dermal or the inhalation route could also be considered. Gases and vapours should be tested only by the inhalation route. A different route of exposure may be used if it is generally regarded as an appropriate route for a particular protocol.

For oral acute toxicity to mammals, guidance regarding the choice of the most appropriate Test Guideline to meet data requirements while reducing the number of animals used and animal suffering can be found in the OECD Guidance Documents on Acute Oral Toxicity Testing (OECD Series on Testing and Assessment Number 24) and on Acute Inhalation Toxicity Testing (OECD Series on Testing and Assessment Number 39). Consideration should be given to the possibility of using data from analogues or repeated dose toxicity studies on the same substance as a substitute for conducting new acute tests.

Regarding genetic toxicity, guidance on testing can be found in sections 2.2.1 of this chapter as well as in Chapter 4, section 4.3 under “Provisional guidance for the initial assessment of health effects.” Results on two different endpoints should be available, generally gene mutation and chromosomal aberration. If any test results on genetic toxicity in vitro are positive, it is necessary to perform appropriate in vivo tests to further explore the reasons for the positive in vitro findings.

For health effects testing the reproduction toxicity requirements may be satisfied through the use of data from several studies. Three typical examples are provided below:

- Requirements are met if existing data on the chemical include a developmental toxicity study and a 90-day repeated dose study that sufficiently documents that reproductive organs were examined histologically and indicate no effects. If results from a developmental toxicity study are not available then such a study is required (e.g. OECD Test Guideline 414).

- When either a 90-day with no evaluation of reproductive organs or a 28-day repeated dose study is the only repeated dose study available, it is recommended that at least a reproduction/developmental toxicity screening test (e.g. OECD Test Guideline 421) be carried out, in order to satisfy the requirements for the reproductive/developmental toxicity endpoint.

- When a repeated-dose toxicity test of 28-days or longer is not available, then a combined repeated dose toxicity test with a reproductive/developmental screening test (e.g. OECD Test Guideline 422) can be carried out to satisfy the requirements for repeated dose and reproductive/developmental toxicity. (This option uses the lowest number of test animals to satisfy both the repeated dose and the reproduction toxicity requirements.)

### 2.3.3 Determining What Chemical to Test

In general, tests should be carried out with the substance as manufactured and to which humans or the environment is exposed. However, several practical issues should be considered in the selection of the actual test substance. Several are summarised below:
To avoid interference from additives and impurities, when practical, it is recommended that tests for physical-chemical properties be conducted on the purest form available that allows the substance to remain stable.

Toxicity tests on SIDS endpoints should generally be carried out on the typical commercial substance with any essential additives (e.g. stabilisers) and impurities it normally contains in order to know the effects of the marketed product. Ideally, the same batch of substance should be used for all tests. If the marketed product contains large proportions of water, mineral oil or other solvents, consideration should be given to their removal from the test substance so that the SIDS chemical may be evaluated at concentrations that have biological relevance.

Highly reactive chemicals may not be stable enough for experiments to be conducted; hence testing with the parent chemical may not be practical. In these cases, it may be useful to identify and selectively examine breakdown products for possible fate/metabolism and potential adverse effects. Where a compound is of limited stability, it may be desirable to design individual ways to test the potential effect of breakdown products for particular endpoints. For aquatic toxicity testing, the instability of the tested chemical may be circumvented by using a flow-through system that continuously dispenses the chemical to test and thus allows measuring toxicity of the sponsored chemical; however a static system allows the assessment of the toxicity of breakdown products, which is also of interest as it reflects the reality. For estimations on environmental fate of hydrolytically instable chemicals, it is usually more pragmatic to use breakdown products if they are identified, but it gives more work to sponsors to go on that side of investigations. For testing aquatic toxicity with reactive substances, see also the Guidance document on aquatic toxicity testing of difficult substances and mixtures (OECD Monograph No 23, Series on Testing and Assessment).

