HPV Challenge Home

Basic Information

HPV Chemical Data - HPV Information System (HPVIS)

Public Use of HPV Chemical Data

EPA Chemical Data Screening, Review, & Characterization

Voluntary Chemical Sponsorships

EPA Regulatory Activities for Unsponsored Chemicals

Related Links

Draft Guidance on Developing Robust Summaries

(October 22, 1999)

The guidance in the following tables are presented exactly as they appear in the official OECD document entitled "*Guidance for Developing Robust Summaries for SIDS Dossiers*" (Document number ENV/JM/EXCH(99)13, dated 10/8/99). EPA provides the following narrative as an introduction to the OECD tables.

Definition/Background

The purpose of the U.S. HPV Chemical Challenge Program is to make hazard data (either existing or newly acquired information) available to the public for all U.S. high production volume chemicals. Most HPV Challenge sponsors will have at least some existing data in the form of full study reports for some or all of the endpoints in the Screening Information Data Set (SIDS). Sponsors need to determine whether available information already adequately describes a given endpoint. EPA guidance for determining data adequacy has already been provided. Once one or more studies have been identified as adequate, then they need to be made public in the Challenge Program. From a practical standpoint, it is not reasonable to attempt to create an electronic version of full study reports (especially old reports that may date to the 1960s or earlier). Instead, electronic summaries of full study reports will be prepared that contain the appropriate technical information for that particular endpoint.

The purpose of this document is to present guidance on what technical information, on an endpoint-by-endpoint basis, is necessary to adequately describe an experiment or study. The term "robust summary" is used to describe this technical content. Robust study summaries are intended to provide sufficient information to allow a technically qualified person to make an independent assessment of a given study report without having to go back to the full study report, and to also allow evaluation of the proposed test plan. A robust study summary therefore reflects the objectives, methods, results, and conclusions of the full study report, which can either be an experiment or in some cases an estimation or prediction method.

Which Studies Require Robust Summaries?

A complete robust study summary should be prepared for at least one key or critical study for each SIDS endpoint that has been considered adequate according to EPA guidance. Robust summaries may also be prepared for other adequate studies that are considered supportive of the key study. When you don't have an adequate study, but some information is available, it is suggested that robust summaries be prepared for each study. In addition, a single "best" study would contain a weight-of-the-evidence analysis in its remarks section (see below) which refers to, and ties together, the other studies.

Origin of the Guidance

The templates for robust study summaries presented in the following pages were based on: (1)

current guidance in the Organization of Economic Cooperation and Development (OECD) SIDS Manual; (2) work carried out by the US EPA in the context of the US HPV Challenge Program; (3) work carried out by the Chemical Manufacturers Association (CMA) and the Business and Industry Association Council (BIAC) relating to both the U.S. Challenge Program and the OECD SIDS program; and (4) work relating to the International Uniform Chemical Information Database (IUCLID) carried out by the European Commission. The draft guidance contained in this document is currently being considered by an international group of scientists associated with the OECD for its usefulness in the OECD SIDS program. Therefore, while there might be some changes made over the next few months, the EPA believes it is useful to place these templates on our website as guidance for early submitters and those who have been following the discussion of this issue over the past year. EPA intends to combine this document with the data adequacy document because the guidance presented herein simply captures the information gleaned during the data adequacy determination.

Robust Study Summary Templates

A series of templates for the different SIDS endpoints have been developed. They have been structured to allow for computerised data entry by describing the items in each robust study summary as "data fields" with allowance for free text. The proposed robust study summary templates have seven sections on: Test Substance, Methods, Results, Conclusion, Data Quality, References, and Other.

In the following pages, templates for the listed SIDS endpoints are provided:

Physical/Chemical Elements

1) Melting point
2) Boiling point
3) Vapor pressure
4) Partition coefficient
5) Water solubility

Environmental Fate and Pathways Elements

6) Photodegradation
7) Stability in water
8) Transport between Environmental Compartments (Fugacity)
9) Biodegradation

Ecotoxicity Elements

10) Acute toxicity to fish
11) Toxicity to aquatic plants
12) Acute toxicity to aquatic invertebrates

Health Elements

13) Acute toxicity
14) Genetic toxicity in vivo(chromosomal aberrations)
15) Genetic toxicity in vitro (gene mutations)
16) Repeat dose toxicity
17) Reproductive Toxicity
18) Developmental Toxicity/Teratogenicity

No templates are currently available for non-SIDS endpoints. Information on these is nevertheless encouraged to be included where available and relevant to the assessment.

