

**REPORTING HAZARD, EXPOSURE AND
SCREENING-LEVEL ASSESSMENT INFORMATION
FOR HPV CHEMICALS TO TECHNICAL AUDIENCES**

Prepared by:

THE ALLIANCE FOR CHEMICAL AWARENESS

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While the ACA believes that the approaches represented here are sound, it is clearly understood that this guidance will not be necessary or even appropriate in certain circumstances. Ultimately, the approach to communicating HPV information will be up to the sole discretion of individual sponsors, and will depend on the sponsor's judgment about the needs of specific audiences to understand the potential hazards of and exposures to a given chemical.

Introduction:

Members of the Alliance for Chemical Awareness (ACA) and other industry groups, the U.S. Environmental Protection Agency (EPA) and Environmental Defense (ED) have agreed on a plan to increase the amount of publicly available screening-level hazard information on U.S. high production volume (HPV) chemicals. HPV chemicals are those manufactured or imported into the U.S. in quantities exceeding a million pounds per year. Data availability and adequacy reviews have already been initiated for many chemicals covered by this initiative, and existing studies are being summarized. The goal is for companies to make initial hazard data sets (based on a standard, OECD recommended list) publicly available on the majority of 2,800 HPV chemicals by 2004. Total cost of the program is estimated to approach \$500 million.

ACA welcomes the high level of cooperation between all parties to produce an effective voluntary program that will provide EPA and the public with an unprecedented amount of information on the potential health and environmental effects of HPV chemicals. The voluntary HPV program is a significant improvement over traditional "command-and-control" regulatory approaches. However, the current program focuses exclusively on the hazards of chemicals. The next important step will be to continue the cooperative approach to ensure risk-based decision-making, particularly through developing and communicating chemical use and exposure information. This additional information would help put hazard information from the HPV Chemical Challenge program into an appropriate risk context. As product stewards, sponsors are encouraged to provide this risk context for the HPV chemicals, and to make this information available to all interested parties.

This document is intended to be used for the preparation of reports for technical audiences. However, even among technical audiences, there will be varying degrees of interest in the details of the assessment. As such, this technical reporting guidance has been structured to provide varying levels of detail to audiences with varying information needs. The initial "layer" of detail provides a summary of the screening evaluation, offering a synopsis of the relevant hazard and exposure information. The second layer of the technical report is embodied in the OECD SIAR format, where an emphasis on the hazard information and an abbreviated review of exposure data leads to a conclusion about the priority of the chemical for further action. Finally, a third layer of reporting that includes expanded descriptions and documentation of the exposure assessment efforts and hazard testing dossiers is illustrated.

Scope and Applicability of This Document:

Currently, there are several programs around the world designed to provide roughly the same type and amount of information on HPV chemicals. However, there are differences, particularly with respect to the amount of exposure information that will be provided. Each of these programs is strictly voluntary, and sponsors are not obligated to provide exposure information in any particular format or level of detail. Nevertheless, where exposure information is provided, it is helpful for sponsors to use reporting formats and approaches that are as consistent and transparent as possible.

Generally speaking, there are four different levels of information that will be provided in these various programs. Those levels can be summarized as follows:

1. “HPV”, which will include, at a minimum, hazard data on 13 endpoints that have been identified by the OECD, plus physical/chemical properties;
2. “HPV-PLUS”, which will include HPV hazard data, plus some general contextual information about use and/or exposure;
3. “SIDS”, which will include, at a minimum, hazard data on 13 endpoints, physical/chemical properties, and a SIDS Initial Assessment Report, plus four basic categories of exposure information (production volume, physical form of product, likely sources of exposure, and use functions/categories);
4. “SIDS-PLUS”, which will include SIDS data, plus more complete exposure information, such as might be appropriate for an initial assessment of the chemical or a chemical use.

In case #1, companies are not expected to provide any use or exposure information. In case #3, the amount and format of exposure information already are fairly well defined by OECD’s guidance on preparation of the SIAR (See Attachment #4). The guidance provided in the following pages is most likely to be helpful to companies that will provide information under case #2 or #4.

Possible Contents of a Technical Report:

- Cover Page
- Summary Chemical Profile
- Hazard and Exposure Data Summary Table
- SIDS Initial Assessment Report (SIAR)
- Expanded Exposure Assessment Addendum (EEAA)
- SIDS Hazard Testing Dossier
- Exposure Evaluation Dossiers

Cover Page:

The Cover Page (see Attachment 1) can display the name and CAS number of the chemical, as well as the name of the sponsor. If the report pertains to a group of chemicals, then all of the individual chemicals and their respective CAS numbers should be reported here. Similarly, if the sponsor were a consortium, it would be appropriate to include the individual company names of the consortium members. It is also advisable to include the revision number and date of last revision.

Summary Chemical Profile:

The Summary Chemical Profile, which follows the cover page (see Attachment 2 for a hypothetical example), summarizes the sponsor's conclusions of the assessment. The Summary Chemical Profile is primarily intended for audiences who only seek a summary of the hazard and exposure screening-level assessments. It should include a summary of properties and hazards of the chemical, a description of the potential exposures and key results of any exposure analysis, the results of the initial screening-level assessment, and a summary of any recommendations. Recommendations will typically be of three types: (1) the chemical is currently of low priority for follow-up work, except for periodic review; or, (2) the chemical is a candidate for more in-depth assessment, or (3) the chemical may be a possible candidate for risk management action.

An overview of the methodologies used for the hazard and exposure analysis, a discussion of the scope and completeness of that analysis, and the relevant, supporting arguments for the recommendations in the Profile might also be appropriate. (Figure 2 in the ACA's Generic Technical Evaluation Framework for Screening-Level Evaluations of Human Exposure to HPV Chemicals provides a conceptual representation of the major routes of exposure that generally are considered when conducting an exposure assessment.)

