

MANUAL FOR INVESTIGATION OF HPV CHEMICALS

CHAPTER 5: PREPARATION OF THE SIDS INITIAL ASSESSMENT REPORT (SIAR) AND SIDS PROFILE ¹

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¹ This document was prepared by the OECD Secretariat based on the agreements reached in the OECD Existing Chemicals Programme up to June 2008.

5.1 Introduction

The SIDS Initial Assessment Report (SIAR) has one primary purpose. It is the document through which the key scientific data on a chemical (or category of chemicals) are presented for scientific and technical review and discussion by Member countries. This review and discussion are concluded at an assessment meeting (SIAM) where data interpretations and conclusions are accepted as proposed or after appropriate revision. The SIAM also recommends whether a chemical is or is not a candidate for further work (with appropriate supporting rationale). The conclusions and recommendations are submitted for endorsement by the Task Force on Existing Chemicals, and then for consideration to and approval and by the Joint Meeting of the OECD Chemicals Committee and Working Party on Chemicals, Pesticides and Biotechnology. The recommendation from the SIAM is transmitted to the Joint Meeting in a SIDS Profile that also contains basic information on the chemical and a brief description of the potential human and environmental hazards.

In 1998 the OECD HPV Chemicals Programme was re-focused to characterise hazardous properties of nominated chemical substances, rather than to conduct initial risk assessments of these substances. The Joint Meeting agreed to refocus the Programme with the objective of increasing the output as well as to make best use of the data and the hazard assessments offered by the International Council of Chemical Associations (ICCA). Detailed exposure information gathering and assessment as well as risk assessment are possible in the post-SIDS part of the OECD HPV Chemicals Programme, provided the chemical has been identified as a candidate for further work. It was foreseen that Member countries would use the conclusions of these initial hazard assessments to determine the need for further work. The use patterns and associated exposure conditions for the substance usually influence the nature of such further work. Further (post-SIDS) work can include national/regional exposure information gathering and assessment as well as testing of endpoints beyond SIDS to assess a concern identified by SIAM. In the majority of cases post-SIDS exposure assessment in follow-up to SIAM will be undertaken nationally (or regionally). It is possible, however, that concerted OECD-wide post-SIDS exposure information gathering and assessment due to the nature of the hazard(s) and the use of the chemical is recommended.

Under the Initiative launched by ICCA, industry has committed to provide SIDS documents (using OECD guidance for preparing SIDS dossiers, SIARs and Profiles) for 1,000 HPV chemicals. A SIAR, while introduced into the SIAM process by a Sponsor country, is commonly drafted by a company (or group of companies) that has committed to develop data and assessments under ICCA in accordance with the procedures of the OECD HPV Chemicals Programme. Governments and industry frequently share in the presentation at the SIAM. Alternatively, Member countries or industry can also take independently the initiative to prepare the SIDS documents and bring them forward to a SIAM, as a direct submission.

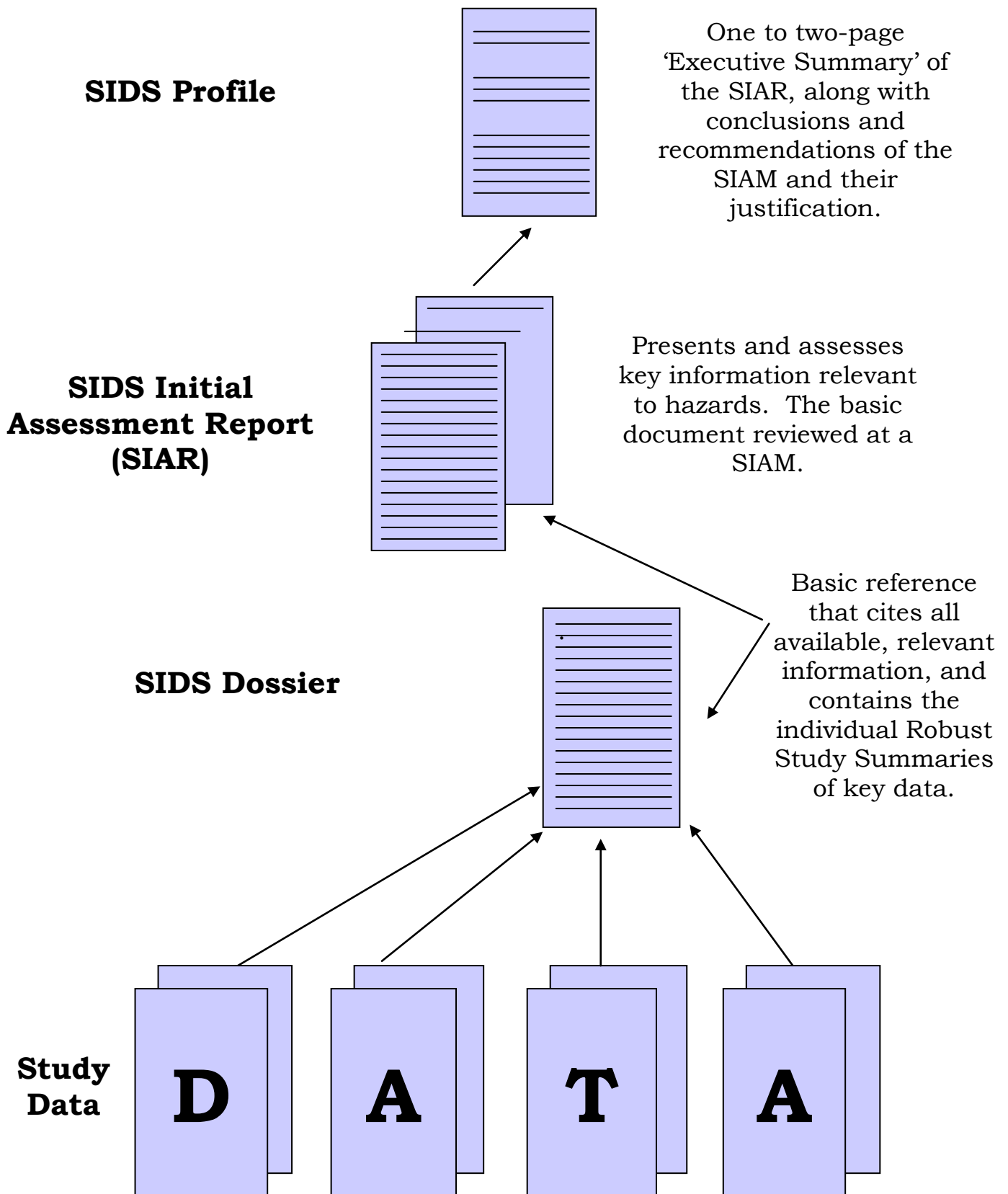
There are primarily three documents involved in the activity of the HPV Chemicals Programme: SIDS Dossier, SIDS Initial Assessment Report, and SIDS Profile. As was discussed in Chapter 2, a SIDS Dossier describes relevant data on a substance, and also contains Robust Study Summaries prepared from key studies. It is the Robust Study Summaries that form the core of information, which is then presented and discussed in a SIAR. The SIAR should be limited to the summary information necessary to reach the hazard conclusions. Finally, a SIDS Initial Assessment Profile, also known as a “SIDS Profile” or SIAP, is a one to a few-page executive summary that transmits the conclusions and recommendations of the SIAM on a chemical to the Joint Meeting for endorsement, while keeping in mind that it is also written for a general public (see also section 5.3.1). The relationship between the various documents relevant to the final scientific review (SIAM) in the OECD Programme is summarised in a simplified manner in Figure 5.1.

The structure and content of both the SIAR and the SIDS Profile are discussed later in this chapter. A format for the SIAR cover page is given in Annex 1 to this chapter and Annex 2 to this chapter contains a format and proposed standard text for the SIDS Profile. Following endorsement of the SIAM conclusions and recommendations by the Joint Meeting, the SIAR is published together with the SIDS Profile and the SIDS Dossier and made available world wide through UNEP Chemicals (<http://www.chem.unep.ch/irptc/sids/OECDSIDS/sidspub.html>)². The SIDS Profile is also published in the HPV database which is found on the EHS public internet site. This ensures that the results of the work on each of the chemicals in the HPV Chemicals Programme can be easily obtained.

The global chemical industry, through its member companies, is a major contributor of information and expertise to the HPV Chemicals Programme. This guidance is therefore intended to assist industry, as well as governments, as they work together in partnerships to complete the goals of the Programme.

² SIARs provide OECD's contribution to the challenge set by the United Nations Conference on the Environment and Development (UNCED) in Chapter 19 of *Agenda 21*. This challenge seeks to ensure that a significant number of internationally agreed assessments on chemicals are available worldwide.

Figure 5.1: Illustration of Documents considered at a SIAM



5.2 Guidance for the Preparation of SIDS Initial Assessment Reports (SIARs)

5.2.1 Overview

The purpose of this section is to provide guidance to Member countries and industry on the nature, structure and content of the SIDS Initial Assessment Report (SIAR) to be prepared under the refocused HPV Chemicals Programme.

The SIAR is based on information provided in the SIDS Dossier (see chapter 2 for guidance on how to select key studies and prepare Robust Study Summaries). Using a standardised format, it sequentially discusses key information for each endpoint that is relevant for the Initial Hazard Assessment by presenting information that is drawn from Robust Study Summaries (key studies) and in some instances from the complete data compilation on that topic that is found in the SIDS Dossier. It integrates relevant data and forms conclusions about the hazardous nature/properties of the chemical for human health and the environment. If certain SIDS endpoints are deemed not relevant for an initial hazard assessment, the SIAR should contain a brief explanation of the reasons.