Explanation of the Templates

Each template identifies the information items that should be included in a robust study summary for that SIDS endpoint. As many items of information as possible should be provided since robust study summaries concern the key study(s) on which the assessment of each SIDS endpoint is based. It is generally expected that the most adequate, reliable, and relevant study for each SIDS endpoint will be clearly identified and reported to the fullest level of the template. In cases where the study is considered inadequate, this should be clearly marked together with the reasons.

Each template is composed of seven sections, each section each of which has two different types of fields: controlled vocabulary and free text. The controlled vocabulary fields are identified in the templates by individual bullets, which are required to be filled out, while the free text field under each section entitled "Remarks"  allows the input of optional information.

Often, the "Remarks" section can be used as a means to further explain the contents of a particular section, much as is done in the "Discussion" portion of a publication in academic journals. For example, under the "Results" section, unexpected results could be further explained in the "Remarks" field (i.e., results seen were due to the complex nature of the test substance, deviations in protocol, etc.).

Test substance

This refers to the identity of the HPV chemical. If the chemical used in the specific test was different from the specific HPV chemical in identity (purity, additives, different solvent carrier, etc), then those differences need to be noted in the Test Substance Remarks field together with the chemical name, CAS number, purity of the materials, additives, and chemical structure as appropriate. If the chemical(s) is listed in the IUCLID system, it would also be useful to have an IUCLID identification number.

Methods

This section refers to the methodologies used to conduct the study. If the study was done according to OECD Test Guidelines, or other widely recognized guidelines, then it does not need to be fully described. For example, only the name of the guideline (e.g., OECD 421) needs to be reported. If there have been deviations from the Test Guideline, then those deviations that will significantly impact either the study reliability or the interpretation of the data need to be individually listed. On the other hand, if a study is based on a guideline that is not widely recognized, more items under the "Remarks" field may need to be included to justify use of the guideline.

There may also be situations in which a single study addresses several endpoints, such as with a study that follows the OECD combined repeat dose/reproduction/developmental Test Guideline 421. In this example, if this single study was to be the key one for each of these endpoints, then three separate robust study summaries would be prepared for each endpoint - all pointing to the same study.

Results

This section has standard items to fill in under discrete bullets, and also a "Remarks" field with additional items that may be needed to adequately assess data for reliability and use. At a minimum, qualitative descriptions of elements where dose-related observations were seen should be described.

Conclusions

This section has a "Remarks" field only, so that the conclusions of the study can be noted if given, together with any comments by the person preparing the robust study summary.

Data Quality

This section can be used to denote the adequacy of data, at the discretion of the person preparing the robust study summary

References

This free text field allows the person preparing the robust study summary to provide the full citation for the critical study on which the robust study summary is based.

Other

This section includes a data field for revisions, a number useful for sorting, and a free text field for general remarks.

PHYSICAL/CHEMICAL ELEMENTS
1) MELTING POINT

TEST SUBSTANCE

- Identity

Remarks field for Test Substance (Use for any pertinent, test substance-specific remarks.)

METHOD

- Method/guideline followed (include calculated as one of the possible methods)
- GLP (Y/N)
- Year (study performed)

Remarks field for Test Conditions (Detail and discuss any significant protocol deviations.)

RESULTS

- Melting point value in °C (include <0°C as an acceptable answer)
- Decomposition (yes-temperature °C/ no /ambiguous)
- Sublimation (yes/no/ambiguous)

Remarks field for Results (Describe additional information that may be needed to confirm data reliability and relevance)

CONCLUSIONS

Remarks field with the ability to identify source of comment, i.e. author and/or submitter

DATA QUALITY

- Reliabilities (Klimisch Code, if used, possibly a flag for key study)

Remarks field for Data Reliability key

REFERENCES (Free Text)

OTHER

- Last changed (administrative field for updating)
- Order number for sorting (administrative field)

Remarks field for General Remarks (Use for any other comments necessary for clarification.)

2) BOILING POINT

TEST SUBSTANCE

- Identity

Remarks field for Test Substance (Use for any pertinent, test substance-specific remarks.)