Hazard and Exposure Data Summary Table:

In addition to the Summary Chemical Profile, a "Hazard and Exposure Data Summary Table can be an effective tool to visually demonstrate both the hazard data, and the results of an exposure analysis. A basic template for such a table is shown in Attachment 3. Although it may repeat information contained in the Summary Chemical Profile and the OECD SIAR (see below), this table is designed to allow a quick review of key data (e.g. properties, hazards, and exposures). There are also placeholders in the table that allow the entry of findings for endpoints that go beyond the required elements for SIDS or the U.S. HPV Challenge program. Sponsors may elect to include such "beyond SIDS" information, when it is relevant and available. However, neither governments, nor the public, should expect this information in all cases.

SIDS Initial Assessment Report (SIAR):

The SIDS Initial Assessment Report (SIAR) is a technical summary of data on the OECD's agreed chemical properties, hazard and exposure endpoints. Since the OECD has developed guidance on the format of the SIAR that has been accepted by industry and governments worldwide, there is no need to re-visit that work. The OECD provisional guidance document for SIAR preparation can be downloaded from the OECD web site at: <http://www.oecd.org/ehs/hpv.htm>. An excerpt from this guidance, containing the recommended reporting format for the SIAR, is contained in Attachment 4.

Expanded Exposure Assessment Addendum (EEAA):

As noted above, the SIAR is a framework for portraying basic screening level hazard and general exposure information about a chemical. However, consistent with the technical framework that ACA is developing and promoting, there may be instances where additional analyses of exposure have been conducted in order to put the results of the HPV hazard testing into a more specific context for decision-making. These findings could be very valuable to interested audiences. Attachment 5 provides a general outline for the reporting of such information in an "Expanded Exposure Assessment Addendum" (EEAA).

The EEAA is intended to supplement, not replace the OECD SIAR. Consistent with the ACA's technical framework, it is organized around the following spectrum of potential chemical exposures:

Human exposures:

1. Occupational settings where HPV chemicals are manufactured, distributed, processed or formulated into end use products;
2. In communities adjoining facilities where HPV chemicals are manufactured, distributed, or processed;
3. As a result of handling chemicals and products during transport;
4. As a result of handling and using end use products containing the chemical; and/or,
5. From indirect sources of the chemical (e.g., drinking water from the dispersed disposal of products, food, natural sources, etc.).

Ecological exposure:

1. In ecosystems adjoining facilities where HPV chemicals are manufactured, distributed, or processed;
2. As a result of the use and disposal of HPV chemical-containing products; and/or,
3. Natural sources of the chemical.

In each instance, sponsors should consider a discussion of the work that was done, including:

- the types of potential exposures evaluated, and the completeness of the analysis (if some potential exposures are not examined, then the reasons why should be discussed);
- the methods used (e.g., qualitative analysis, mathematical modeling, monitoring);
- key results; and,
- the accuracy and reliability of the exposure estimates.

SIDS Hazard Testing Dossier:

The SIDS hazard testing dossier is the collection of hazard data in the form of robust summaries of individual studies. Although many different formats are available, the IUCLID format appears to be favored internationally. The SIDS dossier can be technical and extensive, addressing methodologies, analytical findings, dose response, etc.

Exposure Evaluation Dossiers:

HPV sponsors may want to consider providing reports on individual exposure evaluations, to the extent that they are warranted. Attachment #6 has been developed to assist sponsors in the compilation and documentation of this information. IUCLID has existing fields to enter the general exposure elements included in Outline A.

Attachment 1

Screening-Level Assessment

for

Chemical X
CAS #: 000-00-0

Prepared by:
So and So Consulting

Prepared for:
Chemical X Producers Consortium

Revision: __

Date of Last Revision: _____

Attachment 2

Summary Chemical Profile

The following sections are suggested as possible for inclusion in the Summary Chemical Profile.

- ✓ Chemical Identification Information
- ✓ Background, Summary, and Sponsor's Conclusions
- ✓ Environmental and Human Health Hazard Information
- ✓ Use and Exposure Information
- ✓ Initial Screening-Level Assessment
- ✓ Priority for Further Work

Chemical Identification Information:

[It is recommended that sponsors provide the chemical name, CAS number, and structural formula in this section.]

Background and Summary:

[The sponsor should consider presenting a summary of properties and hazards of the chemical, a description of potential exposures, the result of any exposure analysis relative to the hazards, and recommendations related to the priority of the chemical for further consideration, together with the reasons which support the recommendations. It is recommended that the summary include assessment of the most sensitive relevant endpoint identified in the available data and that it include an indication of the weight of evidence supporting the conclusion. It is recommended that this section be prepared in a concise style, for those audiences that only desire an overview of the hazard, exposure and screening-level assessment processes. The length of this document will depend on the amount of available information.]

Environmental and Human Health Hazard Information:

[Sponsors may want to adapt the following language as a way to introduce a summary of hazard screening information for the chemical.]

“The hazard data used in this study were derived from a compilation of publicly available information, compiled under the voluntary U.S. High Production Volume (HPV) Chemicals Challenge program. The health effects from exposure to this chemical have been screened in a variety of approved methods. The most sensitive relevant endpoint identified in this screening effort was from the study (*insert name of study and the relevant endpoint*). In this study, no adverse health effects were observed at or

below (*insert No Observable Adverse Effect Level*). When tested for ecological effects, scientists observed no effects at levels at and below (*insert Predicted No Effect Concentration*). A detailed summary of the toxicity studies used in this analysis is attached (*provide link to robust summaries*), or from (*insert name of sponsoring organization*).”

Use and Exposure Information:

[Sponsors may want to adapt the following language as a way to introduce a summary of the use and exposure information for the chemical.]

“The exposure assessment component of this analysis encompasses the manufacture, processing, transport, and major uses of this chemical in commerce. As a screening level evaluation, it is based on current information, and is not a comprehensive assessment of every possible use of this material. However, a thorough attempt has been made to identify the significant uses and routes of exposure, and, when appropriate, to quantify them sufficiently to make a comparison to relevant hazard endpoints. A discussion of the completeness of this analysis, the methods used for exposure assessment, and their accuracy and relevance are described in the attached documentation, or are available from the following (*list the sponsoring organization, and provide specific individual contact information*). Where it is appropriate from a scientific standpoint, individual exposures have been summed across different, but related, exposures to provide an aggregate description of the maximum exposure that could be possible for the chemical.