One of the main objectives of the SIAR is to identify and characterise hazards related to SIDS elements and to other non-SIDS elements where this information is available. Although the conclusion of a SIAR on a hazard endpoint should not actually classify a chemical, it should include as far as possible the information related to the degree of an identified effect in order to assist countries in their classification work. The observed adverse effects should therefore be described in detail so that the GHS-system (Harmonised Integrated Hazard Classification System for Chemical Substances and Mixtures) can subsequently be used by Member countries following the completion of the work at the SIAM.

The SIAR also seeks to put hazard(s) into context by including general information on exposure. This exposure information will typically be of limited scope and depth and is not intended to be used as a basis for risk assessment.

NOTE: As stated in chapter 2, the SIDS requirements are fulfilled if exposure information from the Sponsor country is available. Other relevant available information should also be reported in the SIAR and used to put the hazard into context and to derive a recommendation. In this chapter, the expression “available exposure information”, refers to all relevant and readily available exposure information and at a minimum to the information regarding production volume, use pattern and sources of exposure in the Sponsor country.

The SIAR should present and discuss conclusions based on data interpretation, in a transparent and logical manner. These conclusions and accompanying narrative provide the basis for recommendations concerning the priority for additional work.

The SIAR, in addition to its primary use in a SIAM review, is also a vehicle for communication to persons who may be responsible for ensuring the safe manufacture, use and disposal of chemicals. It should enable the reader to quickly grasp the basis of the assessment and the scientific argument supporting the conclusions of the initial hazard assessment.

To ensure consistency and quality of this document, the SIAR should be divided into the sections outlined below.

1. Chemical Identification, Physical/Chemical Properties (if appropriate, a rationale and justification for a category approach should be added in this section)
2. General Information on Exposure
3. Human Health Hazards and Initial Assessment for Human Health
4. Hazards to the Environment and Initial Assessment for the Environment
5. References
6. Annexes (optional)

For a single chemical the overall document should generally be about 30 pages long (excluding annexes). By necessity SIARs for categories will be somewhat longer. Care should be taken to ensure that the SIAR actually describes the relevant hazards, rather than merely repeat the details given in the SIDS Dossier. Where there are multiple sources of data for a SIDS element a weight of evidence narrative should be used to summarise its content. The summary should discuss if there is concordance of results across the studies and if effects were seen at a similar dose range; if results diverge, a plausible basis for such divergence, if any, should be discussed. References for the key studies and any other studies specifically mentioned in the SIAR should be included in the SIAR, to ensure that it is a stand-alone document.

Tables are a useful tool to present study results, particularly when there are multiple studies available for a given endpoint or for a chemical category. Using tables ensures that the text of the SIAR is brief and focuses on the interpretation of the presented data rather than the experimental design and results. When the data summarised in the SIDS Dossier are conflicting or present a range of results, the use of tables in the SIAR is encouraged to highlight the key results. Tables may also be useful to present study results for certain elements, particularly when there are multiple studies available for a given element. This will ensure that the text of the SIAR focuses on the interpretation of the key studies rather than the experimental design and results.

To ensure a harmonised format between initial assessments drafted by different member countries, a template for the SIDS Initial Assessment Report was elaborated. It is an integral part of chapter 5 of the *Manual for Investigation of HPV Chemicals* and can be downloaded from the public OECD internet site [see: http://www.oecd.org/document/7/0,2340,en_2649_34379_1947463_1_1_1_1,00.html].

A statement of the nature and extent of the data available for each SIDS element should be given, including whether data from analogue chemicals (e.g. from a related category) has been used. Where a SIDS element has only partially been filled but other relevant information is available which, taken together, provides an adequate assessment of that SIDS element, e.g. information from closely related analogues, this should also be clearly identified. Where no data are available for a SIDS element, a brief statement such as “No data were found for developmental toxicity....” with a justification or reason presented as to why a new study should not be required.

When reliable and relevant studies are available on non-SIDS elements, the results should be presented and discussed in the SIAR (see Chapter 2 for guidance on how and when data on non-SIDS elements should be presented in the Dossier). There is no obligation to generate *de novo* data on non-SIDS elements.

In principle, only reliable information (e.g. with a reliability score 1 or 2 according to the Klimisch codes) should be used to describe the hazards of a substance (see section 3.1 for more guidance on reliability, relevance and adequacy of available information). Studies which are considered to be unreliable

need to be mentioned only if they give critical results or if they can play a role in the weight-of-evidence assessment on a given endpoint, in the absence of reliable studies; however their reliability score following Klimisch codes need to be clearly mentioned in the SIAR. In case where data are available for a non-SIDS element, but where all these data are not reliable, the presence of these results can simply be stated.

If results are available whose reliability could not be ascertained (e.g. due to missing information on the test conditions, or because a test report is no longer obtainable) but which might be relevant because they support other available and reliable results, they can be mentioned in the SIAR, but with a clear indication that their reliability could not be established. Such results would normally be assigned Klimisch code (4) not assignable. For transparency reasons, it is important to state why the reliability could not be assigned.

In some cases, as explained in section 3.1.6 (Weight-of-evidence analysis), there may be several results available on a given endpoint, none of which would be acceptable by itself due to some deficiency. Collectively however, if for example the results confirm each other, they could satisfy the data element for SIDS. In the SIAR this should be highlighted and discussed.

Where a category of chemicals is being assessed together, the category should be presented in one overall SIAR supplemented as necessary with appropriate information for each member of the category contained within the corresponding SIDS Dossier. It is highly relevant for a chemical category to present individual chemicals data from the key studies and for a given endpoint in a tabular format in the SIAR for an overview of the read-across application.

5.2.2 Structure and Content of the SIAR

A Cover Page (see Annex 1 to this chapter as well as the overall template for the SIDS Initial Assessment report) should precede the SIAR and present:

- The prior history of the chemical in the programme, i.e. how the chemical or category was sponsored and brought into the SIDS programme;
- Details of the quality check process and a description of shared partnerships between government and industry, where applicable. The quality check discussion should describe how data in the SIDS Dossier (including Robust Study Summaries) was extracted from the original study data and how the reliability of the results was checked.

Other formats than the one described below can be accepted if they comply with the objectives of the SIAR, i.e. outline the rationale for the hazard conclusions.

1. Identity

This section of the SIAR should include the following basic information on the chemical in a table format:

- Identification of the chemical(s) (e.g. CAS number(s), name(s), structural and molecular formula where applicable, etc.).
- Composition of the chemical(s) being assessed:
- For a single chemical: degree of purity, known impurities or additives, difference of impurities among products.

- For mixtures: percentages or range of percentages of mixture components, known impurities or additives, differences among products.
- For streams: typical descriptors, known impurities or additives, differences among products.
- Basic elements of physical-chemical properties (e.g. water solubility, Log K_{ow} , vapour pressure, etc.). As for most substances Log K_{ow} will be the parameter on which the classification for bioaccumulation potential will be based, the validity of the available results should be discussed and a “recommended value” should be proposed.

In the event that a chemical category is proposed or data from an analogue is used, section 1 should contain a category/analogue justification/rationale. It should be approximately 1 to 2 paragraphs and present the basic principles, concepts and rationale that support such an approach. In the event a complicated concept is being proposed additional information beyond the 1 to 2 paragraphs should be presented as an Annex to the SIAR. The section may also present similar or analogous chemicals for which data are available and with which the HPV chemical under consideration could be compared. When a category of chemicals is being assessed together, the relevant information in this section should be presented for each member of the category, along with a summary of the justification for using the category. Each member of the category should be clearly identified, using consistent nomenclature and other references throughout. Data may be used for related chemicals outside of the category.

2. General Information on Exposure

Available exposure information should be provided to clearly summarise the uses and the potential sources of exposure during the life cycle of the chemical as outlined below. Information on potential human and environmental exposure should be described at a general level of detail. It is not necessary to conduct exposure modelling or monitoring for the purposes of the SIDS initial assessment. However, when more detailed relevant information is available, it should be noted in the SIAR, so that its availability is known. Alternatively, such information could be annexed to the SIDS Dossier.

When a hazardous substance is indicated to be a low priority for further work based on exposure considerations, the following aspects should be considered and clearly addressed in Sections 2.1-2.3 of the SIAR:

- If information is available on sources of exposure (workers, consumers, environment), it should always be specified whether it is related to a given site or whether it can be considered to be generic for a given use. For the latter case, a justification should be put forward.
- The extent to which information provided is based on actual measurement of releases or exposures, modelling or other estimation methods, or expert judgment should be clearly indicated.
- When describing the sources of potential exposure to humans and the environment, the availability of exposure information relating to transport between sites and storage at production and use sites should be addressed and the available information should be qualified as to its scope and degree of completeness.
- Similarly if information is available on exposure reduction measures, it should always be specified whether this is related to a given site or whether it can be considered to be generic for a given use. For the latter case, a justification should be put forward.
- The specific producers and/or users to which any information provided applies should be identified.

As for hazard data, the source of exposure information should always be provided.