METHOD

- Method (include calculated as one of the possible methods)
- GLP (Y/N)
- Year (study performed)

Remarks field for Test Conditions (Detail and discuss any signification protocol deviations.)

RESULTS

- Boiling point value in °C (include >300°C as acceptable answer)
- Pressure
- Pressure unit
- Decomposition (yes/no/ambiguous)

Remarks field for Results (Describe additional information that may be needed to adequately assess data for reliability and use.)

CONCLUSIONS

Remarks field with the ability to identify source of comment, i.e. author and/or submitter

DATA QUALITY

- Reliabilities (Klimisch Code, if used, possibly a flag if 'key study')

Remarks field for Data Reliability

REFERENCES (Free Text)

OTHER

- Last changed (administrative field for updating)
- Order number for sorting (administrative field)

Remarks field for General Remarks (Use for any comments necessary for clarification.)

3) VAPOUR PRESSURE

TEST SUBSTANCE

- Identity

Remarks field for Test Substance (Use for any pertinent, test substance-specific remarks.)

METHOD

- Method (include calculated as one of the possible methods)
- GLP (Y/N)
- Year (study performed)

Remarks field for Test Conditions (Detail and discuss any significant protocol deviations.)

RESULTS

- Vapor Pressure value (include < 1 x 10^{-5} Pa as an acceptable answer)
- Temperature °C
- Decomposition (yes/no/ambiguous)

Remarks field for Results (Describe additional information that may be needed to adequately assess data for reliability and use.)

CONCLUSIONS

Remarks field with the ability to identify source of comment, i.e. author and/or submitter

DATA QUALITY

- Reliabilities (Klimisch Code, if used, possibly a flag if 'key study')

Remarks field for Data Reliability

REFERENCES (Free Text)

OTHER

- Last changed (administrative field for updating)
- Order number for sorting (administrative field)

Remarks field for General Remarks (Use for any comments necessary for clarification.)

4) PARTITION COEFFICIENT

TEST SUBSTANCE

- Identity

Remarks field for Test Substance (Use for any pertinent, test substance-specific remarks).

METHOD

- Method (include calculated as one of the possible methods)
- GLP (Y/N)
- Year (study performed)

Remarks field for Test Conditions (Detail and discuss any signification protocol deviations.)

RESULTS

- Log P_{ow}
- Temperature °C

Remarks field for Results (Describe additional information that may be needed to adequately assess data for reliability and use. In particular note if compound is surface active, dissociative, insoluble in water, etc.)

CONCLUSIONS

Remarks field with the ability to identify source of comment, i.e. author and/or submitter

DATA QUALITY

- Reliabilities (Klimisch Code, if used, possibly a flag if 'key study')

Remarks field for Data Reliability

REFERENCES (Free Text)

OTHER

- Last changed (administrative field for updating)
- Order number for sorting (administrative field)

Remarks field for General Remarks (Use for any comments necessary for clarification.)

5) WATER SOLUBILITY

TEST SUBSTANCE

- Identity

Remarks field for Test Substance (Use for any pertinent, test substance-specific remarks.)

METHOD

- Method (include calculated as one of the possible methods)
- GLP (Y/N)
- Year (study performed)

Remarks field for Test Conditions (Detail and discuss any signification protocol deviations.)

RESULTS

- Value (mg/L) at temperature °C
- Description of solubility (e.g., miscible to soluble to not soluble) (see Note 6 below)
- pH value and concentration at temperature °C
- pKa value at 25 °C

Remarks field for Results (Describe additional information that may be needed to adequately assess data for reliability and use.)

CONCLUSIONS

Remarks field with the ability to identify source of comment, i.e. author and/or submitter

DATA QUALITY

- Reliabilities (Klimisch Code, if used, possibly a flag if 'key study')

Remarks field for Data Reliability

REFERENCES (Free Text)

OTHER

- Last changed (administrative field for updating)
- Order number for sorting (administrative field)

Remarks field for General Remarks (Use for any comments necessary for clarification.)

ENVIRONMENTAL FATE AND PATHWAY ELEMENTS

6) PHOTODEGRADATION

TEST SUBSTANCE

- **Identity**

Remarks field for Test Substance (Use for any pertinent, test substance-specific remarks.)