Data from analogues

It is appropriate to investigate the use of analogues or surrogates to assist in providing supplemental data to reduce possible testing needs. The OECD Guidance Document on Grouping of Chemicals should be consulted for guidance on using analogues (OECD Monograph No.80, Series on Testing and Assessment). In some situations data from another chemical can be used, such as:

- isomers that have similar structure activity profiles;
- closely related homologues;
- relevant precursors and breakdown products, along with information on metabolism and degradation.

The data of the related compound should be inserted in the SIDS dossier for the chemical if the analogue has not yet been assessed in the OECD Cooperative Chemicals Assessment Programme; otherwise a reference to the published SIDS Dossier for that chemical may suffice. The SIDS Dossier should clearly state the identity (chemical name and CAS No.) of the related compound. When data for an analogue chemical are used to fill one or more endpoints, the data for the analogue’s other endpoints (e.g. physical-chemical properties, metabolism, toxicity profile, etc.) should be compared and discussed in relation to the main chemical to shed light on the similarities and differences in the properties of the main chemical and its analogue. This comparison is usually described in the assessment report (SIAR/ITAR) and in the profile containing summary conclusions (SIAP/ITAP); the assessment report and the profile are described in Chapters 5 and 6.

Chemical Categories

A chemical category is a group of chemicals whose physicochemical and toxicological properties are likely to be similar or follow a regular pattern as a result of structural similarity. These structural similarities may
create a predictable pattern in any or all of the following parameters: physicochemical properties, environmental fate and environmental effects, and/or human health effects. The similarities should be based on the following:

- common functional group(s) (e.g. aldehyde, epoxide, ester, specific metal ion);
- common constituents or chemical classes, similar carbon range numbers. This is frequently the case with complex substances often known as “substances of Unknown or Variable composition, Complex reaction products or Biological material” (UVCB substances);
- an incremental and constant change in chemical structure across individual discrete/pure chemicals included in the category (e.g. a chain-length category), resulting in a predictable change in physicochemical properties, e.g. boiling point range;
- the likelihood of common precursors and/or breakdown products, via physical or biological processes, which result in structurally similar chemicals (e.g. the “metabolic pathway approach” of examining related chemicals such as alcohol/aldehyde/acid or ester/alcohol/acid or salt/acid).

Categories can sometimes apply to series of chemical reaction products or chemical mixtures that are, again, related in some regular fashion. Analogous to the basic “discrete chemical” category model, some (but not all) of the individual mixtures may undergo testing in a mixture category (e.g. linear alkylbenzene mixtures).

If the available test results show that the chemicals in the category behave in a similar or predictable manner, then interpolation and/or extrapolation can be used to assess the chemicals in lieu of conducting additional screening-level testing.

A clear explanation needs to be provided as to why a category is being proposed and how the presented data are going to be used in relation to the category and the testing plan. The category may also be applicable and justifiable for some endpoints and not others; it should be very clearly stated in the SIAR/ITAR what is covered under the chemical category and why, and how data are used and for which endpoints. Occasionally, a large chemical category may be divided in sub-categories for which adequate justification of boundaries is needed (see the example of long chain primary alcohols). It is recommended that a SIDS Dossier be prepared for each individual chemical within the category. In section 1.03 of the SIDS Dossiers of each chemical forming the category, the identity of the substances forming the category should be listed together with the rationale behind the formation of the category. At a minimum, data on each chemical’s physical chemical properties should be provided.

For the preparation of the SIDS Dossiers for each individual chemical within the category, each Dossier would only contain the information and Robust Study Summaries which are available for each specific substance forming the category. In situations where data from another chemical within the category is used to complete an endpoint, a reference to the SIDS Dossier(s) containing the data would be inserted in each of the dossiers in which the endpoint is not filled with data. If information from another related chemical outside of the category is used to complete an endpoint, the study results of the related compound should be inserted in the SIDS dossier for the chemical, clearly stating the identity (chemical name and CAS No.) of the related compound being used to fill the endpoint.

The use of a Data Matrix can help to illustrate the extent to which analogue data is used to fill data gaps. A data Matrix is usually reported in the assessment report. Further guidance can be found in the Guidance for the Development and Use of Chemical Categories in the HPV Chemicals Programme (see Chapter 3).