2.1 Production Volumes and Use Pattern

At a minimum, the following information must be provided to put the human health and environmental hazard information into context:

- Estimated production/import volume in the Sponsor country (in tonnes per year) or, for assessments prepared under voluntary industry programmes, in the country where the lead company is located (see section 1.5 of the SIDS Dossier).
- Use categories and/or functions in the Sponsor country or, for assessments prepared under voluntary industry programmes, in the country where the lead company is located (see section 1.6 of the SIDS Dossier).

The following supporting information, if reported, would significantly improve the usefulness of the SIAR:

- an estimate of the percentage of the production volume for each use in the Sponsor country or, for assessments prepared under voluntary industry programmes, in the country where the lead company is located;
- the OECD and global annual production quantities 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;
- number and production capacities of producers in other countries if verifiable;
- brief general description of manufacture/production;
- physical form of product(s) as transported or as purchased and used by the consumer;
- the use pattern in other countries, if verifiable.

If only the production/import volume and use pattern in the Sponsor country (or, for assessments prepared under voluntary industry programmes, the country where the lead company is located) are available, it should be clearly indicated that the production/import volume and use pattern in other OECD countries is unknown or not provided. If the information provided pertains to a country other than the Sponsor country, that country should be prominently indicated as distinct from the Sponsor country.

Information on the actual use of a substance, in terms of volumes, number of products, composition of products and the use and industry categories where the substance can be found, might also be available from product registers. Of special importance is the information on down-stream uses and consumer availability.

However, each of the product registers has their special characteristics that must be taken into account when interpreting the product register data. There are some uncertainties associated with the concentrations in products and the volumes of products and substances that arise from the way the data are reported. Other sources of uncertainty are due to wrong or no reporting, time delays in updating of the product register databases and due to the fact that primarily only dangerous substances are recorded.

To be able to judge on the usefulness of data from product registers, at least the following information would need to be available:

- Product Register (Name and Country);
- Description of the product use(s), chemical functions, concentrations in products and volumes per use as specifically as possible. If the product may be used by consumers, it should be indicated;
- Date (year) the information being submitted was collected, and date (year) of the last update.

2.2 Environmental exposure and fate

Sources of potential releases to the environment as well as the most likely compartment of release (see section 1.7 of the SIDS Dossier) should be discussed qualitatively in this section. The whole life-cycle of the substance should be taken into consideration. Available information on releases into the environment, or monitoring data can be summarised in this section.

Information about environmental fate and pathways should be provided based on the available information on potential sources of release to the environment, use categories and physical-chemical properties, as well as the following specific test or estimation results:

- Photodegradation
- Stability in Water
- Transport between Environmental Compartments, and
- Biodegradation.

When presenting data that has been obtained via modelling, the SIAR should clearly state the specific model and version used. Input values are more appropriately placed in the SIDS Dossier.

The results of all testing or modelled data should be clearly summarised in a final paragraph so that the reader may easily understand the overall behaviour of the chemical in the environment.

The GHS-system introduces the concept of rapidly degradable substances including pass levels for such substances. This requires that additional data compared to the concept of ready and inherent biodegradability is presented if available:

- 10 days time window for all ready biodegradability tests;
- information on degradation products in some cases where it has to be shown that these products are not classified as hazardous to the aquatic compartment;
- MITI II results after 14 days and Zahn-Wellens-Test results after 7 days, for non-readily biodegradable substances.

If this information is not available, it should be highlighted.

If results of bioaccumulation studies are available, they should be critically discussed and a recommended BCF should be proposed.

2.3 Exposure to Humans

Generally, available information should be presented and discussed for occupational and consumer populations (see section 1.7 of SIDS Dossier). When presenting occupational exposure information, existing relevant workplace exposure limit values (e.g. TLV, MAK) may be presented, along with job tasks associated with the highest potential exposure. Non-occupational exposure should address direct exposure from use of products that contain the chemical, (e.g., is the chemical polymerised, bound or otherwise immobilised?), and indirect exposure, such as via food, water and air, or because the chemical is naturally occurring. If available information suggests certain factors may be associated with high potential exposures (for example, a specific use pattern or contact pathway, such as presence in certain diet constituents), this information should be included in the discussion. In describing sources of human exposure, the exposure pathway should be described for each source.

3. Human Health Hazards

3.1 Effects on Human Health

Results of toxicity tests and other information should be summarised and discussed in the order shown below:

- a) Toxicokinetics and metabolism and mode of action (if known)
- b) Acute Toxicity
- c) Irritation (if available)
- d) Sensitisation (if available)
- e) Repeated Dose Toxicity
- f) Genetic Toxicity
- g) Reproduction/Developmental Toxicity and
- h) Other valid and reliable information that is available, e.g. Neurotoxicity, Carcinogenicity, etc...

Each of these elements should be clearly identified by the use of sub-headings and further separated by similar study type (for example, oral, dermal, and inhalation routes of exposure). There should be remarks about the experimental results, discussion and conclusions for each SIDS element. The SIAR should summarise the conclusions on each specific element before proceeding to discuss the next element. The intent is not to repeat the detail of the information given in the SIDS Dossier but to briefly highlight the key aspects. For the purpose of hazard identification, it is important to report the toxicological effects that are seen as well as the actual doses that produced these effects, especially for repeated dose toxicity and reproduction/developmental toxicity. If human data are available, they should be described separately from non-human data under the relevant endpoint.

Summary tables are recommended, when more than one adequate or key study is available. The table should be placed in the body of the document (rather than in an annex) and summarise the relevant data used to reach the conclusion presented in the SIAR. Any text used in support of the conclusions may also accompany this tabulated data, if necessary. When the SIAR interpretation of a study differs from that of the study author, the SIAR should contain sufficient information describing the alternative interpretation and a narrative supporting the reason(s) for a difference in interpretation. In addition, this same approach should be taken when there are multiple studies available which vary significantly in addressing a given endpoint.

In cases where there is immediate and/or significant breakdown of the chemical(s) being assessed, the potential toxicological significance of breakdown products or metabolites should be discussed in section "Toxicokinetics and metabolism and mode of action". When the test substance rapidly metabolises or breaks down under the test conditions, the data presented in the SIAR (for the parent chemical) should reflect the toxicities or effects of the breakdown products.

Evaluation of the test results on Repeated Dose toxicity and Reproduction/Developmental toxicity as well as other relevant endpoints should include a judgement on the No-Observed-Adverse-Effect Level (NOAEL) and Lowest-Observed-Adverse-Effect Level (LOAEL). Such a judgement should be made taking into account statistical significance, other adverse effects as well as information on whether dose-response relationship was observed. Where the combined Repeated Dose toxicity and Reproductive/Developmental toxicity testing has been carried out (OECD Test Guideline 422, 'Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test'), care must be taken to separately present results of systemic effects of repeated dosing and the developmental and reproductive effects. In addition, OECD Test Guideline 422 primarily is a screening level test; therefore, the effect should be reported along with the degree of certainty or uncertainty placed on that result by the

toxicologist. Given the modest size of each dose group, requiring strong levels of statistical significance is not appropriate.

Where relevant and reliable data are available on non-SIDS elements such as irritation, skin sensitisation, neurotoxicity, and carcinogenicity, they should be presented and conclusions summarised in the manner discussed in the preceding paragraphs.

4. Hazards to the Environment

4.1 Aquatic effects

Results of ecotoxicity tests and other information are summarised and discussed, including:

- Acute (short-term) toxicity to Fish, *Daphnia* and Algae, and
- Available subchronic/chronic (prolonged/long-term) toxicity data on Fish, *Daphnia* and Algae.

Results from tests with other aquatic species, especially micro-organisms, should also be reported if relevant.

In the discussion, a qualitative consideration of the following items is recommended if the relevant data are available:

- The toxic mode of action of the chemical, and
- The possibility to cause chronic effects based on physical-chemical properties, stability, relationship between acute toxicity and time, release pattern, degradation products, etc.

Each separate SIDS element should be presented in its own section or paragraph. When presenting data that has been obtained via modelling, the SIAR should clearly state the specific model and version used. Input values are more appropriately placed in the SIDS Dossier.

The results of all testing or modelled data should be clearly summarised in a final paragraph so that the reader may clearly be able to understand the overall toxicity of the chemical in the aquatic environment.

Predicted No Effect Concentrations (PNECs) are not required. However they may be included for information purposes. If provided, the PNEC value for the aquatic environment should be derived consistently by applying relevant assessment factors. These assessment factors depend on the adequacy of the data available. PNECs are useful in a screening level assessment because they allow a judgement to be made on the concentration where critical effects may be expected to be seen in the aquatic environment. Deriving these values takes into account the range of information about the full aquatic ecosystem. The reason for choosing a particular assessment factor should be stated in the SIAR. Guidance on the derivation of PNECs can be found in section 4.2. The PEC/PNEC ratio is a risk-based calculation and therefore not appropriate for the SIAR or SIDS Profile.

4.2 Terrestrial effects

If information is available which shows that significant exposure to the terrestrial environment is expected, information on acute toxicity to earthworms and terrestrial plants should be provided (see Chapter 2, section 2.3.2). Other relevant available test results, e.g. toxicity to soil micro-organisms, should

also be reported in this section. There is no agreed OECD guidance for the assessment of terrestrial effects. If a PNEC for soil is proposed in the SIAR, the underlying procedure used to derive a PNEC should be described and referenced. The reason for choosing a particular assessment factor should be stated in the SIAR as well.