METHOD

- **Method/guideline followed (include calculated as one of the possible methods)**
- **Type (test type)**
- **GLP (Y/N)**
- **Year (study performed)**
- **Light Source**
- **Light Spectrum (nm)**
- **Relative Intensity based on Intensity of Sunlight**
- **Spectrum of substance (max lambda, max epsilon and epsilon 295)**

Remarks field for Test Conditions. Detail and discuss any significant protocol deviations. Detail differences from the guideline followed including the following as appropriate:

- **Test medium (air, water, soil, other - specify)**
- **Duration**
- **Positive Controls**
- **Negative Controls**

RESULTS

- **Concentration of Substance**
- **Temperature °C**
- **Direct photolysis**
  - **Half-life t ½ (preferred)**
  - **Degradation % after**
  - **Quantum yield**
- **Indirect photolysis**
  - **Sensitizer (type)**
  - **Concentration of sensitizer**
  - **Rate Constant**
  - **Degradation % after**

- **Breakdown products (yes/no) If yes describe breakdown products and whether they were transient or stable in the Remarks field for Results.**

Remarks field for Results (Describe additional information that may be needed to adequately assess data for reliability and use.)

CONCLUSIONS

Remarks field with the ability to identify source of comment, i.e. author and/or submitter

DATA QUALITY

- **Reliabilities (Klimisch Code, if used, possibly a flag if 'key study')**

Remarks field for Data Reliability

REFERENCES (Free Text)

- **Last changes (administrative field for updating)**
- **Order number for sorting (administrative field)**

Remarks field for General Remarks (Use for any other comments necessary for clarification.)

7) STABILITY IN WATER

TEST SUBSTANCE

- **Identity**

Remarks field for Test Substance (Use for any pertinent, test substance-specific remarks.)

METHOD

- **Method/guideline followed (include calculated as one of the possible methods)**
- **Type (test type)**
- **GLP (Y/N)**
- **Year (study performed)**

Remarks field for Test Conditions. Detail and discuss any significant protocol deviations. Detail differences from the guideline followed including the following as appropriate:

- Duration (days)
- Positive Controls

- Negative Controls
- Analytical procedures

RESULTS

- Nominal
- Measured value (the value with units preferably as mg/L)
- Degradation % at a specified pH and temperature °C % after a specified time or
- Half-life ($t_{(1/2)}$ in days or hours at a specific pH (pH 4, 7, 9, and other) and temperature)
- Breakdown products (yes/no) If yes describe breakdown products and whether they were transient or stable in the Remarks field for Results.

Remarks field for Results (Describe additional information that may be needed to adequately assess data for reliability and use.)

CONCLUSIONS

Remarks field with the ability to identify source of comment, i.e. author and/or submitter

DATA QUALITY

- Reliabilities (Klimisch Code, if used, possibly a flag if 'key study')

Remarks field for Data Reliability

REFERENCES (Free Text)

OTHER

- Last changed (administrative field for updating)
- Order number for sorting (administrative field)

Remarks field for General Remarks (Use for any other comments necessary for clarification.)

8) TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS(FUGACITY)

TEST SUBSTANCE

- Identity

Remarks field for Test Substance (Use for any pertinent, test substance-specific remarks.)

METHOD

- Test (test type)

- **Method (Y/N)**
- **Year (study performed)**

Remarks field for Test Conditions. Detail the model used (title, version and date) and the input parameters (chemical-specific, environmental conditions) as necessary.

RESULTS

- **Media**
- **Estimated Distribution and Media Concentration (levels II/III)**

Remarks field for Results. Describe additional information that may be needed to adequately assess data for reliability and use including the following if available:

- Absorption coefficient
- Desorption
- Volatility

CONCLUSIONS

Remarks field with the ability to identify source of comment, i.e. author and/or submitter

DATA QUALITY

- **Reliabilities (Klimisch Code, if used, possibly a flag if 'key study')**

Remarks field for Data Reliability

REFERENCES (Free Text)

OTHER

- **Last changed (administrative field for updating)**
- **Order number for sorting (administrative field)**

Remarks field for General Remarks (Use for any other comments necessary for clarification.)

9) BIODEGRADATION

TEST SUBSTANCE

- **Identity**

Remarks field for Test Substance (Use for any pertinent, test substance-specific remarks.)