Applicability of the chemical category: The basis for category proposals varies depending on the specific reasons for forming a category. Experience to date has shown that a chemical category proposal may be acceptable for one set of the SIDS elements but not others. As an example, a chemical may be manufactured and produced similarly, have similar physical-chemical properties and environmental fate, but may be expected to react differently in the aquatic environment or behave differently concerning health.
toxicity. In these cases, it is recommended that the Sponsor thoroughly evaluate the chemicals proposed in the category to determine if possible sub-categories may be required for specific endpoints.

2.3.4 Review of the SIDS Plan

Once the available data are collected in the initial SIDS Dossier they are evaluated and a determination made on the need for additional testing. These decisions, and the logic used in their formulation are assembled in a SIDS Plan. Wherever the sponsor has ascertained that adequate data for a SIDS element are not available and testing is considered unnecessary (e.g. due to limited exposure, use of data from analogues, a category approach), it shall seek agreement from the other SIDS Contact Points, together with full justification and relevant supporting data. This can be done via the community discussion group. The statement should provide detailed argument explaining why testing is not needed. Arguments for not testing must be well developed and convincing. When this SIDS Plan is submitted it should be supported by an initial version of the chemical’s SIDS Dossier with Robust Study Summaries (described in the next section and in Annex 1) that shows SIDS data gaps and whether testing is required.

Once the testing plan has been agreed on the Electronic Discussion Group, any additional testing is to be conducted and results incorporated in the SIDS Dossier.

2.4 THE SIDS DOSSIER

The SIDS Dossier is the basic reference document that contains or cites all readily available data/information on the chemical under investigation, following a pre-defined structure or format. As a basic reference it initially underpins the SIDS Plan and ultimately, with revision, the SIAR (see Chapter 5). To facilitate review of data in the OECD Cooperative Chemicals Assessment Programme it is important that SIDS Dossiers be prepared using a harmonised format. Such format guidance is provided in Annex 1. In addition, Annex 2 provides guidance for entering data into SIDS Dossiers using the IUCLID software (see guidance below).

The SIDS Dossier frequently develops in two stages: initial collection and formatting of data; and an updating or revision stage. In the updating stage the SIDS Dossier is revised through the inclusion of data from new SIDS testing, SAR analyses etc. Robust Study Summaries are developed and included in the SIDS Dossier for selected key studies as discussed below. Templates for Robust Study Summaries are found in Annex 1.

2.4.1 Data Collection and Preferred Software

The SIDS Dossier provides information about each SIDS element together with non-SIDS elements (where such information is available and relevant to the assessment) in a standardised format. As described above, SIDS information is organised under five headings: Substance information; Physical-chemical properties; Environmental fate; Environmental toxicity; and Mammalian toxicity.

The IUCLID software\(^9\) is the preferred format for entering data, and developing a SIDS Dossier, using the standard templates. The dossier can be submitted preferably as an exported electronic IUCLID file, or as a hard copy printed directly from IUCLID. By using the IUCLID software for data collection, efficiencies are gained at the data submission stage. Step-by-step procedures for preparing a SIDS Dossier using the IUCLID software are provided from the IUCLID Internet site at the following URL: http://iuclid.eu/index.php?fuseaction=home.documentation#usermanual.

\(^9\) IUCLID - International Uniform Chemical Information Database
Information presented in a SIDS Dossier should be sufficiently reported and referenced with respect to the substance tested, methods used, endpoints examined and results obtained so as to allow reviewers to make an informed judgement of the suitability of the data for its intended use.

All studies containing data relevant to a SIDS element should be cited in the SIDS Dossier. When more than one study exists for a data element, a brief description of the reliability and adequacy of the studies should be presented. Consistency of the study data results should also be summarised.