Based on an analysis of existing information, ___ % of the current production volume of this chemical is commonly used as a (*provide application*) in (*describe products*). (*Repeat as often as necessary to include all uses that have been evaluated; applications can be batched as appropriate*). As a result, the normal way(s) by which someone could come into contact with this chemical is/are from (*provide exposure route*) while (*describe activity related to exposure*). Considering the uses mentioned above, it is estimated that someone handling this chemical, or using the products containing this material could be expected to be exposed to about (*provide exposure estimate*) of this chemical

When this chemical enters the environment, it will likely (*provide environmental fate information*).”

Initial Screening-Level Assessment:

[Sponsors may want to adapt the following approach as a means to relate hazard information to the estimated exposure levels.]

“A summary of the screening level exposure comparison to hazard no effect levels is provided in the table below.”

Results of Screening Level Use/Exposure Comparison for Chemical X			
Use or Exposure	Estimated Exposure Level	Relevant Hazard Endpoint and “No Adverse Effect Level”	Exposure/Hazard Ratio (If Calculated)

Priority for Further Work:

[Sponsors may want to consider providing a statement on the priority of the chemical for further work. This could include the adaptation of language such as the following.]

<p>“Based on the results, the estimated (aggregate) human exposure levels expected during the manufacture, processing or intended uses of Compound X evaluated in this report are ###-fold less than the lowest dose of Compound X showing no adverse health effect in currently available hazard studies. Considering the completeness, accuracy, and relevance of both the hazard and exposure evaluations, Compound X is recommended as a low priority for further work at this time. “</p> <p style="text-align: center;">OR:</p> <p>“Based on the results, the estimated (aggregate) human exposure levels expected during the manufacture, processing or intended uses of Compound X evaluated in this report (exceed or approximated) the lowest dose of Compound X showing no adverse health effect in currently available hazard studies. Considering the completeness, accuracy and relevance of the exposure and hazard assessments, Compound X is a candidate for more refined follow-up study with respect to its hazard and/or exposure potential. “</p> <p style="text-align: center;">OR:</p> <p>“Based on the results, the estimated (aggregate) human exposure levels expected during the manufacture, processing or intended uses of Compound X evaluated in this report exceed the lowest dose of Compound X showing no adverse health effect in currently available hazard studies. Considering the completeness, accuracy and relevance of the exposure and hazard assessments, Compound X may be a candidate for risk management action.”</p>
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[Similar summaries need to be added for ecological effects, as relevant.]

Attachment 3

Hazard and Exposure Data Summary Table

(Note: This summary table should explicitly identify which data are derived from Structure Activity Relationships, which exposure data are derived from models, and whether or not those models have been validated)

CHEMICAL NAME:		
CAS NO:		
PHYSICAL-CHEMICAL ELEMENTS	PROTOCOL	RESULTS
Melting Point		°C
Boiling Point		°C (at kPa)
Vapor Pressure		kPa at °C
Partition Coefficient		Log K _{ow}
Water Solubility		mg/l at °C

ENVIRONMENTAL FATE AND PATHWAY ELEMENTS	PROTOCOL	RESULTS
Photodegradation		In air T _{1/2} = hours
Stability in Water		T _{1/2} =min
Transport and Distribution between Environmental Compartments		In Air % In Water % In Sediment % In Soil % In Biota %
Biodegradation		
Additional data (as available)		

ECOTOXICITY ELEMENTS	SPECIES	PROTOCOL	RESULTS
Acute Toxicity to Fish			LC ₅₀ (24 hr) = mg/l LC ₅₀ (48 hr) = mg/l LC ₅₀ (72 hr) = mg/l LC ₅₀ (96 hr) = mg/l
Toxicity to Aquatic Plants (Algae)			EC ₅₀ (hr) = mg/l NOEC (hr) = mg/l
Acute Toxicity to Aquatic Invertebrates (Daphnia)			LC ₅₀ (24 hr) = mg/l LC ₅₀ (48 hr) = mg/l

HEALTH ELEMENTS	SPECIES	PROTOCOL	RESULTS
Acute Toxicity			LD ₅₀ = mg/kg
Repeat Dose Toxicity			NOAEL = mg/kg
Genetic Toxicity In Vivo (chromosomal aberrations)			
Genetic Toxicity In Vitro (gene mutations)			+ or -
Reproductive Toxicity			NOAEL = mg/kg (General toxicity) NOAEL = mg/kg (parental) NOAEL = mg/kg (F1 generation)

Developmental Toxicity/Teratogenicity			NOAEL = mg/kg (General toxicity) NOAEL = mg/kg (Pregnancy/litter) NOAEL = mg/kg (Fetal data)
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ADDITIONAL HAZARDS DATA (AS AVAILABLE)	SPECIES	PROTOCOL	RESULTS
PHYSICAL-CHEMICAL			
ENVIRONMENTAL FATE AND PATHWAYS			
ECOTOXICITY			
HEALTH			

(Note: The following sections may need to be repeated as necessary to capture a variety of exposure scenarios. Instructions should be provided, directing reader to robust summaries on which these evaluations are based.)

EXPOSURE INFORMATION (AS AVAILABLE)	KEY RESULTS
Evaluation of Human Exposures	<ul style="list-style-type: none"> • Brief description of which routes have relevant exposures, and the completeness of the analysis, including discussion of routes that were not examined, and why. Industrial hygiene data should be included, if available. • Type of method(s) (measurement and modeling) used to assess exposure for each route. • Summary of findings (e.g., in mg/kg/d)
Evaluation of Ecological Exposures	<ul style="list-style-type: none"> • Brief description of which routes have relevant exposures, and the completeness of the analysis, including discussion of routes that were not examined, and why. • Type of method(s) used to assess exposure for each route. • Summary of findings (e.g., in mg/kg/d)

Attachment 4

OECD Guidance for the Preparation of SIARS for Hazard Assessment Annex 1: Proposed Structure and Content of the SIDS Initial Assessment Report (SIAR)

NOTE: Full document can be downloaded from <http://www.oecd.org/ehs/hpv.htm>, under "Interim Manual for Investigation of HPV Chemicals Policy and Guidance Documents."