METHOD

- **Method/guideline followed (include calculated as one of the possible methods)**
- **Test Type (test type/aerobic/anaerobic)**
- **GLP (Y/N)**
- **Year (study performed)**
- **Contact time (units)**
- **Innoculum**

Remarks field for Test Conditions. Detail and discuss any significant protocol deviations, whether there was bacterial inhibition, and detail differences from the guideline followed including the following as appropriate:

- Innoculum (concentration and source)

· Fresh activated sludge
· Sludge from SCAS test (concentration and time of adaptation),
or
· Other

- Concentration of test chemical, vehicle used, pre-acclimation conditions
- Temperature of incubation °C
- Dosing procedure
- Sampling frequency
- Appropriate controls and blank system used?
- Analytical method used to measure biodegradation
- Method of calculating measured concentrations (i.e., arithmetic mean, geometric mean, etc.)

RESULTS

- **Degradation % after time**
- **Results**
- **Kinetic (for sample, positive and negative controls)**

- For each time period %

- **Breakdown products (yes/no) If yes describe breakdown products and whether they were transient or stable in the Remarks field for Results.**

Remarks field for Results (Describe additional information that may be needed to adequately assess data for reliability and use, e.g. lag time, observed inhibition, excessive biodegradation, excessive standard deviation, kinetics, time required for 10% degradation and total degradation at the end of the test.)

CONCLUSIONS

Remarks field with the ability to identify source of comment, i.e. author and/or submitter

DATA QUALITY

- **Reliabilities (Klimisch Code, if used, possibly a flag if 'key study')**

Remarks field for Data Reliability

REFERENCES (Free Text)

OTHER

- **Last changed (administrative field for updating)**
- **Order number for sorting (administrative field)**

Remarks field for General Remarks (Use for any other comments necessary for clarification.)

ECOTOXICITY ELEMENTS

10) ACUTE TOXICITY TO FISH

TEST SUBSTANCE

- **Identity**

Remarks field for Test Substance (Use for any pertinent, test substance-specific remarks.)

METHOD

- **Method/guideline followed (experimental/calculated)**
- **Type (test type)**
- **GLP (Y/N)**
- **Year (study performed)**
- **Species/Strain/Supplier**
- **Analytical monitoring**
- **Exposure period (unit)**
- **Statistical methods**

Remarks field for Test Conditions. Detail and discuss any significant protocol deviations, and detail differences from the guideline followed including the following as appropriate:

- Test fish (Age/length/weight, loading, pretreatment) - Test conditions, e.g.

· Details of test (static, semi-static, flow-through)
· Dilution water source

· Dilution water chemistry (hardness, alkalinity, pH, TOC, TSS, salinity)
· Stock and test solution and how they are prepared
· Concentrations dosing rate, flow-through rate, in what medium
· Vehicle/solvent and concentrations
· Stability of the test chemical solutions
· Exposure vessel type (e.g., size, headspace, sealed, aeration, lighting, # per treatment)
· Number of replicates, fish per replicate
· Water chemistry in test (D.O., pH) in the control and one concentration where effects were observed

- Test temperature range - Method of calculating mean measured concentrations (i.e. arithmetic mean, geometric mean, etc.)

RESULTS

- **Nominal concentrations (as mg/L)**
- **Measured concentrations (as mg/L)**
- **Unit (results expressed in what unit)**
- **Element value (e.g. LC_{50}, LC_{0}, LL_{50}, or LL_{0} at 48, 72 and 96 hours, etc., based on measured or nominal concentrations)**
- **Statistical results, as appropriate**

Remarks field for Results. Discuss if element effect concentration is greater than materials solubility. Describe additional information that may be needed to adequately assess data for reliability and use, including the following, if available:

- Biological observations
- Table showing cumulative mortality
- Lowest test substance concentration causing 100% mortality
- Mortality of controls
- Abnormal responses
- Reference substances (if used) - results
- Any observations, such as precipitation that might cause a difference between measured and nominal values.

CONCLUSIONS

Remarks field with the ability to identify source of comment, i.e. author and/or submitter

DATA QUALITY

- **Reliabilities (Klimisch Code, if used, possibly a flag if 'key study')**

Remarks field for Data Reliability

REFERENCES (Free Text)

OTHER

- **Last changed (administrative field for updating)**
- **Order number for sorting (administrative field)**

Remarks field for General Remarks (Use for any other comments necessary for clarification.)