4.3 Other Environmental Effects

Other relevant and reliable ecotoxicological information on non-SIDS elements that is available (e.g. avian effects) should also be taken into account and discussed depending on the use of the chemical. If there is a bioaccumulation potential, a discussion on the possibility of secondary poisoning (potential impact of substances on top predators due to accumulation through the food chains) should be included.

If specific information is not available, a qualitative evaluation based on physical-chemical properties and estimation from analogues can be given but is not required.

5. References

The SIAR reference list should be concise and contain only the studies used in the SIAR, since the SIDS Dossier provides the comprehensive reference list.

5.3 Guidance for the Preparation of a SIDS Initial Assessment Profile

5.3.1 Overview

The SIDS Profile is a brief (i.e., a few pages) executive summary of the SIDS Initial Assessment Report (SIAR) targeted at a general audience. A draft SIDS Profile is prepared by the Sponsor country, then discussed (and, if necessary, revised) at the SIAM. Once the SIDS Profile is approved at the SIAM the document is forwarded to the Joint Meeting for endorsement. The SIDS Profile should be as clear and concise as possible, and avoid the use of excessive technical terminology.

Detailed information on the format and content of the SIDS Profile is provided below. Annex 2 to this chapter contains a format for the SIDS Profile.

5.3.2 Structure and Content of the Profile

This section provides guidance on the structure and content of the SIDS Profile. The purpose of the SIDS Profile is to summarise, for a general audience, the main conclusions on the hazards identified in the SIAR together with the available exposure information necessary to put these hazards into context. These summary statements must support a recommendation regarding the need (or not) for further work. If further work is recommended the reasons for this recommendation together with the nature of further work should be clearly stated.

All Profiles should use the same format and structure to allow for ultimately transparent communication of information to a general audience, but also quick and efficient discussions when presented for agreement at SIAM. The Profile should present only the most important information about all SIDS elements and relevant non-SIDS elements. The information required consists of the following types:

- Identification of the chemical(s)
- Category or analogue rationale (if appropriate)
- Human health hazard information on toxicological elements (SIDS and relevant non-SIDS elements)
- Environment hazard information on ecotoxicological elements and environmental fate (SIDS and relevant non-SIDS elements). The most relevant physical/chemical properties should be described at the beginning of this section.
- General information on exposure to the chemical (see subsection 5.2).
- Recommendation and rationale for the recommendation and nature of further work recommended.

It is neither desirable nor appropriate for the SIDS Profile to repeat all the detailed information for SIDS and non-SIDS elements provided in the SIAR. Where no hazards are found, the SIDS Profile should only succinctly summarise the data. For example, a summary might say: "...chemical x was found to be not acutely toxic at doses below 1,000 mg/kg when exposure was by the oral and dermal route in rats, mice and rabbits". Conversely, when data in the SIAR identifies a potential hazard concern for a SIDS element, then the SIDS Profile should describe the hazard with sufficient detail and clarity to be informative, keeping in mind that the information is aimed at a general audience. Examples of text are proposed below under the *Human health* section.

Other attributes of a Profile include:

- A focus on hazard assessment,
- Avoid references to risk assessment (e.g., margins of safety, PEC/PNEC ratio, etc.),
- Use, to the degree possible, of language that is understandable by a lay reader,
- Information to assist countries in classification work. While the terminology and units found in the classification criteria of the Globally Harmonized System of classification criteria of the Harmonized Integrated Hazard Classification System for Chemicals (United Nations, New York and Geneva, 2007 (2nd revised edition) [see http://www.unece.org/trans/danger/publi/ghs/ghs_welcome_e.htm] should be used, the actual classification of chemicals either at a SIAM or in a SIDS Profile should be avoided; and
- NOAEL, LOAEL and L(E)C₅₀ values for key studies.

SIDS Profile structure and content should include the following:

Identification of the chemical(s)

This is the very first section of the SIAP that is presented in a two-column format (see Annex 2). This section indicates the chemical(s) name, CAS number(s) and structure(s).

Analogue/Category Rationale

This section should be included for assessments which rely in part or entirely on data from (non-sponsored) analogue chemicals to fill SIDS endpoint datagaps, or for category assessments.

Analogue: a brief overview should be included of the SIDS datagaps for the sponsored chemical, a description of the analogue, and a justification for read-across of the data for these endpoints from the analogue to the sponsored chemical.

Category assessments: a brief overview of the basis for the category, including details of read across data of chemicals within the category. (see also section 5.2.2).

Physical-chemical properties

The SIAP should indicate whether endpoint values were calculated (e.g., via (Q)SARs) or measured experimentally. Also the SIAP should state the test substance (e.g., the parent compound or a hydrolysis product) and what products were analysed during the test.

The most relevant basic physical/chemical property information on the chemical should be presented first in this section. For substances that are not pure (e.g. non isolable substances, complex mixtures, substances supplied as aqueous solutions), their composition should be summarized briefly. The following properties and their order should be: physical state at standard ambient temperature, melting point, boiling point, vapour pressure, water solubility, *n*-octanol/water distribution coefficient (preferentially as $\log K_{ow}$). Temperature- and pressure dependent physical/chemical data should be reported preferentially for standard ambient temperature (i.e. 298.15 K, 25°C) and pressure (i.e. 1013 hPa) conditions. For substances that may dissociate in aqueous environments, the dissociation constant (e.g., pKa for acids) should be mentioned. Also the predominant form/species of the substance in neutral pH environment may be indicated for clarity.

Human Health

This section should not be a repetition of the individual study summaries, but should provide only a succinct summary of hazards identified in the key study described in the SIAR that are relevant for human health, and should be presented in a way that is clear and unambiguous. The rationale and argumentation for selection of the key study is better placed in the SIDS Dossier or the SIAR, including a justification in case of conflicting results. In case no reliable key study have been identified in the SIAR, (Q)SAR predictions and/or data from analogue chemicals should be considered in a weight of evidence approach. Studies of lower reliability (reliability “4” studies) may also be considered in such a weight of evidence approach. Results of the following toxicity tests and any other information including human data should be summarised and presented, in the following sequential order:

- Acute Toxicity
- Repeated Dose Toxicity
- Genetic Toxicity
- Reproduction Toxicity (including Fertility and Developmental Toxicity)
- Where relevant and valid, available data on non-SIDS elements such as toxicokinetics data (e.g., Absorption, Distribution, Metabolisation, Excretion), corrosivity, skin and eye irritation³, respiratory tract irritation, sensitisation, carcinogenicity, (developmental) neurotoxicity, epidemiological studies or biomonitoring studies, should also be stated and the results and conclusions summarised and presented in a similar manner. The order of the additional endpoints should reflect the IUCLID format (e.g., toxicokinetics before all endpoints; skin irritation, eye irritation and skin sensitization after acute toxicity; carcinogenicity after genetic toxicity).

Where a toxicokinetic study is not available, it is possible to make general observations regarding absorption and metabolism, taking account of the chemical structure, physicochemical and the available toxicodynamic information. Where there is evidence of mutagenicity *in vivo* on e.g. chromosome aberration, micronuclei, but no information on carcinogenicity, the SIAP should include a statement in the carcinogenicity section indicating a potential concern for this endpoint. However, expert judgement should be applied in making such statement.

When several studies exist for the same endpoint and route of exposure, the key study should be reported in the SIAP with appropriate details (see below). In addition, a very brief description of additional studies, their effects and associated doses/concentrations should be included for studies with reliability score of 1 or 2, especially if additional effects are identified. On rare occasions, studies with reliability score of 4 may be needed *i)* in a weight-of-evidence approach, or *ii)* if the study identifies significant results not seen in the key study AND there is a good reason why details of the study cannot be obtained.

Information for each endpoint and route of exposure investigated should, as far as possible, be reported in a standard format. It should include the actual doses at which adverse effects were observed along with a description of the adverse effects, as well as conclusive statements that support the results, for example statements on whether the substance is to be regarded as a reproductive toxicant, a genotoxic, etc. All SIDS endpoints should be stated. An example for a repeated dose toxicity study, carried out in conformity with test guidelines, is presented below:

“In a repeated dose [oral/dermal/inhalation] toxicity study in [rats/mice] [following guideline name], the substance was administered [via gavage/via the diet/via drinking water/via inhalation (nose only or

³ For irritation, adjectives to qualify the severity of the observed effect should be used in accordance with the classification terminology of the GHS.

whole body)/via dermal route] to (number of animals/sex/dose or concentration) at 0, w, x, y and z mg/kg bw/day or mg/L/day⁴, for n [days/weeks] for [xx weeks/months]). [Death/no death] was observed in [either sex, males, females]. [Clinical effects A, B, C and D were observed in [males/females] at dose levels x, y, z mg/kg bw/day] OR [There was no effect observed upon haematological, clinical biochemistry or histopathological examination at any dose]. Based on effect A, the LOAEL and NOAEL for repeated dose [oral/dermal/inhalation] toxicity were considered to be x and y mg/kg bw/day or mg/L/day, respectively.”

Major deviations from OECD Test Guidelines should be reflected in the summary of the endpoint in the SIAR and SIDS Dossier. However, the SIAP should include any deviations that might significantly affect results (e.g., administration of a test substance to rats on gestation days 7-20 versus 5-15).