1. IDENTITY

This chapter should include the following basic information on the chemical:

- Identification of the chemical (e.g. CAS number, name, molecular formula, etc.)
- Composition of the chemical being assessed (e.g. degree of purity, known impurities or additives, difference of impurities among products)
- Basic elements of physical-chemical properties (e.g. water solubility, P_{ow} , vapor pressure, etc.)

It may also suggest 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 chapter 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 the SIAR.

2. GENERAL INFORMATION ON EXPOSURE

Readily available information on exposure to the chemical in the Sponsor country should be summarized for the clear understanding of the potential sources of exposure during the life cycle of the chemical. Although additional relevant information should be provided if available, such as international data on production/import volumes and use categories, the following must be provided as much as possible to enable the human health and environmental hazard information to be put in context:

- estimated national production or import volume;
- use categories and/or functions;
- physical form of marketed product(s); and
- source(s) of potential release to the environment.

If available, information on potential human exposure and exposure to the environment should be described but at a general level of detail. It is not necessary to conduct exposure modeling or monitoring for the purposes of the SIDS initial assessment. However, when more detailed relevant information is available to the Sponsor country or members of industry consortia, it should be referenced in the SIAR document, so that its availability is known. Alternatively, such information could be annexed to the SIDS Dossier.

Specific guidance is available on the assessment of chemicals used solely as closed system intermediates (Sub-section 3.6 in the SIDS Manual)

2.1 Environmental Exposure and Fate

Information about environmental fate and pathways should be provided based on the information on potential sources of release to the environment in the Sponsor country, use categories and physical-chemical properties, and the following specific tests:

- photodegradation
- stability in water
- transport between environmental compartments; and
- biodegradation

2.2 Human Exposure

The human populations for which there is a potential exposure to the chemical should be identified with specific consideration of occupational exposure, consumer exposure and indirect exposure of man via the environment. These considerations should be based on readily available general information on exposure, the use pattern and physical-chemical properties of the chemical.

Potential sources of occupational and consumer exposure known to the Sponsor country should be highlighted. Available workplace exposure limit values (e.g. TLV, MAK) already determined could be stated here for illustrative purposes. The possibility of indirect human exposure (via food, water and air) should be considered and discussed if relevant.

3. HUMAN HEALTH HAZARDS

3.1 Effects on Human Health

Results of toxicity tests and other information should be summarized and discussed, including:

- a) toxicokinetics and metabolism and mechanism of action (if known);
- b) acute toxicity;
- c) repeated dose toxicity;
- d) reproduction/developmental toxicity;
- e) genetic toxicity; and
- f) any other information that is available, e.g. experience with human exposure.

Each of these elements should be clearly identified by the use of sub-headings and the SIAR should summarize the conclusions on each specific element before going on to discuss the next. For example, there should be remarks about the experimental results, discussion and conclusions for each SIDS element. Again the intent is not to repeat the detail of the information given in the SIDS Dossier but to briefly highlight the key aspects. If human data are available, they should be described separately from non-human data under the relevant SIDS element. Where more than one adequate or key study is available, it may be useful to present a table summarizing the data considered in reaching the conclusion for each element, together with accompanying text if necessary.

From the test results on repeated dose toxicity and reproduction/developmental toxicity, a judgement on the No-Observable-Adverse-Effect Level (NOAEL) and Lowest-Observable-Adverse-Effect Level (LOAEL) should be made. However, this information should be presented in the context of the adverse effects, information on the dose-response relationship and an assessment of whether any adverse effects are considered compound - related. Where combined repeated dose toxicity and reproductive/developmental toxicity testing has been carried out (OECD Test Guideline 421), care must be taken to separately consider systemic effects of repeated toxicity, developmental and reproductive effects. The toxicological significance of breakdown products or metabolites should be discussed where appropriate.

Where relevant data are available on non-SIDS elements such as irritation, skin sensitization and carcinogenicity, this also should be stated and the results, discussion and conclusions summarized in a similar manner.

4. HAZARDS TO THE ENVIRONMENT

4.1 Aquatic effects

Results of ecotoxicity tests and other information are summarized 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;

Other ecotoxicity information should be provided, if available. In the discussion, a qualitative consideration of the following 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.

Predicted No Effect Concentrations (PNECs) provide useful information for Sponsor countries to conduct their own local environmental risk assessment, and so are encouraged to be included for information where possible.

The PNEC value for the aquatic environment should be derived by applying relevant assessment factors. These assessment factors depend on the adequacy of the data available (reference). PNECs are useful in a screening level assessment because they allow a judgement to be made on the concentrations where critical effects may be expected 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 must be stated in the SIAR.

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.

4.3 Other Environmental Effects

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

If specific information is not available (e.g. due to chemicals being difficult to test or unstable), a qualitative evaluation based on physical-chemical properties and estimation from analogues can be given but is not required.

5. CONCLUSIONS AND RECOMMENDATIONS

5.1 Conclusions

The SIAR should provide a separate section summarizing the overall conclusions of the initial assessment, which provides a summary of the conclusions about each relevant SIDS element for human health and the environment together with information on exposure and on non-SIDS elements, where available.

Specifically the conclusions should provide:

- a summary description of the hazards of the chemical written with sufficient detail and clarity as to be informative, and to assist countries with classification work and other hazard-based national decision making; and
- a summary of the exposure information, primarily from the Sponsor country that will put the hazard information into context (e.g. on use).