11) TOXICITY TO AQUATIC PLANTS (E.G., ALGAE)

TEST SUBSTANCE

- **Identity**

Remarks field for Test Substance (Use for any pertinent, test substance-specific remarks.)

METHOD

- **Method/guideline followed (experimental/calculated)**
- **Test type (static/other)**
- **GLP (Y/N)**
- **Year (study performed)**
- **Species/strain # and source**
- **Element basis (i.e. number of cells/ml, area under the curve, growth rate, etc.)**
- **Exposure period, date of start and end of the test [Duration]**
- **Analytical monitoring**
- **Statistical methods**

Remarks field for Test Conditions. Detail and discuss any significant protocol deviations and detail differences from the guideline followed including the following as appropriate:

- Test organisms

· Laboratory culture
· Method of cultivation
· Controls

- Test Conditions

· Test temperature range
· Growth/test medium chemistry (hardness, alkalinity, pH, TOC, TSS, dissolved oxygen, salinity, EDTA)
· Dilution water source
· Exposure vessel type (e.g., size, headspace, sealed, aeration, #

per treatment)
· Water chemistry in test (pH) in at least one replicate of each concentration (at start and end of the test)
· Stock solutions preparation (vehicle, solvent, concentrations)
· Light levels and quality during exposure

- Test design (number of replicates, concentrations)
- Method of calculating mean measured concentrations (i.e. arithmetic mean, geometric mean, etc.)

RESULTS

- **Nominal concentrations in mg/L**
- **Measured concentrations in mg/L**
- **Unit [results expressed in what unit]**
- **Element value (e.g. ErC_{50}, ErL_{50}, EbC_{50}, EbL_{50}, EC_{10}-CD, EL_{10}-CD, EC_{50}-CD, EL_{50}-CD, EL_{90}-CD, EC_{90}-CD, EC_0, or EL_0 at 24, 48, 72 or 96 hours) Note whether cells removed prior to measurement.**
- **NOEC, LOEC, or NOEL, LOEL**
- **Was control response satisfactory (yes/no/unknown)**
- **Statistical results, as appropriate**

Remarks field for Results. Discuss if element effect concentration is not less than materials solubility. Describe additional information that may be needed to adequately assess data for reliability and use including the following:

- Biological observations
· Cell density at each flask at each measuring point
· Growth curves

Percent biomass/growth rate inhibition per concentration
Observations

CONCLUSIONS

Remarks field with the ability to identify source of comment, i.e. author and/or submitter

DATA QUALITY

- **Reliabilities (Klimisch Code, if used, possibly a flag if 'key study')**
- **Remarks field for Data Reliability**

REFERENCES (Free Text)

OTHER

- **Last changed (administrative field for updating)**
- **Order number for sorting (administrative field)**

Remarks field for General Remarks (Use for any other comments necessary for clarification.)

12) ACUTE TOXICITY TO AQUATIC INVERTEBRATES (E.G., DAPHNIA)

TEST SUBSTANCE

- **Identity**

Remarks field for Test Substance (Use for any pertinent, test substance-specific remarks.

METHOD

- **Method/guideline followed (experimental/calculated)**
- **Test type**
- **GLP (Y/N)**
- **Year (study performed)**
- **Analytical procedures**
- **Species/Strain**
- **Test details (static, semi-static, dosing rate, flow-through rate, etc.)**
- **Statistical methods**

Remarks field for Test Conditions. Detail and discuss any significant protocol deviations and detail differences from the guideline followed including the following as appropriate:

- Test organisms

· source, supplier, any pretreatment, breeding method
· Age at study initiation
· Control group

- Test conditions

· Stock solutions preparation (vehicle, solvent, concentrations) and stability
· Test temperature range
· Exposure vessel type (e.g., size, headspace, sealed, aeration, # per treatment)
· Dilution water source
· Dilution water chemistry (hardness, alkalinity, pH, TOC, TSS, salinity, Ca/Mg ratio, Na/K ratio)
· Lighting (quality, intensity and periodicity)
· Water chemistry in test (D.O., pH) in the control and at least one concentration where effects were observed

- Element (unit) basis (i.e. immobilization)