The reliability of data in the SIDS Dossiers should be determined by the Sponsor using the criteria set out in Chapter 3 under “Guidance for Determining the Quality of Data for the SIDS Dossiers: Reliability, Relevance and Adequacy.” The following general principles should be used in reviewing and documenting the quality of the data in the SIDS Dossier:

- Each SIDS Contact Point in a Sponsor country should have the opportunity to evaluate the reliability, relevance and adequacy of key and supporting data for a chemical(s). In principle, all OECD member countries will rely upon their evaluation of the quality, if the study is sufficiently documented in the Robust Study Summary contained in the SIDS Dossier. The templates for Robust Study Summaries discussed below include a section which describes the rationale for the reliability of the study as well as the process by which the “reliability” decision was taken.

- In general the supporting data and reports will not be kept confidential [see also OECD Council Act C(83)98(Final) and its OECD List of Non-Confidential Data on Chemicals]. In exceptional cases where data are confidential the data will be made available for review under the conditions set out in the OECD Council Act concerning Exchange of Confidential Data on Chemicals [C(83)97(Final)]. This Council Act applies to specific experts in each country who receive the data.

When a study fails to meet core data adequacy criteria, minimum information should still be provided, e.g. comments explaining why the study is considered inadequate. It is important to record the existence of studies - even if regarded as inadequate - because in some contexts, they may be used to provide sufficient information on a SIDS element, avoiding the need for additional testing. This is particularly true where there may be good data from chemical analogues to give support for the study result.

2.4.2 Robust Study Summaries and Template Prediction Reporting Format

The Robust Study Summary is the most efficient way of providing sufficient information on a study that will allow assessors to judge the reliability and adequacy of the study. In SIDS Dossiers, Robust Study Summaries are important for the adequate presentation of any study relevant for hazard assessment. This is in general true for “key studies,” which are the basis for the data analysis presented in the SIAR (see section on Key Studies below).

A Robust Study Summary should reflect the objectives, methods, results and conclusions of a full study report. Information within a Robust Study Summary should be provided in sufficient detail to allow a technically qualified person to make an independent assessment on its reliability and completeness - minimising the need to go back to the full study report. Given the central role of Robust Study Summaries in providing the basis for the assessment of a chemical in the Cooperative Chemicals Assessment Programme. In exceptional circumstances member countries reviewing the SIDS assessment may request the original study from the sponsor.

In principle, at least one key study should be summarised in the form of a complete Robust Study Summary for each SIDS element. Under special data conditions, it may be necessary to prepare also Robust Study Summaries for inadequate or invalid studies as further outlined in section on Key Studies. Where data on certain elements for the sponsored chemical are not available and surrogate information is to be used, the SIDS Dossier should contain Robust Study Summaries of data on the related compounds (see section 2.3.3) and the identity of the related compounds should be clearly stated under the test substance heading.

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A series of templates for Robust Study Summaries have been developed for all of the SIDS elements. They have been structured to allow for computerised data entry via IUCLID by describing the items in each Robust Study Summary as “data fields” with allowance for free text. The Robust Study Summary templates have eight sections: Test Substance, Method, Test Conditions, Results, Conclusions, Reliability, References, and Remarks. Templates provide a convenient data management tool by providing prompts for the type of information to include. This will increase the quality of the SIDS Dossier and description of the study overall.

The Robust Study Summary also allows for remarks on the adequacy and relevance of a study. By including detailed information in the IUCLID, the information in the SIAR can remain more concise and focus on interpretation of results.

The following descriptions of information to be provided in the SIDS Dossier are applicable to all elements, whether they are SIDS or non-SIDS endpoints and whether there is a Robust Study Summary template available or not.

**Test Substance**: This refers to the identity of the chemical. Where possible the purity, percentages of known impurities, and details of any vehicle used should be given. If the chemical used in the specific test was different from the commercial product (purity, additives, different solvent carrier, etc), then those differences need to be noted. This notation is inserted in the Test Substance Remarks field. If the chemical(s) are listed in EINECS, it would also be useful to have its identification number.