5.2 Recommendations

The recommendations of the Sponsor country regarding the need for further work on the chemical should be clearly stated, together with the rationale and an indication of the nature of possible further work.

These recommendations will be discussed and agreed to, or modified as appropriate by the SIAM and endorsed by the Joint Meeting of the Chemicals Committee and the Working Party on Chemicals, Pesticides and Biotechnology, through the Task Force on Existing Chemicals.

The recommendations will be of two types, either:

- a) the chemical is currently of low priority for further work; or
- b) the chemical is a candidate for further work.

In the case of a recommendation for further work, the work can be of different types (depending on the hazards and general exposure information about the chemical). In most cases the initial focus will be on further work undertaken at a national and/or regional level, however international level activities may also be considered in some situations.

6. REFERENCES

References for the key studies relied upon in the SIAR should be included in the report. However, the reader should be made aware that the SIDS Dossier provides a comprehensive listing of references and information for any particular chemical.

Attachment 5

Suggested Approaches for Preparing an Expanded Exposure Assessment Addendum (EEAA)

Introduction

The purpose of the EEAA is to provide a more detailed discussion of any exposure analysis that is available, beyond the basic information called for in the SIAR. It is not a requirement of the OECD SIAR or EPA Challenge program, but may be provided at the option of the sponsor. The intent of the EEAA is to provide supporting exposure information beyond that expected from the SIAR or EPA challenge programs, and thereby help reduce the uncertainty associated with decisions as to whether or not further work on HPV chemicals is warranted.

Note that not all of the section headings suggested in this addendum may be relevant for a given situation. They are provided only for the purpose of encouraging consistency in reporting. Individual sponsors should adapt those relevant sections of the format that apply to their specific situation.

The elements of the addendum are based on identifying areas where human or ecosystem exposure to the subject chemical could occur. The ACA has identified the following basic routes of potential human exposure (described in greater detail in its technical framework report):

- Industrial occupational settings;
- Exposure to communities adjoining industrial facilities;
- As a result of using end products containing the chemical; and/or,
- From indirect sources of the chemical (e.g., drinking water, food, natural sources, etc.).

It has also identified potential routes of ecological exposures due to:

- Emissions from industrial facilities;
- The use and disposal of products; and,
- Natural sources of the chemical.

The following sections provide an overview of how an EEAA can be structured along the lines of these potential exposure routes. In each instance, the types of potential exposures that are identified, the completeness of the evaluation, a description of the methods used to estimate exposure (e.g., qualitative estimation, mathematical modeling, monitoring), the results, and a discussion of the accuracy and reliability of the exposure estimates should be provided. Factors to be considered with respect to the accuracy and reliability of the exposure estimates may include:

- Have the exposure methods been independently reviewed and are they publicly available (e.g., approved by a regulatory agency, or published in the peer reviewed scientific literature)?
- In the case of modeling estimates: what is the basis of the model, has it been validated, is it generic or specific to a particular type of exposure, to what extent were default assumptions used versus observed habits and practices information, what is the estimated precision of the model, etc?
- In the case of direct monitoring: what were the design and methods of sampling and analysis, the quality assurance controls considered, the estimated precision (the level of uncertainty?) of the measurements, etc?

These issues help the audience understand the level of uncertainty of analysis for decision-making, and how they may be compared to the hazard data (which, of course, also has limits of precision and accuracy that should be considered). Figure 2 of the ACA's Generic Technical Evaluation Framework for Screening-Level Evaluations of Human Exposure to HPV Chemicals provides a representation of the major routes of exposure that should be considered when conducting an exposure assessment.

HPV sponsors may want to consider providing reports on individual exposure evaluations, to the extent that they are warranted. Attachment #6 has been developed to assist sponsors in the compilation and documentation of this information.

Human Exposure Assessment:

The human exposure assessment section of the EEAA provides a summary of the qualitative, and where performed, the quantitative assessment of key potential exposure routes for the compound. Where a quantitative evaluation is performed, values should be presented in units that facilitate comparisons with relevant hazard data (e.g. mg/kg/day). As noted above, in the course of describing the exposure calculations and methods used, it is useful to identify areas of uncertainty where default assumptions were used, and their potential to overestimate or underestimate exposure.

In cases where multiple exposures are known to exist and are toxicologically relevant, it may also be appropriate to provide an estimate of the aggregate human exposure to the compound via the three main types of exposure listed below. If such a summation of exposures is not necessary, a rationale for this decision would be informative. Similarly, it may also be appropriate to include a discussion of special populations that may be disproportionately exposed, or who are more sensitive to the chemical than average.

Identification of Key Human Exposures – Completeness of the Evaluation

This section should provide an overview of the key human exposures evaluated, in summary form. It should also evaluate the completeness of the analysis, for example:

- To what extent has the total production of the chemical been considered in the evaluation?
- Are there gaps in the evaluation?
- If there are gaps, what was the reason they occurred (e.g., were data on a potential exposures not available, or was there insufficient information or analytical tools available)?
- To what extent might any gaps influence decision making?

Exposures Related to the Production, Handling, or Formulation of the Chemical in Industrial Facilities:

*Occupational (exposure of workers during production, handling and formulation of the individual chemical)

Summarize the major routes of occupational exposure that could lead to human contact with the compound (e.g. inhalation of vapors during chemical production). If occupational exposures present limited or no exposure potential, it is suggested that the rationale and back-up information be provided to demonstrate the same. If occupational exposures are deemed to be contributors to human exposure, these estimates of exposure(s) should be summarized, and the method(s) used to estimate the exposure (e.g. modeling, monitoring, etc.) should be described.

*Community (public exposure as a result of environmental releases to adjoining areas during production, handling and formulation of the individual chemical)

Summarize the major routes of community exposure (e.g., emissions from chemical production processes) that could lead to human contact with the compound by individuals living near facilities where the chemical is produced, handled, or processed. If community exposures present limited or no exposure potential, it is suggested that the rationale and back-up information be provided to demonstrate the same. If community exposures are deemed to be contributors to human exposure, these estimates of exposure(s) should be summarized, and the method(s) used to estimate the exposure (e.g. modeling, monitoring, etc.) should be described.