- Test design (number of replicates, individuals per replicate, concentrations)
- Method of calculating mean measured concentrations (i.e. arithmetic mean, geometric mean, etc.)
- Exposure period
- Analytical monitoring

RESULTS

- **Nominal concentrations in mg/L**
- **Measured concentrations in mg/L**
- **Unit [results expressed in what unit]**
- **EC50, EL50, LC0, LL0, at 24, 48 hours**
- **Statistical results, as appropriate**

Remarks field for Results. Discuss if element effect concentration is not less than materials solubility. Describe additional information that may be needed to adequately assess data for reliability and use including the following as appropriate:

- Biological observations

· Number immobilized as compared to the number exposed
· Concentration response with 95% confidence limits
· Cumulative immobilization
· Was control response satisfactory (yes/no/unknown)

CONCLUSIONS

Remarks field with the ability to identify source of comment, i.e. author and/or submitter

DATA QUALITY

- **Reliabilities (Klimisch Code, if used, possibly a flag if 'key study')**

Remarks field for Data Reliability

REFERENCES (Free Text)

OTHER

- **Last changed (administrative field for updating)**
- **Order number for sorting (administrative field)**

Remarks field for General Remarks (Use for any other comments necessary for clarification.)

HEALTH ELEMENTS

13) ACUTE TOXICITY

TEST SUBSTANCE

- **Identity**

Remarks field for Test Substance (Use for any pertinent, test substance-specific remarks.)

METHOD

- **Method/guideline followed (experimental/calculated)**
- **Type (test type)**
- **GLP (Y/N)**
- **Year (study performed)**
- **Species/Strain**
- **Sex**
- **No. of animals per sex per dose**
- **Vehicle**
- **Route of administration (if inhalation - aerosol, vapor, gas, particulate)**

Remarks field for Test Conditions. Detail and discuss any significant protocol deviations and detail differences from the guideline followed including the following as appropriate:

- Age
- Doses (OECD guidelines 401 and 425 do not provide dose levels, so these must be described in detail)
- Doses per time period
- Volume administered or concentration
- Post dose observation period
- Exposure duration (for inhalation studies).

RESULTS

- **Value [LD50 or LC50] with confidence limits if calculated**
- **Number of deaths at each dose level**

Remarks field for Results. Describe additional information that may be needed to adequately assess data for reliability and use, including the following, if available:

- Time of death (provide individual animal time if less than 24 hours after dosing)
- Description, severity, time of onset and duration of clinical signs at each dose level
- Necropsy findings, included doses affected, severity and number of animals affected
- Potential target organs (if identified in the report)

- If both sexes tested, results should be compared

CONCLUSIONS

Remarks field with the ability to identify source of comment, i.e. author and/or submitter

DATA QUALITY

- Reliabilities (Klimisch Code, if used, possibly a flag if 'key study')

Remarks field for Data Reliability

REFERENCES (Free Text)

OTHER

- Last changed (administrative field for updating)
- Order number for sorting (administrative field)

Remarks field for General Remarks (Use for any other comments necessary for clarification.)

GENETIC TOXICITY ELEMENTS

14) GENETIC TOXICITY IN VIVO (CHROMOSOMAL ABERRATIONS)

TEST SUBSTANCE

- Identity

Remarks field for Test Substance (Use for any pertinent, test substance-specific remarks.)

METHOD

- Method/guideline followed
- Type (test type)
- GLP (Y/N)
- Year (study performed)
- Species
- Strain
- Sex
- Route of administration (if inhalation - aerosol, vapor, gas, particulate)
- Doses/concentration levels
- Exposure period
- Statistical methods

Remarks field for Test Conditions. Detail and discuss any significant protocol deviations and detail differences from the guideline followed including the following as appropriate:

- **Age at study initiation**
- **No. of animals per dose**
- **Vehicle**
- **Duration of test**
- **Frequency of treatment**
- **Sampling times and number of samples**
- **Control groups and treatment**
- **Clinical observations performed (clinical pathology, functional observations, etc.)**
- **Organs examined at necropsy (macroscopic and microscopic)**
- **Criteria for evaluating results (for example, cell types examined, number of cells counted in a mouse micronucleus test)**
- **Criteria for selection of M.T.D.**