**Method**: This section refers to the methodologies used to conduct the study. If the study was done according to OECD Test Guidelines or other widely recognised standard test methods/guidelines (e.g. OECD, ISO, DIN, APHA, and EPA), this should be identified. The year of publication of the guideline should be reported as well, as revisions of Test Guidelines may change the method used. In these instances where an OECD Guideline was used, a full description of the method is not needed; only the name of the guideline, e.g. OECD 421, “Reproduction/Developmental Toxicity Screening Test” needs to be reported. The same considerations apply for studies run under standard guidelines that have since been superseded or deleted. When a non-standard method has been used, details of the method, equivalent to those in an OECD Test Guideline, should be provided. If such information is not available this fact should be noted.

When the test method allows variations for certain test parameters (e.g. species), the variations chosen should be indicated. In the case of aquatic toxicity tests, it is important to indicate under Analytical monitoring whether nominal or measured concentrations were used.

If there have been deviations from the Test Guideline, then those deviations that will significantly impact either the study reliability or the interpretation of the data need to be individually listed. There may also be situations in which a single study addresses several elements, such as with a study that follows the OECD combined repeat dose/reproduction/developmental (OECD Test Guideline 421). If a key study is available addressing more than one SIDS element, then several Robust Study Summaries would be prepared. Thus the Results and Conclusions sections would be different depending on the endpoint but the Method and Reference section would be the same in each case.

**Test Conditions**: Any relevant information on test conditions, e.g. for aquatic toxicity testing: temperature, pH, flow-through or static renewal, can be listed under this heading. For aquatic toxicity studies, the test preparation of difficult to test substances (e.g. insoluble chemical, unstable chemicals) should be described with particular care as it often helps interpretation of test results.

**Results**: This section includes standard items to be filled in under discrete bullets for additional items that may be needed to adequately assess data for reliability and use. Qualitative descriptions of elements where dose-related observations were seen should be described and a NOAEL and LOAEL stated (where relevant) for critical effects together with the rationale for selection of these values (e.g. biological
significance, lack of genotoxicity, etc.). A quantitative description of the extent of changes measured compared to control may also help and if available from the study, this information should be reported in the Robust Study Summary. If the control values measured were outside the historical change, this is an important feature to report. In addition, should a study include effects that were not considered to be biological or statistically significant, an explanation should be given.

Expressing results by phrases such as "insoluble in water" is discouraged. A limit test should be performed under such circumstances so that a positive expression, such as "< 0.1 mg/l (analytical limit)", can be entered. Calculated values must be identified and the calculation method should be cited. If a statistical reanalysis of the data was performed by the reviewer, this should be mentioned separately.

Conclusions: The conclusions of the author of the study can be noted, together with any comments of the person preparing the Robust Study Summary. The conclusions of the submitter or reviewer of the data should be clearly separated if these are different from the conclusions of the author, by indicating the origin of the comments.

Reliability: This section can be used to denote the adequacy of data, at the discretion of the person preparing the summary. Data reliability codes can be used, as described in Chapter 3 under Guidance for Determining the Quality of Data for the SIDS Dossier. The rationale for the reliability code should be described clearly as should the process by which the "Reliability" decision was made. A rationale supporting selection of the “key study” should be given (where applicable) and how the Robust Study Summary was confirmed as an accurate reflection of the original study data should be described in this section.

References: This free text field is to be used by the person preparing the SIDS Dossier to cite full references for the critical studies on which the summary is based. The source of information used to respond to the endpoint should be identified. In general, information should be taken from primary sources and quoting from secondary references such as a book or a review article should be avoided. References should include the title of the article, the journal where study appears, volume and page numbers, and date of report or publication. Where appropriate, "unpublished report," its authors and their affiliation should be used. Lesser details can be cross-referenced within the appropriate individual data element.

Only one study should be summarised per Robust Study Summary. In cases where multiple studies are available, separate Robust Study Summaries should be prepared. However, if more than one reference is available describing the available study (such as the original study and published articles of the study results), then it would be appropriate to have one single study summary with multiple references.

Remark: This section includes a free text field for general remarks.

Note that the structure and items given in the robust summary templates are intended to provide guidance on the type of information to be included, but do not exactly mirror the corresponding IUCLID subchapter screens. The items provided in the templates either correspond with defined fields in IUCLID or must be entered in IUCLID free text fields. The type of information described in OECD templates under "Remarks" normally must be entered into IUCLID free text fields. The most appropriate free text type should be selected, e.g. "Test Conditions", "Results" etc. Only information that does not fit into a specific free text type should be entered in free text type "Remarks".