This section should also include a concluding sentence describing the overall human health hazards, such as: “The available animal data suggest a potential for compound X to result in [developmental toxicity/reproductive toxicity, genotoxic or non-genotoxic carcinogenicity].

If available and relevant, a summary of (developmental) neurotoxicity studies, epidemiological studies or biomonitoring studies should also be presented and placed in the human health section according to which endpoint they address.

Environment

All SIDS endpoints should be stated. For some compounds, it may be important to include certain non-SIDS endpoints as discussed below. The SIAP should indicate whether endpoint values were calculated (e.g., via (Q)SARs) or measured experimentally. Also the SIAP should state the test substance (e.g., the parent compound or a hydrolysis product) and what products were analysed during the test

Information on Environmental Fate and Pathways and tests for the following endpoints should be provided:

- Degradation, specifically:
 - Abiotic in water (hydrolysis); the half-life, temperature and pH conditions should be stated; if measured, the identified hydrolysis products should be stated here.
 - Air (photodegradation); the half-life and type of photolysis (direct or indirect photolysis by reaction with OH radicals and/or ozone); and
 - Biodegradation, aerobic (and anaerobic, if measured) along with classification, i.e. whether the substance is readily biodegradable or not, and the extent of biodegradation in percent of the initial amount at the end of the test period (number of days). If the substance is considered readily biodegradable, it should be indicated, if possible and applicable, whether the 10-day window was met.

- Distribution and transport between environmental compartments.

Indicate the modelled transport values as well as the model used. Although the Henry’s Law Constant is not a required SIDS endpoint, it is useful for determining the likelihood of volatilization. Therefore, it should be reported, with a statement on the likelihood of volatilisation from water. Likewise,

⁴ For inhalation exposure, units used in the GHS should also be used in the SIAP, e.g., ppmV (gas), mg/L (vapour, dust and mist).

the log K_{oc} is a useful measure to help estimate adsorption to organic matter in soil and sediment, and should also be discussed in most cases.

Modelled environmental fate values should be described by presenting numerical values for the distribution between the target compartments, as well as the model used. For Level III models the loading ratios (i.e. emission to air, water and/or soil) should be stated. Environmental fate models should be used only for substances that are within the applicability domain of the model. If there is a bioaccumulation potential expected (estimated using the Log K_{ow} or measured), then information related to the possibility for adverse effects attributed to secondary/long-term accumulation (poisoning) should be included in this section of the profile. Bioconcentration factors (BCF) - either measured or estimated values using the partition coefficient (log K_{ow}) - may be useful here as well. When reporting the measured BCF, the basis of the result should be given (i.e., kinetic or steady state, whole fish or lipid, etc.) as well as the method used and any extra important details, such as whether the result was based on measurement of radioactivity (in case radiolabelled material was used) or on analytical measurement of the actual chemical.

Results for ecotoxicity tests and other relevant information should also be summarised and presented in this section. When several studies exist for the same endpoint and fate of the substance, only the key study should be reported in the SIAP. The rationale and argumentation for the selection of the key study is better placed in the SIDS Dossier or the SIAR, including a justification in case of conflicting results. Information for each endpoint and fate of the substance investigated should, as far as possible, be reported in a standard way. The key study should be reported in the SIAP with appropriate details (see below). In addition, a very brief description of additional studies, their effects and associated doses/concentrations should be included for studies with reliability score of 1 or 2, especially if additional effects are identified. Results from ecotoxicity tests include:

- Aquatic Toxicity, specifically:
 - Acute toxicity to fish, aquatic invertebrates and aquatic plants. Available LC_{50}/EC_{50} values for the key studies, indicating study duration and species. The SIAP should focus on the standard species identified in OECD Test Guidelines. It is considered acceptable to present data for various species along with ranges for multiple acceptable studies. In some cases, available LC_{50}/EC_{50} values for other species may also be relevant to report if more sensitive or for a weight-of-evidence approach.
 - Available chronic toxicity data on fish, aquatic invertebrates and aquatic plants should also be provided, as well as NOEC values. The SIAP should focus on the standard species identified in OECD Test Guidelines, but should also highlight any non-standard species test results considered relevant to the conclusion.

It is important to indicate whether reported values represent measured or nominal concentrations. In the case of unstable test substances or substances tested as mixtures, the chemical identity on which the result is based should be clearly stated. For substances with very low solubility and difficult to test substances (e.g. substances that are not stable under test conditions), a brief reference to the preparation of the test solution is useful (e.g. type and concentration of dispersant used, loading rate, or WAF, etc.).

- If appropriate, available data or information on terrestrial toxicity, for example information on acute toxicity to earthworms and terrestrial plants, toxicity to sediment-dwelling organisms or any likely avian effects, should also be provided. Information on well-known ecological damage and/or contamination in relation to the substance and/or its metabolites should be noted (e.g. eutrophication, acidification, global warming, tropospheric ozone formation /ozone layer depletion, potential formation of very fine particulate matter (PM 2.5), endocrine disrupting properties, etc.)

Exposure

The SIDS Profile should summarize the exposure information presented in the SIAR. At a minimum, the exposure information in the SIDS Profile should include the available information on production volume, major use functions/categories and sources of potential exposure, including environmental releases and occupational/consumer exposure. As in the SIAR, it is necessary to transparently describe and qualify the scope of the available exposure information to the extent possible. If only the production/import volume and use pattern in the Sponsor country (or the country where the lead company is located) are available, it should be clearly indicated that the production/import volume and use pattern in other OECD countries is unknown. If the information provided pertains to a country other than the Sponsor country, that country should be prominently indicated as distinct from the Sponsor country.

Recommendations and Rationale for the Recommendation and Nature of the Further Work Recommended

The 'Recommendation' section of the SIAP proposes one of two possible statements regarding the need for further work on the chemical. The recommendation options, based on the conclusions and their context, are either that **the chemical is currently of low priority for further work** or that **the chemical is a candidate for further work**. This recommendation will be discussed and agreed or modified as appropriate by SIAM.

The recommendation is usually based on two aspects of the substance: its hazard profile and its exposure potential. The criteria described in the Harmonized Integrated Hazard Classification System for Chemical Substances and Mixtures [GHS, see: <http://www.oecd.org/env/classify>] may be used as a general background reference for judging the hazard of a substance for the purpose of deriving consistent recommendations for substances assessed in the OECD HPV Chemicals Programme. It should be kept in mind that no classification is performed in the context of the OECD HPV Chemicals Programme. Guidance on how to derive recommendations can be proposed for different specific situations as outlined below.

Non-hazardous substances

For non-hazardous substances, the recommendation would normally be that the substance is of low priority for further work. However depending on the exposure profile and information on the actual levels of exposure, a recommendation for further work may be warranted.

Hazardous substances with a low exposure potential

For hazardous substances, the identified environmental and human hazards need to be put into context using the available exposure information. If the exposure potential is low, e.g. for closed system intermediates, or because appropriate risk management measures are being applied, it can often be concluded that the chemical is of low priority for further work.

In the refocused SIDS programme, exposure information from the Sponsor country is sufficient to fulfill the SIDS elements. Therefore it can be difficult to decide on a recommendation due to the uncertainty of the exposure situation in other member countries. The uncertainty behind the recommendation can be highlighted. For example if based on the information available to the Sponsor country a hazardous substance is used solely as a chemical intermediate, the recommendation could be that the substance is currently of low priority for further work. The uncertainty behind the recommendation should be highlighted by stating that the recommendation is based on limited exposure information and

that further work might be necessary in member countries with a different exposure situation or where no information is available. A prerequisite for basing the recommendation on anticipated low exposure is that the extent of the available exposure information is described in a very transparent manner in the SIAR as well as in the SIDS Profile.

Hazardous substances with a high exposure potential

A hazardous substance with a high exposure potential will normally be a candidate for further work (for exceptions, see “Other situations” below). For substances which are candidates for further work, the post-SIDS work expected should be clearly described and the reasons why such work is needed should be outlined. Examples of specific further work recommended could include additional exposure information gathering, in-depth risk assessment, exposure reduction measures or post-SIDS testing.

Some hazards are specifically relevant in the context of recommending that a substance is a candidate for further work. For hazards to human health, these would be hazards related to severe irreversible effects or with no or very low thresholds:

- acute toxicity (e.g. LD50 in rodents \leq 300 mg/kg)
- eye/skin corrosion
- sensitisation (skin, respiratory)
- mutagenicity
- carcinogenicity
- reproductive toxicity
- specific target-organ toxicity after single exposure and/or repeated exposure.

For hazards to the aquatic environment these would be hazards related to acute toxicity (e.g. L(E)C50 \leq 100 mg/l) in conjunction with a high bioaccumulation potential or lack of rapid degradation as well as severe acute toxicity (e.g. L(E)C₅₀ \leq 1 mg/l) independent of biodegradation and bioaccumulation.

Some identified hazards are less relevant in the context of recommending that a substance is a candidate for further work. For hazards to human health, these would be hazards related to reversible, transient and non-lasting effects (e.g. dermal irritation: reversible effects in dermal tissue; eye irritation). The same would apply if the acute toxicity of the chemical is so low that it may become evident only at high exposure levels, which are not reached under normal conditions of manufacture or use (e.g. LD50 in rodents $>$ 300 mg/kg). For hazards to the aquatic environment, these would be hazards related to acute toxicity which may become evident only at higher exposure levels (e.g. L(E)C50 $>$ 1 mg/l), which are usually not reached under normal conditions of manufacture or use in conjunction with a low bioaccumulation potential and rapid degradation.