Exposures Related to the Handling of Chemicals and Products During Transport:

Summarize the major routes of exposure that could lead to human contact with the compound during transfer and transport (e.g. contact during the transfer of chemicals from bulk

storage containers, during repackaging operations, etc.) If transport-related exposures present limited or no exposure potential, it is suggested that the rationale and back-up information be provided to demonstrate the same. If such exposures are deemed to be contributors to human exposure, the calculations that depict such exposure(s) should be summarized, and the method(s) used to estimate the exposure (e.g. modeling, monitoring, etc.) should be described.

Exposures Related to the Handling and Use of End Products Containing the Chemical:

*Industrial (exposure of workers during the handling and use of end products intended for consumption in industrial facilities (e.g., machine tool cleaning solvents))

Summarize the major routes of exposure that could lead to human contact with the compound as a consequence of using an industrial product containing the chemical (e.g. inhalation of vapors during the use of an industrial paint, or cleaning solvent). If industrial product exposures present limited or no exposure potential, it is suggested that the rationale and back-up information be provided to demonstrate the same. If industrial product exposures are deemed to be contributors to human exposure, these estimates of exposure(s) should be summarized, and the method(s) used to estimate the exposure (e.g. modeling, monitoring, etc.) should be described.

*Institutional/Commercial (exposure of workers and users of facilities resulting from the use of products intended for institutions or commercial applications (e.g., janitorial products, dry-cleaning products))

Summarize the major routes of exposure that could lead to human contact with the compound as a consequence of using an institutional product containing the chemical (e.g. inhalation of vapors during the use of an industrial paint, or cleaning solvent). If institutional product exposures present limited or no exposure potential, it is suggested that the rationale and back-up information be provided to demonstrate the same. If institutional product exposures are deemed to be contributors to human exposure, these estimates of exposure(s) should be summarized, and the method(s) used to estimate the exposure (e.g. modeling, monitoring, etc.) should be described.

*Consumer (exposure of individuals, as the result of using household or personal care consumer goods)

Summarize the major routes of consumer exposure that could lead to human contact with the compound (e.g. contact during the use of cleaning products, personal care products, gardening products, etc.) If consumer exposures present limited or no exposure potential, it is suggested that the rationale and back-up information be provided to demonstrate the same. If

consumer exposures are deemed to be contributors to human exposure, the calculations that depict such exposure(s) should be summarized, and the method(s) used to estimate the exposure (e.g. modeling, monitoring, etc.) should be described.

Additional Considerations:

***Other Environmental Exposures**

In certain situations, it may be appropriate to consider indirect exposure to the chemical via various environmental media due to dispersed sources of the chemical (e.g. air, drinking water, and food from emissions due to the disposal of chemical products, or natural sources). The major routes of indirect environmental exposure that could lead to human contact with the compound, arising from situations other than those considered under community exposure, should be described (e.g. drinking water containing the compound.) If other environmental exposures present limited or no exposure potential, a statement and rationale along with the back-up information necessary to demonstrate the same should be provided. If other environmental exposures are deemed to be contributors to human exposure, the calculations that depict such exposure(s) and the method(s) used to estimate these exposures (e.g. modeling, monitoring, etc.) should be summarized.

***Aggregate Exposures**

In some instances, certain chemicals may present the potential for human exposure through a number of different exposure routes simultaneously. In these situations, it may be necessary to consider these aggregate exposures as part of the exposure assessment. If aggregate exposures are considered, the calculations that depict such exposure(s) should be summarized, and the method(s) used to estimate the exposures (e.g. modeling, monitoring, etc.) should be described. If multiple exposures are not expected to occur, it is recommended that the rationale and back-up information to demonstrate the same be provided.

***Special Populations**

In some instances, certain chemicals may present the potential for special populations (e.g. children) to be disproportionately exposed, or for exposure to occur in populations that are more sensitive to the chemical than average. These situations should be specifically identified as part of the technical reporting.

Ecological Exposure Assessment:

The ecological exposures section of the EEAA is focused on exposures to organisms in the environment, as a consequence of releases to ecosystems. As for human exposures, either

qualitative or quantitative analysis may be used to characterize releases to ecosystems, and resulting exposures. Where quantitative analysis is used, results should be expressed in terms that are relevant to the hazard data (e.g., mg/l in the case of chemicals in river water). Aggregate exposures (e.g., from multiple sources in the same ecosystem) may also be considered. The following sections outline the key routes of ecological exposure that can be evaluated.

Identification of Key Ecological Exposures – Completeness of the Analysis

As in human exposures, provide a summary of key ecological emissions and exposures, and an evaluation of any missing information.

Ecosystem Exposures Related to Emissions from the Production, Handling, or Formulation of the Chemical in Industrial Facilities

[TO BE COMPLETED]

Ecosystem Exposures Related to the Use and Disposal of Products Containing an HPV Chemical

[TO BE COMPLETED]

Other Sources of Ecological Exposure (e.g., from Natural Production)

[TO BE COMPLETED]

Hazard/Exposure-Based Human Screening Assessment:

The enhanced reporting may include an assessment of the hazard data in relation to the estimated exposure information. In such cases, it is recommended that the authors: 1) Describe the critical (most sensitive relevant) toxicological end point used for the compound relative to the types of exposures, and cite the appropriate health criterion (e.g. NOAEL, slope factor, RfD, etc.); 2) Relate relevant individual and/or aggregate exposures to the toxicological thresholds; 3) Provide a summary statement regarding the relationship of the estimated exposure level to the health criterion. (e.g. the estimated level of exposure is X times lower/higher than the No Observed Adverse Effect Level in studies on experimental animals.) (See related guidance on example statements); and, 4) Provide an evaluation of the accuracy and precision of these findings (e.g., whether the methods used to estimate exposure would have tended to overestimate or underestimate exposure, the extent to which any incomplete aspects of the exposure evaluation are important, etc.), and the impact that such factors would tend to have on the conclusions being reached regarding any recommendations for future work.