Reporting format for (Q)SAR predictions

When no or limited experimental data are available, an estimation may be possible using (Q)SAR results. In order to facilitate the regulatory acceptance of (Q)SAR predictions, it is necessary to provide a minimum set of information on the prediction model used and its suitability for predicting an effect for a given chemical and endpoint.

Target substance: the identity and characteristics of the target substance should be provided, including the CAS number and other regulatory numbers, the chemical name and synonyms, the structural formula, the structure codes (SMILES), the quality of structure identity and databases used.
General information: date and author(s) of the report.

Category definition and structural analogues [in case of grouping chemicals for read across]: requires definition of the applicability domain of the chemical category [functional group, type of reaction (e.g., nucleophilic substitution), parametric boundaries (e.g., boundaries for Log Kow), endpoints covered by the category and category members], a category justification and a data matrix showing for which chemicals experimental data is available.

Prediction: The information provided in this section will allow the assessor to judge the adequacy of the prediction. The prediction is documented following the OECD principles: (1) a defined endpoint, (2) an unambiguous algorithm, (3) the applicability domain as defined by the SAR, (4) uncertainty of the prediction, (5) chemical and biological mechanisms.

Adequacy: the user is free to manually add information on the regulatory purpose, the approach for the regulatory interpretation of the model result, the outcome and conclusions.

A Template Prediction Reporting Format (TPRF) has been developed as part of the OECD (Q)SAR Application Toolbox. The use of the TPRF ensures provision of complete information for the assessor to judge the suitability/adequacy of the prediction for a given chemical. The TPRF is the equivalent of the Robust Study Summary for test data.

The TPRF can be generated by the OECD (Q)SAR Application Toolbox. The headings and sub-headings are automatically created and the user may manually edit some of the fields. Some fields are automatically filled-in (e.g. applicability domain of the category).

It is not mandatory to use a TPRF for reporting (Q)SAR predictions. However a (Q)SAR prediction should be supported by a minimum set of information following the OECD principles mentioned above.

Key studies

In general, a key study is the study that has been identified as most suitable to describe an endpoint from the perspective of quality, completeness and representativity of data. When several study results are available on a specific endpoint (maybe using different species or routes of exposure), they can be used together to derive a more sound hazard assessment. However, they can also originate from different periods of time and laboratories, can be of different quality and can be performed according to different guidelines. Therefore, each study’s value to the hazard assessment has to be judged individually.

Considerations for key studies

The prerequisites for a key study concept related to toxicological and ecotoxicological studies are that:

a) it is in accordance with the principles laid down in the relevant Test-Guidelines;
b) it is a tiered (see figure 2.1) and transparent approach that ensures that at least one reliable study is defined as a key study for each SIDS element;
c) it is flexible so it can accommodate special data conditions and hazard assessment requirements following consultations with a SIDS Contact Point.
Figure 2.1 provides a decision tree for defining the level of detail for reporting key studies and non-key studies.

**Fig. 2.1.-** Decision tree for defining the level of detail for reporting of key and non-key studies

![Decision Tree](image)

All available significant studies should be referenced in the dossier. For non-key, less substantive studies, summaries need not be as robust for weight of evidence support. A study summary with a minimum level of detail is sufficient. For studies that are flawed, but indicate critical results, Robust Study Summaries highlighting the weaknesses of the studies need to be elaborated. These considerations apply primarily to SIDS elements, but should also be made for other endpoints.

**Toxicological studies**

If there are several reliable tests (for example, for acute oral toxicity testing on the same species), the most appropriate test should be identified as key study. Among a set of well-documented and well-conducted studies, the key study for a specific endpoint is normally defined as the study that results in the lowest no-effect value (below which no effects were seen for that endpoint in that or any other study) or the lowest effect dose (e.g. LD₅₀ or LC₅₀) (indicating highest toxicity) and the characteristic signs of toxicity for the substance in the relevant species, or as the study with the highest sensitivity (for example, a Magnusson and Kligman test instead of a Buehler test). The most sensitive species should normally be used, except in those cases where evidence is available that the given effect(s) are species specific and are not relevant for human health evaluation.