For substances for which only these “lesser hazards” have been identified, a recommendation for further work might not be warranted. A brief narrative should explain the rationale that supports the recommendation for low priority for further work, according to the reasons outlined above.

Independent of the recommendation-making process in the OECD HPV Chemicals Programme, there are exposure scenarios where hazards considered to be less relevant when recommending further work may be expressed e.g. use of aerosols in uncontrolled conditions, during sampling of enclosed systems. It is therefore essential that these “lesser hazards” are flagged so that they can be noted by chemical safety professionals and users.

Other situations

Internationally agreed classification criteria do not exist for some hazards, e.g. neurotoxicity, or immunotoxicity. There may therefore be cases when a recommendation for further work for human health

is warranted, despite the fact that the substance does not pose a hazard according to the current classification criteria. In the same way, for the environment, the GHS only provides guidance on identifying hazards for the aquatic environment. Further work may also be recommended for substances which pose a hazard to the terrestrial or benthic environment or which have potential for adverse effects on the atmosphere such as ozone depletion or which have a potential for endocrine disruption. Also, further work could be recommended for substances which show severe chronic toxicity in long-term aquatic toxicity tests. Furthermore, there may be cases where further work would be recommended for very persistent and bioaccumulative substances for which available data do not show acute or chronic toxicity. In each of these cases, a scientific justification is to be given on a case-by-case basis.

There may be cases where high exposure suggests a need for post-SIDS testing in the absence of definite information regarding hazards. Further work could be recommended for example when the properties of a substance indicate a high potential for exposure to soil or sediment but there is no information available on its toxicity to soil or sediment dwelling organisms or if hazardous properties towards soil or sediment organisms can be estimated.

A recommendation of low priority for further work can also be appropriate for hazardous substances if it is thought that labelling or other types of regulatory controls or management options are in place in OECD member countries that adequately address the hazard concern.

For any of these more specific situations, an explicit rationale for deriving the recommendation should be provided.

The ‘Recommendation’ can only be one of the two possible statements regarding the need for further work on the chemical, based on the conclusions set out in the Profile:

“The chemical is currently of low priority for further work”

or

“The chemical is a candidate for further work”

No other statements should be used. This recommendation will be discussed and agreed or altered as appropriate by, and at, the SIAM.

The rationale that was used to derive the recommendation as described in the SIAR should then be summarised in this section. Some more guidance and proposals for specific language are presented below.

Chemicals considered to be candidates for further work

If further work is recommended, this section should contain a concise statement or phrase that clearly states the post-SIDS work expected and why such work is needed. Examples of specific work could include additional exposure information gathering, in-depth risk assessment, risk management or post-SIDS testing.

The procedures regarding post-SIDS work are outlined in Chapter 6. If further work on exposure assessment or risk assessment is recommended:

- the recommendation for further work on exposure assessment is addressed to all member countries and is always considered to be post-SIDS work;
- member countries are invited to use the recommendation for their national/regional priority setting;

- the decision whether to perform further exposure assessment and/or risk assessment as a follow-up to a recommendation from the OECD HPV Chemicals Programme is taken up by member countries in the context of their national/regional priority setting;
- if member countries decide to perform further exposure assessment and/or risk assessment, they are invited to inform the Secretariat and the other member countries about the activity and the outcome of the national/regional work.

Chemicals considered to be currently of low priority for further work

Some examples of language that can be used in this section for four specific cases are given below.

1. For substances with a low hazard profile, the rationale could be:

This chemical is currently of low priority for further work because of its low hazard profile.

2. For substances for which only hazards were identified which do not automatically warrant a recommendation for further work, the identified hazards should nevertheless be highlighted. The language for the rationale could be:

The chemical possesses properties indicating a hazard for (human health and/or the environment). These hazards do not warrant further work as they are related to reversible / transient / non-lasting effects / acute toxicity which may become evident only at high exposure level [select as appropriate]. They should nevertheless be noted by chemical safety professionals and users.

If it is not already obvious from the summary of the conclusions, the hazards can be explicitly mentioned.

For chemicals for which only hazards related to aquatic toxicity were identified (acute aquatic EC/LC50 values between 1 and 100 mg/l) which do not warrant a recommendation for further work due to rapid degradation and a low potential for bioaccumulation, the following wording could be used for the rationale:

The chemical has properties indicating a hazard for the environment (acute aquatic EC/LC50 values between 1 and 100 mg/l). However the chemical is of low priority for further work for the environment because of its rapid biodegradation and its limited potential for bioaccumulation.

3. Substances which are hazardous, but for which it is anticipated that their exposure to man and the environment is low, can be considered to be of low priority for further work. The main difficulty arises from obtaining exposure information and from the uncertainty of the exposure potential of a substance if only very limited information regarding the exposure profile is available. The recommendation can only be based on the available knowledge. The following language could be used where necessary, to highlight the uncertainty behind the recommendation:

The chemical possesses properties indicating a hazard for (human health and/or the environment). Based on data presented by the Sponsor country (relating to production {by [number] producers}/{in [number] countries} which accounts for {[number] %}/{unknown fraction} of {global production}/{production in OECD countries} and relating to the use

pattern in one/several/[number] [OECD] country[ies]), exposure to (humans and/or the environment) is anticipated to be low, and therefore this chemical is currently of low priority for further work. Countries may desire to investigate any exposure scenarios that were not presented by Sponsor countries.

If it is not already obvious from the summary of the conclusions, the hazards should be explicitly mentioned.

A prerequisite for basing the recommendation on anticipated low exposure is that the extent of the available exposure information is described in a very transparent manner in the SIAR as well as in the SIDS Profile.

4. A recommendation of low priority for further work can also be appropriate for some hazardous substances if it is thought that regulatory controls or risk management options are in place in OECD member countries that adequately addresses the hazard concern. This option is limited to substances which are corrosive or skin sensitizers and for which adequate labelling is in place for the substances as well as mixtures containing them. Specific language indicating that the recommendation of low priority for further work is based on the prerequisite of presumed adequate labelling in place, should be used, on a case-by-case basis, to explain this situation. One possible example for language for the rationale could be:

The chemical possesses properties indicating a hazard for (human health and/or the environment). Based on data presented by the Sponsor country, adequate risk management measures are being applied. Countries may desire to check their own risk management measures to find out whether there is a need for additional measures.

A prerequisite for basing the recommendation on anticipated risk management measures is that the extent of the available information on risk management is described in a very transparent manner in the SIAR as well as in the SIDS Profile.

Another example, relevant for the situation where the use which potentially gives rise to exposure is regulated in other fora, e.g. use as a pharmaceutical or use as a plant protection agent:

The chemical possesses properties indicating a hazard for (human health and/or the environment). However the main use of the substance is known to be regulated and it is recommended that the information on possible total exposure from regulated and non-regulated use be shared with regulatory agencies.

If it is not already obvious from the summary of the conclusions, the hazards should be explicitly mentioned.

5.4. Preparing SIARs and SIDS Profiles when Assessing Categories or Using Analogue Data

When data from analogues are used (see also section 2.3.4 in Chapter 2), or when a category approach is used to present a similar group of chemical(s) (see also section 2.3.5 in Chapter 2) the rationale or justification should be succinctly explained in the SIAR. This justification should be located directly after the cover page in the first section, which covers the identification of the chemical. When multiple chemicals are to be presented, the data on each chemical(s) should be clearly indicated in a table that is formatted to allow for a clear “read across” of the data, e.g., a table that has a column for each chemical in the category and rows within each column that displays data on that specific chemical for each SIDS

element or non-SIDS element if relevant. Alternatively, the columns could contain the data and the rows can contain the category chemicals.

At the end of the Chemical Identification section, it is recommended that an additional section be included entitled: Section **1.1, Category/Analogue Rational**. In this section, the sponsor should present a brief narrative as to why these chemicals are to be considered similar or part of a category approach. This may be based on multiple factors; however, each factor should be clearly and concisely stated.

Since the SIAR is prepared after the data have been collected, it is assumed that the Sponsor is aware of the strengths and possible weakness of the category as a group. In some instances a category may be acceptable for one set of SIDS endpoints but not others. As an example, chemicals may be manufactured and produced in a similar way, have similar physical-chemical properties and environmental fate, but be expected to react differently in the aquatic environment or behave differently as concerns health toxicity. In such cases, the sponsor should thoroughly evaluate the chemicals proposed for the category to determine if possible sub-categories may be required for specific endpoints. Alternatively, the sponsor may propose to evaluate one set of endpoints as a category, and another set of endpoints separately. (If sub-categories are used, they should be clearly stated in Section 1.1 of the SIAR.)

When analogue data is to be used to complete a SIDS element, it should be clearly stated that no data are available for “chemical A” but that analogue data for “chemical B” has been used due to chemical similarities. This should be done in the SIAR, at the respective location in which the SIDS element is to be presented.

When a category is being presented, discussion of each chemical for which data are available should be presented separately. As an example, for the section on repeated dose toxicity, where five chemicals form the category and three chemicals have multiple data available, the data entry should present a separate paragraph for each of the three chemicals with data. Details regarding the available studies should be located within each individual paragraph. A final paragraph should be added at the end of the repeated dose toxicity section, which shows how these data can be extrapolated (extended) to the two remaining chemicals, along with similarities and differences in the data on the three chemicals. When differences are noted, explanations should be given to attempt to characterise the difference, for example, “the minor differences in the NOAELs of each study may be attributed to an increase in molecular weight of the substance and the ability of the substance to be available for consumption, or due to different routes of exposure.” This method of presentation should be employed for each SIDS element for which data for multiple chemicals are available.