Attachment 6

Suggested Approaches for Summarizing Individual Exposure Evaluations

Introduction

There is little debate among scientists that exposure is an integral part of understanding chemical safety. However, until recently, there has not been a great deal of consistency in how exposure information was reported, especially the results of individual monitoring and modeling studies. Such consistency would be desirable for government, the chemical industry, and the public.

The purpose of this document is to provide a consistent approach for summarizing individual exposure evaluations via “Exposure Reporting Outlines” for sponsors who choose to provide this level of detail. The studies reported through these Outlines, are connected to and are discussed in the Attachment 5 narrative. Such summaries are intended primarily for technical audiences who are interested in the details of a particular study. They are not a requirement of the OECD SIAR or EPA Challenge program, but may be provided at the option of the sponsor. The intent of the Reporting Outlines is to provide a way to share exposure information beyond that expected from the SIAR or EPA Challenge programs and thereby help reduce the uncertainty associated with decisions as to whether or not further work on HPV chemicals is warranted.

Note that not all of the Outlines or their elements suggested in this addendum may be relevant for a given situation. They are provided only for the purpose of encouraging consistency in reporting. Individual sponsors may adapt those relevant sections of the format that apply to their specific situation.

Attachment 6 is intended to provide a user-friendly, consistent method for reporting summaries of individual studies of exposure data and information. It is envisioned that the exposure reporting outline would be a flexible, yet relatively standardized format. It includes consumer, occupational, and/or environmental information in summary form, and provides a basis for communicating screening and potentially detailed assessments of chemicals. The full detail of an individual study would not be included within the summary. However, the completed outline would direct the reader on where to get more detailed information. Flexibility in developing the outline and accompanying guidance is needed to ensure that the outline will be sufficient for screening level assessments. The Outlines address three general types of exposure information:

- **General Exposure-Related Information (Outline A):** This Outline is used to provide general exposure-related information on chemical manufacturing and product use. This information describes the chemical, its physical form, estimated volume, functions and product category uses, and potential releases and exposures. It can also include information related to controls in place that

reduce or prevent releases and exposures.

- **Monitoring Evaluations (Outline B):** These are quantitative evaluations of exposure where direct measurements of a chemical are made from samples collected under a specific exposure scenario (e.g. occupational exposure during chemical manufacturing).
- **Modeling Evaluations (Outline C):** These are primarily quantitative evaluations of exposure where mathematical models are used to predict exposure to a chemical for a specific exposure scenario (e.g. aquatic exposure following wastewater treatment). Modeling evaluations are frequently used for specific end-use product exposure information beyond the general information in Outline A. Details addressed in elements (9) Description of modeled scenario and (11) Input parameters in this outline are the typical factors used in performing an exposure assessment for a chemical in a particular product use. If a chemical were used in five different products, then the outline could be filled out to provide the five different modeling scenarios.

These Outlines provide a suggested flow of information, and would be accompanied by guidance to help the user in completing the outline. For example, a description of the data element, and examples of language that might be helpful in describing aspects such as data quality would be suggested. In designing the attached exposure study outlines, several basic principles that are usually addressed, either qualitatively, or quantitatively, in scientific reports should be considered. These basic principles are consistency in reporting exposure summary information, completeness, transparency, and the quality of the assessment, including data quality.

- **Completeness:** A full screening-level assessment of exposure covers direct consumer exposure; direct occupational exposure; indirect human exposure; and concentrations in environmental compartments. In the context of scientific reporting here, completeness refers to a description of: 1) which areas were studied; 2) which areas do not need to be studied with an explanation of why not; and 3) which areas were otherwise not studied, e.g., due to insufficient information. Ideally, the reader would have a very clear picture of those exposure scenarios that were included in the summary, those that were not, and an understanding why certain scenarios were not included.
- **Transparency:** Transparency, or showing your work, is essential for repeatability and full understanding by the reader. It is difficult to evaluate any type of conclusion without knowing how the information and conclusions were derived. Ideally, the summary should enable the reader to independently reach the same conclusions.
- **Assessment Quality:** No one method is appropriate for all scientific inquiry. Each method has some sort of scope and limitations. Precision, or repeatability, is a core scientific principle. Even qualitative descriptions of precision can provide insight to help predict ranges of probability, including the likelihood of exposure. Ideally the summary will enable the reader to understand the limitations, precision, and accuracy of the data and information.
Quality of Monitoring Data. Monitoring studies often employ Quality Assurance and Quality Control procedures and sampling and analytical chemistry methods, which are accepted and well documented. Often studies are designed with a specific objective in mind (e.g., comprehensive

monitoring study to develop a distribution of exposures, study for exploratory purposes, study to identify peak exposures). Effective communication of a study's results normally includes a clear statement of the applicability and limitations of the study.

Quality of Modeled Data. Predictive models are widely used to provide quantitative estimates of exposure for expected scenarios. Models range from basic approaches that rely heavily on conservative default assumptions to highly sophisticated tools that are specifically aimed at a given scenario and use measured site and/or scenario specific input parameters. Exposure modeling needs to be done with caution, by experts. Many models have not been validated. Some have been peer reviewed either informally or via a formal external peer review process. Selection of input values for models may limit the applicability of a model for certain types of decisions.

Reporting Outlines

The following is a general description of the purpose of each of the three Outlines, and how they could be used together when reporting exposure findings.

Outline A: GENERAL EXPOSURE-RELATED INFORMATION

The major purpose of this Outline (Outline A) is to provide general exposure-related information on chemical manufacturing and product use. This general information describes the chemical, its physical form, estimated volume, functions and product category uses. The Outline can also be used to qualitatively assess the potential for releases or exposures and to discuss factors that can mitigate or exacerbate releases or exposures. The IUCLID system can accommodate all of the information identified in Outline A.