It might be necessary for several studies to be considered as key studies for the same endpoint (for example, when data is available on several species or different routes of exposure or if different results are observed in valid tests).
Ecotoxicological studies

A short summary (including the main results and an indication of the reliability) of all studies performed should be provided in the SIDS Dossier. The key study should be selected and summarised in greater detail according to the Robust Study Templates. If there are several reliable studies based on different test guidelines on the same endpoint, the key study should be selected from the method with the highest sensitivity. It might be necessary for several studies to be considered as key studies for the same endpoint (for example, when data is available on several species). The environmental hazard assessment will focus on the most critical value for each endpoint. For example when more than one $LC_{50}/EC_{50}$ value is available, the lowest result from a valid study is chosen and a Robust Study Summary is developed for the corresponding study. Robust Study Summaries need also be elaborated for studies giving more critical results but which are considered inadequate or invalid. For endpoints with many available data and for which a conclusion is taken on a weight of evidence approach (e.g. ready biodegradation) it might be necessary to produce Robust Study Summaries for all available test results.

2.4.3 Notes on reporting existing data on non-SIDS endpoints in the SIDS Dossier

Introduction and general principles

There is a common acceptance that the standard SIDS package can and should be augmented by additional available data where these can help the understanding of the hazards of the particular substance. It is recognised, however, that, without guidance, the scope of these additional data will be open to considerable interpretation.

For transparency, all available and relevant data should be referenced in the SIDS dossier and should be used for the hazard assessment. Studies that are invalid or have other shortcomings should still be documented. Non-SIDS data is expected to be treated in the same way as SIDS elements, with some assessment of the study validity and relevance, with justification, and preparation of Robust Study Summary(ies) for key study(ies), as described in section 2.4.1-2.4.3.

Additional testing does not need to be conducted on non-SIDS endpoints for the initial assessment; however, any available information on non-SIDS endpoint need to be reported in the assessment.

It is difficult to provide a definition of information that is ‘relevant’ to the hazard assessment and expert judgement should be used during the information collection stage. Data that is likely to have a significant effect on the overall conclusion of the hazard assessment is certainly relevant, but information that supports the conclusions from the SIDS may also be relevant (for example, analytical chemistry data that supports conclusions about the stability of the substance). In some cases, the information may be readily discounted as irrelevant to the assessment, for example when a chemical is tested for properties that are not relevant to the environmental or health hazards.

Endpoints relating to environmental effects, fate and behaviour, including relevant physico-chemical properties

It is not possible to provide a definitive list of non-SIDS endpoints that may be relevant to an environmental hazard assessment, due to the wide range of studies available in the published literature. Information on the toxicity, environmental fate and behaviour of a chemical are all relevant to its hazard assessment and the following list provides an indication of non-SIDS endpoints that could be considered as relevant. In general terms, any data that could reasonably be expected to influence the determination of a predicted environmental exposure or effect concentration should be included.
Short and Long-term Ecological Effects

Toxicity to aquatic organisms: short and long-term toxicity to both standard and non-standard species, including tests conducted to standard national and international guidelines. Such tests would include:

- Short-term (acute) toxicity to non-standard species and taxa
- Long-term (chronic) toxicity to standard and non-standard species
- Other long-term toxicity where end-points are not covered above, or show a different level of toxicity (e.g. endocrine disruption)
- Short and long-term toxicity to sediment dwelling organisms
- Short and long-term toxicity to amphibia

Toxicity to soil organisms: short and long-term toxicity to both standard and non-standard species, including tests conducted to standard national and international guidelines. Such tests would include:

- Effects on mortality and reproduction of earthworm
- Effects on higher plants
- Effects on soil micro-organisms
- Effects on soil arthropods, e.g. Collembola