In addition, it is important to take into consideration any other external peer reviewed assessments of any chemical presented as an analogue or category. In some circumstances, chemicals that were previously reviewed in the SIDS programme or for which IPCS assessment documents are available are being used. It is important that the sponsor recognises the complexities of such evaluations and ensures that, when these chemical data are used as an analogue or for a category, the results of such evaluations can be rationalised with the new presentation of data. (For example, a chemical presented at SIAM 10 is used as an analogue for a chemical presented at SIAM 13 for multiple health endpoints. The chemical from SIAM 10 was determined to be a mutagen and had positive results in a two-year bioassay. The chemical being presented at SIAM 13 should have similar conclusions, unless other newer data are available, or unless a clear and thorough explanation is provided. It is important that consistency be emphasised when presenting these data.)

When presenting conclusions, each chemical should be considered independently of the others. There should be a separate paragraph for individual chemicals as well as for subcategories of chemicals. It is recognised, however, that one or more chemicals in a category may have limited data. Therefore any

conclusions drawn for such chemicals will be derived from data available from the other category members. A final paragraph should be provided which makes an overall conclusion and recommendation regarding the whole category.

If a chemical category is being presented for consideration at a SIAM, the draft SIDS Profile should provide a brief summary of the category rationale. Similarly, if data from an analogue was used to fulfil the SIDS requirements, the rationale for using the analogue data should be summarised in the SIDS Profile.

When presenting categories and analogues, each individual chemical and CAS number should be presented in the Profile. (If there are many substances within a category, molecular structures should be shown in the Chemical Identity section of the SIAR only, in order to keep the SIDS Profile as simple as possible.) The beginning section of the Profile should be modified to accommodate this need.

In addition, in the “Category/Analogue Rationale”, the first section that should be presented is a brief statement regarding the chemicals’ similarities and why they are to be considered a good category or analogue. In order to fully follow through on this approach, a final section should be added at the end of the overall discussion, which indicates the conclusions and recommendations on the category as a whole. To be specific, this section must clearly indicate the strengths and weakness of the data provided and if additional work might be needed. If further work is recommended, the specific chemical on which the work should be conducted should be mentioned.

ANNEX 1

Format for COVER PAGE

SIDS Initial Assessment Report
for
SIAM ...
(Location and Date of meeting)

1. Chemical Name:	
2. CAS No.:	
3. Sponsor Country:	Name the sponsor country and SIDS Contact Point.
4. Shared Partnership With:	If applicable, add the name of the industry sponsor/consortia. If not applicable leave blank, and skip to “7. Review Prior to SIAM”.
5. Roles/Responsibilities of the Partners:	
<ul style="list-style-type: none"> Name of industry sponsor/consortium. 	Provide the name and contact information for the industry partner (contact point and consortium members).
<ul style="list-style-type: none"> Process used. 	Briefly discuss: roles/responsibilities of the parties; who drafted the documents; and how the documents were reviewed for accuracy, completeness and quality.
6. Sponsorship History	
<ul style="list-style-type: none"> How was the chemical or category brought into the OECD HPV Chemicals Programme? 	Describe the history of how the chemical(s) came to the SIDS Program. Was it through the ICCA Initiative? Did the government contact industry? Was the chemical part of another assessment program (e.g., EU RA, or IPCS CICAD)?
7. Review Process Prior to the SIAM:	Briefly describe whether the Electronic Discussion Group was utilized for pre-review of any part of the case. [e.g. the SIDS Plan /category rationale/... was posted on the Pre-SIAM EDG for comments by the other OECD Member countries. Responses to these comments were also posted to the Pre-SIAM EDG.]
8. Quality Check Process	<p>Briefly describe the quality check process, including:</p> <ul style="list-style-type: none"> how data in the SIDS Dossier (including Robust Study Summaries) was extracted from the original study data how the reliability of the results was checked <p>[e.g. government agencies of the Sponsor country/the independent peer review body “...” performed spot checks on randomly selected endpoints and compared original studies with data in the SIDS Dossier (including the Robust Study Summaries, the validation of studies and the selection of key studies)]</p>
9. Date of Submission:	To the OECD Secretariat for posting on the SIAM electronic discussion group
10. Comments:	Other remarks should be written here

ANNEX 2
FORMAT FOR THE SIDS PROFILE

CAS No. (Nos.)	
Chemical Name(s)	
Structural Formula	
SUMMARY CONCLUSIONS OF THE SIAR	
<p>Analogue/Category rationale</p> <p><i>[This section should be included for assessments which rely in part or entirely on data from (non-sponsored) analogue chemicals to fill SIDS endpoint data gaps, or for category assessments.]</i></p> <p><i><u>Analogue:</u> a brief overview should be included of the SIDS data gaps for the sponsored chemical, a description of the analogue, and a justification for read-across of the data for these endpoints from the analogue to the sponsored chemical.</i></p> <p><i><u>Category assessments:</u> a brief overview of the basis for the category, including details of read across data of chemicals within the category. (see also section 5.2.2).]</i></p> <p>Physical-chemical properties</p> <p>“Chemical X is a [colour] [solid/liquid/gas/crystal/powder/etc.] with a melting point of XXX °C, a boiling point of XXX °C and a [measured/calculated] vapour pressure of XXX Pa at 25 °C. The [measured/calculated] octanol-water partition coefficient (log K_{ow}) is XXX, and the water solubility is XXX mg/L at 20 °C.”</p> <p><i>[For substances that are not pure (e.g. non isolable substances, complex mixtures, substances supplied as aqueous solutions) their composition should be summarised briefly.]</i></p> <p>Human Health</p> <p>Toxicokinetics data if available. <i>[Where a toxicokinetic study is not available, it is possible to make general observations regarding absorption and metabolism, taking account of the chemical structure, physicochemical and the available toxicodynamic information. The assessment should include: potential for absorption, whether it is likely to be widely distributed, consideration of metabolism and likely routes of excretion. It is also very useful to provide a view on potential in utero exposure, and also exposure via the breast milk.]</i></p> <p><i>[Acute toxicity] “The [oral/dermal/inhalation] LD₅₀ values were XXX [mg/kg bw or mg/L¹ (for inhalation specify whether vapour, dust or mist)] for male and XXX [mg/kg bw or mg/L⁵] for female [mice/rat]. The substance caused [describe relevant clinical effects and findings at necropsy].”</i></p> <p><i>[Experimental data on skin and eye irritation in animals, if available] E.g., “Chemical X was [slightly/mildly/...] [skin/eye] irritating/corrosive. [Describe symptoms] were observed in a skin irritation assay performed in rabbit.”</i></p> <p><i>[Indicate whether effects were transient and reversible or not] OR [“No experimental data are available for skin and eye irritation in animals.”]</i></p> <p><i>[If relevant, a statement on the potential for respiratory tract irritation may be included.]</i></p> <p><i>[Experimental data on skin sensitization, if available] E.g., “Chemical X [was/was not] skin sensitizing. [The skin sensitization assays performed were all negative.] or [Chemical X gave positive results for skin sensitization in a [test name] in [test species]] or [In humans, some cases of sensitisation from topical contact with the chemical X have been described.]” or [No experimental data are available for skin sensitization in animals.]</i></p>	

⁵ For inhalation exposure, units used in the GHS should also be used in the SIAP, e.g., ppmV (gas), mg/L (vapour, dust and mist).

“The repeated dose toxicity of the chemical X has been investigated in [one/ x] studies. In a repeated dose [oral/dermal/inhalation] toxicity study in [rats/mice/rabbits] following [guideline name/OECD TG No.], the substance was administered [via gavage/via the diet/via drinking water/via inhalation (nose only or whole body) /via dermal route] to (number of animals/sex/dose or concentration) at 0, w, x, y and z mg/kg bw/day or mg/L¹/day, for n [days/weeks] for [xx weeks/months]. [Death/no death] was observed in [either sex/males/females]. Treatment related effects [clinical signs, increased/decreased body weight gain, food consumption, haematology, clinical biochemistry, organ weight changes, macroscopical/histopathological findings] were observed in [males/females] at dose levels x, y, z mg/kg bw/day] OR [There were no treatment related effects observed at any dose]. Based on effect(s)... the [NOAEL or LOAEL] for repeated dose [oral/dermal/inhalation] toxicity was considered to be x and y mg/kg bw/day or mg/L/day¹.”

“In a [bacterial reverse mutation assay/Ames test with multiple strains of *Salmonella typhimurium* / OECD TG No./etc.], Chemical X was [positive/negative] both with and without metabolic activation. An *in vitro* chromosomal aberration test using [test name and conditions] was [positive/negative] with and without metabolic activation. An *in vivo* micronucleus assay [test name and conditions] was [positive/negative] up to the maximum tolerated dose. Based on these results, Chemical X is considered to be [genotoxic/ non genotoxic] *in vitro/in vivo*.”