Outline B: MONITORING EVALUATIONS

Monitoring evaluations cover studies in which data are the result of measurements of the chemical in a particular exposure scenario (e.g., occupational exposure during chemical manufacturing, consumer habits and practices study.) Monitoring information can be used directly to estimate exposures. It is also used to validate a model, or as an input for a particular model. This Outline provides a flexible approach that includes fields that address the various types of monitoring studies. The fields are flexible enough to include monitoring in any type of medium, to include simple matrices such as air or water, or complex ones like blood or tissue. In the context of exposure, an estimate could be related to the concentration of a chemical measured in a medium, an exposure concentration (e.g. with units of ppm-hours), a potential dose estimated from an exposure concentration, an absorbed dose (estimated or measured), or any other type of exposure/dose estimate.

Outline C: MODELING EVALUATIONS

Modeling evaluations cover studies in which data are the result of mathematical predictions of the chemical in a particular exposure scenario (e.g. aquatic exposure following wastewater treatment).

Although the word model is often associated with scientific computer software applications, it can also be used to describe one or more algorithms or mathematical equations used to make estimations of real-life scenarios. As noted above, scientists routinely use data from monitoring studies to validate exposure models, although not necessarily for the specific chemical of interest. Monitoring data can also be used as inputs for some models to improve the quality of the prediction. There are also models that use the outputs of other models as inputs. The Modeling Outline is flexible to allow a sponsor to describe the diverse approaches to modeling exposure. In the context of exposure, an estimate could be related to the concentration of a chemical found in a medium, an exposure concentration (e.g. with units of ppm-hours) a potential dose, an absorbed dose, or any other type of exposure/dose estimate.

Modeling Evaluations are frequently used to provide specific end-use product exposure information beyond the general information in Outline A. The details addressed in outline elements (9) Description of modeled scenario and (11) Input parameters are the typical factors used in performing an exposure assessment for a chemical in a particular product use. The results of the exposure assessment for that product use are also documented here, together with the methodology and discussion of assessment quality. If a chemical were used in five different products, then the outline would be filled out to provide the five different modeling scenarios.

Outline A: General Chemical Manufacturing and Use Exposure-Related Information

I. Identification Information	
(1) Assessment Identification and Date	
II. Scope	
(2) Activity	(e.g. manufacture of the chemical, a chemical use)
(3) Coverage	(e.g. single company, group of companies, entire U.S.)
III. Chemical information	
(4) Chemical Category	
(5) Chemical Name (s)	(e.g. Name on TSCA Inventory, IUPAC, synonyms)
(6) CAS Number (s)	
(7) Other Constituents (If Applicable)	(e.g. Name, CAS#, percentage range)
(8) Physical Form	(e.g. Liquid, solid, suspension.)
IV. Production, Import and Use	
(9) Estimated Volume (kg/year)	
(10) Function/Product Use Categories	(e.g. surfactant in paint, flame retardant in plastic)
V. Potential Releases and Exposures	
(11) General description of Potential Releases and Exposures	
(12) Discussion of Factors that Mitigate or Exacerbate Releases and Exposures	
(13) Remarks	(e.g. Citations, resources, references)

(Where no information is available or element is not relevant, it may be indicated by NIA, NR)

Outline B: Monitoring Evaluations

I. Identification Information	
(1) Assessment Identification and Date	
(2) Chemical Category	
(3) Chemical Name (s)	(Name on TSCA Inventory, IUPAC, synonyms)
(4) CAS Number (s)	
II. Monitoring Objective	
(5) Monitoring Study Objective	(e.g. Goal, scope)
III. Sampling and Analytical Methods	
(6) Sampling	(e.g. Dates, duration, number of samples)
(7) Method/Procedure	(e.g. NIOSH, ASTM, instrumentation, documentation, variations.)
IV. Description and Results	
(8) Description of Scenario Monitored	(e.g. Scenario being monitored, setting, population characterization,)
(9) Medium Sampled	(e.g. Air, water, wastewater, groundwater, soil, clothing or cloth patches, blood, tissue, work surfaces)
(10) Exposure Scenario Parameters	(e.g. Physical form of chemical, likely route, duration and frequency of exposure, amount of product used, use concentration)
(11) Results	(e.g. Media Concentration, Potential Dose, basis)
(12) Data Reliability	(e.g. Precision, accuracy, uncertainty, limitations, completeness)
(13) Remarks	(e.g. Citations, resources, study notes)

(Where no information is available or element is not relevant, it may be indicated by NIA, NR)

Outline C: Modeling Evaluations

I. Identification Information	
(1) Assessment Identification and Date	
(2) Chemical Category	
(3) Chemical Name (s)	(e.g. Name on TSCA Inventory, IUPAC, synonyms)
(4) CAS Number (s)	
II. Modeling Objective	
(5) Modeling Study Objective	(e.g. Goal, scope)
III. Description of Model	
(6) Tool or Model	Name (e.g. E-FAST, Calendex™) Brief description of tool
(7) Validation/Peer Review	(e.g. Evaluation with monitoring data, peer review process)
(8) Availability and Documentation	(e.g. Web sites, company names, reviews, evaluations)
IV. Description, Inputs and Results	
(9) Description of Modeled Scenario	(e.g. Scenario/product type being modeled, setting, population characterization)
(10) Exposure Medium Modeled	(Air, soil, clothing, blood, tissue, etc.)
(11) Input parameters	(e.g. Sources, approx. volume in this scenario, physical form of chemical, likely route, duration and frequency of exposure, amount of product used and chemical concentration, known or recommended use concentration, disposal route to the environment., assumptions, defaults, default changes, rationale for parameter selection.)
(12) Results	(e.g. Concentration, dose, basis)
(13) Reliability	(e.g. Precision, accuracy, uncertainty, limitations, completeness.)
(14) Remarks	(e.g. Citations, resources, study notes)

(Where no information is available or element is not relevant, it may be indicated by NIA, NR)