Toxicity to terrestrial animals (not covered in health section): short and long-term toxicity to both standard and non-standard species, including tests conducted to standard national and international guidelines. Such tests would include:

- Effects on avian mortality and reproduction

Toxicity to micro-organisms: short and long-term toxicity to both standard and non-standard species, including tests conducted to standard national and international guidelines. Such tests would include:

- Activated sludge respiration inhibition test
- Soil micro-organisms, Nitrogen and Carbon transformation tests
- Activated sludge simulation tests
- Growth inhibition tests with protozoans

Atmospheric effects: where significant release to the atmosphere is possible, and information exists on ozone depleting potential, photochemical ozone creation, and/or global warming potential, this should be included in the assessment (it may be possible to predict some of these properties in the absence of data). Effects on plants and other organisms due to atmospheric exposure should be considered for volatile substances.

Environmental Fate and Behaviour

Partitioning and Mobility: information relating to partitioning and mobility in environmental compartments, including tests conducted to standard national and international guidelines. Such tests would include:

- Adsorption/desorption studies, such as Koc determination

Degradability: information relating to degradation in the environment, including tests conducted to standard national and international guidelines. Such tests would include:

- Biodegradability in biological waste water treatment plants, freshwater, seawater, groundwater, sediment and soil: non-SIDS screening tests and tests simulating environmental conditions
- Anaerobic biodegradation

The term “standard species” is here used to refer to species used in standard national or international test guidelines.
• Abiotic degradation data in environmental media, e.g. photodegradation in water

Bioaccumulation: information relating to bioconcentration, bioaccumulation, and biomagnification, including tests conducted to standard national and international guidelines. Such tests would include:

• Determination of bioconcentration factors in fish and other species
• Data from other studies such as feeding studies

Monitoring data: if available, monitoring of levels in the environment and biota should be included where this can be used to confirm the hazardous properties of the chemical, such as persistence or bioaccumulation.

Presentation of Environmental Information

Those endpoints with OECD Test Guidelines would be considered a priority and should be included in the hazard assessment. For example, long-term aquatic (including sediment) toxicity, toxicity to microorganisms and to soil-dwelling organisms, avian toxicity and environmentally relevant mammalian toxicity. Other toxicity data should be reviewed for its relevance to the assessment but the presumption must be that it should be included unless clearly not relevant. Additional information on the fate and behaviour would include adsorption-desorption, measured bioconcentration factors, and degradation studies. In addition, tests on non-standard test species such as amphibians should be included.

Endpoints relating to human health, including relevant physical chemical properties

In addition to SIDS elements, the following endpoints could be relevant for the overall assessment of a substance and existing data should be reported and assessed.

• Relative density
• Flammability (including reactions with water to liberate flammable gases or pyrophoric properties)
• Explosive properties
• Viscosity (for hydrocarbons)
• Surface tension (of an aqueous solution)
• Toxicokinetics (including absorption, distribution, metabolism, excretion and physiologically based pharmacokinetic modelling)
• Corrosivity/Irritation (skin, eye and respiratory tract)
• Sensitisation
• Carcinogenicity
• Neurotoxicity
• Other - In some circumstances there might be mechanistic/explanatory studies available that may have a very detailed (e.g. biochemical mechanism; effect on isolated mitochondria) and/or general applicability (e.g. endocrine disrupting potential).

One can reference information about a particular endpoint in various ways. Two examples are:

Repeated dose toxicity

This endpoint can be informed by a wide range of experimental studies in animals from several days duration, to more prolonged and even lifetime studies. In addition, relevant human data may be available, e.g. from epidemiology studies. Effects such as neurotoxicity or immunotoxicity may have been identified, or studied in some detail, in the repeated dose studies; these then comprise part of the repeated dose toxicity endpoint.

Mutagenicity
This can be informed by a range of *in vitro* or *in vivo* studies that may evaluate different mechanisms of mutagenicity (e.g. gene mutation, chromosome abnormalities, DNA damage, etc). In addition, useful information can be obtained from structure activity considerations (would the compound or a metabolite be expected to react with DNA?). Occasionally there may be some relevant human data.