[“No data are available for the carcinogenicity of Chemical X.”] OR [“The carcinogenic potential of the chemical X has been investigated in [one/ x] studies. In a [oral/dermal/inhalation] carcinogenicity study in [rats/mice/] [following guideline name], the substance was administered [via gavage/via the diet/via drinking water/via inhalation (nose only or whole body) /via dermal route] to (number of animals/sex/dose or concentration) at 0, w, x, y and z mg/kg bw/day or mg/L¹/day, for n [days/weeks] for [xx weeks/months]. [Death/no death] was observed in [either sex/males/females]. [Summarize treatment related effects with dose response as in the repeated dose toxicity study with an emphasis on neoplastic findings] OR [There was no treatment related effects observed at any dose]. Based on these results, Chemical X is considered to have [a/no] carcinogenic potential.”

“The reproductive toxicity of the substance X has been well investigated in [a standard one/two generation study] /[in a reproductive and developmental toxicity screening test] in rats [test name/OECD TG No.]. In this study, chemical X was administered [via gavage/via the diet/via drinking water/via inhalation (nose only or whole body)] to (number of animals/sex/dose or concentration) at 0, w, x, y and z mg/kg bw/day or mg/L/day⁶, for n [days/weeks] for [xx weeks/months]. [Death/no death] was observed in [either sex/males/females]. [Describe effects on fertility with dose-response if observed] OR [No adverse effects on reproductive parameters were observed up to the highest dose tested]. [Describe effects on development with dose-response if observed] OR [No adverse effect on development were observed up to the highest dose tested] [Describe effects on general toxicity with dose response as described for the repeated dose toxicity study] OR [There were no treatment related effects on parental animals observed at any dose]. Based on effect(s)..., the [NOAEL or LOAEL] for [general/maternal/paternal] toxicity was considered to be x and y mg/kg bw/day or mg/L/day in [males/females]. Based on effect(s)...the [NOAEL or LOAEL] for reproductive toxicity was considered to be x and y mg/kg bw/day or mg/L/day, in [males/females]. Based on effect(s)...,the [NOAEL or LOAEL] for developmental toxicity was considered to be x and y mg/kg bw/day or mg/L/day in [males/females]. Based on these results, Chemical X is considered [to be/not to be] a[reproductive/developmental] toxicant.”

[Results of developmental toxicity can also be presented separately]: “The developmental toxicity of substance X has been well investigated in standard studies in [rats and/or rabbits] (or in a screening test) following [test name/OECD TG No.]. [Describe effects and dose response if developmental effects are observed.] OR [No evidence of developmental toxicity was observed in [rats and/or in rabbits] at doses of up to XX and YY mg/kg/day respectively.] In [rats and/or in rabbits] maternal toxicity was observed at doses of XX and YY mg/kg/day, respectively. Based on effect(s)...the [NOAEL or LOAEL] for developmental toxicity was considered to be x and y mg/kg bw/day or mg/L/day. Based on effect(s)..., the [NOAEL or LOAEL] for maternal toxicity was considered to be x and y mg/kg bw/day or mg/L/day. Overall, substance X [is/is not] a developmental toxicant.”

[In case no reliable studies have been identified in the SIAR, (Q)SAR predictions and/or data from analogue chemicals should be considered in a weight of evidence approach. Studies of lower reliability (reliability “4” studies) may also be included in such a weight of evidence approach.]

⁶ For inhalation exposure, units used in the GHS should also be used in the SIAP, e.g., ppmV (gas), mg/L (vapour, dust and mist).

Environment

“The hydrolysis half-life for this compound is X hours/days” or “A hydrolysis test [test name/OECD TG No.] showed no hydrolysis at pH4, pH7 and pH9 at XX °C for X days. [For acids: “As the dissociation constant (pKa) is XX, Chemical X mainly exists in its [undissociated/dissociated] form at environmentally relevant pH values”].

In the atmosphere, indirect photo-oxidation by reaction with hydroxyl radicals is predicted to occur with a half-life of XX days/hours. A [test name/OECD TG No.] resulted in XX % biodegradation after 28 days. Chemical X [is/is not] readily biodegradable under aerobic conditions.”

“A level III fugacity model calculation with equal and continuous distributions to air, water and soil compartments suggests that Chemical X will distribute mainly to the [air/water/soil/sediments] (XX %) and [air/water/soil/sediments] (XX%) compartments with minor distribution to the [air/water/soil/sediments] compartment (XX%) and negligible amount in the [air/water/soil/sediments] compartment. If released only to the [air/water/soil/sediments] compartment, Chemical X stays in the [air/water/soil/sediments] compartment (XX%) with negligible amounts in other compartments. A Henry’s law constant of XX Pa.m³/mole at 25 °C suggests that volatilization of Chemical X from the water phase [is/is not] expected to be high. [A K_{oc} of XX was estimated based on the log K_{ow} and indicates a [low/high/moderate] potential for accumulation in soil.”

“The bioaccumulation potential seems to be [low/high] based on a BCF value of XX estimated with BCFWIN] or [Chemical X [is/is not] expected to bioaccumulate in the aquatic environment based on a measured bioconcentration factor of XX.]”

“The following acute toxicity test results have been determined for aquatic species:

e.g., Fish [test species]; 96 h LC₅₀ = XX mg/L (measured/nominal)
Invertebrate [test species] 48 h LC₅₀ = XX mg/L (measured/nominal)
Algae [test species] 72 h ErC₅₀ = XX mg/L (growth rate method) (measured/nominal)
Algae [test species] 72 h EbC₅₀ = XX mg/L (area under growth curve method)

The following chronic toxicity test results have been determined (test name/OECD TG No.):
[Species name] duration of exposure, NOEC = XX mg/L (measured/nominal)

[In the case of unstable substances, or substances tested as mixtures, the chemical identity on which the result is based should be clearly stated.]

Exposure

Chemical X is commercially produced with an annual production volume of XXXX tonnes in [Sponsor country]. Worldwide production volume [is not available/was estimated to be approximately XXXX tonnes/year in year XXXX]. Chemical X is mainly produced by [production process]. Chemical X is used for [use pattern(s)]. [Monitoring/No monitoring] data for effluents, surface water in occupational settings from are available from the production and processing sites in [Sponsor country]. [Occupational exposure through [exposure routes] is possible]. [Consumer exposure is considered to be negligible] or [Consumer exposure may occur through [exposure pathways]]. [Environmental exposure through [exposure media/route] is possible/considered negligible.]

**RECOMMENDATION AND RATIONALE FOR THE RECOMMENDATION AND NATURE
OF FURTHER WORK RECOMMENDED**

Human Health

[The chemical is currently of low priority for further work] or [The chemical is a candidate for further work]

[*Select rationale as appropriate*]:

[This chemical is currently of low priority for further work because of its low hazard profile.]

OR

[The chemical possesses properties indicating a hazard for human health (specify hazards identified). These hazards do not warrant further work as they are related to reversible / transient / non-lasting effects / acute toxicity which may become evident only at high exposure level They should nevertheless be noted by chemical safety professionals and users.]

OR

[The chemical possesses properties indicating a hazard for human health (specify hazards identified). Based on data presented by the Sponsor country (relating to production {by[number] producers}/{in [number] countries} which accounts for {[number]%}/{unknown fraction} of {global production}/{production in OECD countries} and relating to the use pattern in one/several/[number] [OECD] country[ies]}), exposure to humans is anticipated to be low, and therefore this chemical is currently of low priority for further work. Countries may desire to investigate any exposure scenarios that were not presented by Sponsor countries.]

OR

[The chemical possesses properties indicating a hazard for human health (specify hazards identified). Based on data presented by the Sponsor country, adequate risk management measures are being applied. Countries may desire to check their own risk management measures to find out whether there is a need for additional measures.]

OR

[The chemical possesses properties indicating a hazard for human health (specify hazards identified). However the main use of the substance is known to be regulated and it is recommended that the information on possible total exposure from regulated and non-regulated use be shared with regulatory agencies.]

Environment

[The chemical is currently of low priority for further work] or [The chemical is a candidate for further work].

[*Select rationale as appropriate*]:

[This chemical is currently of low priority for further work because of its low hazard profile.]

OR

[The chemical possesses properties indicating a hazard for the environment (specify hazards identified). These hazards do not warrant further work as they are related to pH effects which may become evident only at high exposure level They should nevertheless be noted by chemical safety professionals and users.]

OR

[The chemical possesses properties indicating a hazard for the environment (specify hazards identified). . Based on data presented by the Sponsor country (relating to production {by[number] producers}/{in [number] countries} which accounts for {[number]%}/{unknown fraction} of {global

production}/{production in OECD countries} and relating to the use pattern in one/several/[number] [OECD] country[ies]}, exposure to the environment is anticipated to be low, and therefore this chemical is currently of low priority for further work. Countries may desire to investigate any exposure scenarios that were not presented by Sponsor countries.]

OR

[The chemical has properties indicating a hazard for the environment (acute aquatic toxicity values between 1 and 100 mg/L). However the chemical is of low priority for further work for the environment because of its rapid biodegradation and its limited potential for bioaccumulation.]

OR

[The chemical possesses properties indicating a hazard for the environment (specify hazards identified). However the main use of the substance is known to be regulated and it is recommended that the information on possible total exposure from regulated and non-regulated use be shared with regulatory agencies.]

Note: This document may only be reproduced integrally. The conclusions and recommendations (and their rationale) in this document are intended to be mutually supportive, and should be understood and interpreted together.