RESULTS

- **Effect on mitotic index or PCE/NCE ratio by dose level by sex**
- **Genotoxic effects (positive, negative, unconfirmed, dose-response, equivocal)**
- **NOAEL(NOEL) (C)/LOAEL(LOEL) (C)**
- **Statistical results, as appropriate**

Remarks field for Results Describe additional information that may be needed to adequately assess data for reliability and use, including the following, if available:

- **Mortality at each dose level by sex**
- **Mutant/aberration/mPCE/polyploidy frequency, as appropriate**
- **Description, severity, time of onset and duration of clinical signs at each dose level and sex**
- **Body weight changes by dose and sex**
- **Food/water consumption changes by dose and sex**

CONCLUSIONS

Remarks field with the ability to identify source of comment, i.e. author and/or submitter

DATA QUALITY

- **Reliabilities (Klimisch Code, if used, possibly a flag if 'key study')**

Remarks field for Data Reliability

REFERENCES (Free Text)

OTHER

- **Last changed (administrative field for updating)**
- **Order number for sorting (administrative field)**

Remarks field for General Remarks (Use for any other comments necessary for clarification.)

15) GENETIC TOXICITY IN VITRO (GENE MUTATIONS)

TEST SUBSTANCE

- **Identity**

Remarks field for Test Substance (Use for any pertinent, test substance-specific remarks.)

METHOD

- **Method/guideline followed**
- **Type (e.g. reverse mutation assay, gene mutation study, cytogenetic assay, mammalian cell gene mutation assay, cytogenetic assay, etc.)**
- **System of testing [bacterial, non bacterial]**
- **GLP (Y/N)**
- **Year (study performed)**
- **Species/Strain or cell type and or cell line, bacterial or non-bacterial**
- **Metabolic activation**

  - Species and cell type
  - Quantity
  - Induced or not induced

- **Concentrations tested**
- **Statistical Methods**

Remarks field for Test Conditions. Detail and discuss any significant protocol deviations. Detail differences from the guideline followed including the following as appropriate:

- Test Design

· Number of replicates
· Frequency of Dosing
· Positive and negative control groups and treatment
· Number of metaphases analyzed
- Solvent

- Description of follow up repeat study
- Criteria for evaluating results (e.g. cell evaluated per dose group)

RESULTS

- Result
- Cytotoxic concentration
  - With metabolic activation
  - Without metabolic activation
- Genotoxic effects (e.g. positive, negative, unconfirmed, dose-response, equivocal)
  - With metabolic activation
  - Without metabolic activation
- Statistical results, as appropriate

Remarks field for Results. Note test-specific confounding factors such as pH, osmolarity, whether substance is volatile, water soluble, precipitated, etc., particularly if they effect the selection of test concentrations or interpretation of the results. Describe additional information that may be needed to adequately assess data for reliability and use include the following if available. Provide at a minimum qualitative descriptions of elements where dose effect related observations were seen.

- Frequency of reversions/mutations/aberrations, polyploidy as appropriate
- Precipitation concentration if applicable
- Mitotic index

CONCLUSIONS

Remarks field with the ability to identify source of comment, i.e. author and/or submitter

DATA QUALITY

- Reliabilities (Klimisch Code, if used, possibly a flag if 'key study')

Remarks field for Data Reliability

REFERENCES (Free Text)

OTHER

- Last changed (administrative field for updating)
- Order number for sorting (administrative field)

Remarks field for General Remarks (Use for any other comments necessary for clarification.)

16) REPEATED DOSE TOXICITY

TEST SUBSTANCE

- **Identity**

Remarks field for Test Substance (Use for any pertinent, test substance-specific remarks.)

METHOD

- **Method/guideline followed**
- **Test type**
- **GLP (Y/N)**
- **Year (study performed)**
- **Species**
- **Strain**
- **Route of administration, oral (gavage, drinking water, feed), dermal, inhalation (aerosol, vapor, gas, particulate), other**
- **Duration of test**
- **Doses/concentration levels**
- **Sex**
- **Exposure period**
- **Frequency of treatment**
- **Control group and treatment**
- **Post exposure observation period**
- **Statistical methods**

Remarks field for Test Conditions. Detail and discuss any significant protocol deviations and detail differences from the guideline followed including the following as appropriate:

- Test Subjects

· Age at study initiation
· No. of animals per sex per dose

- Study Design

· Vehicle
· Satellite groups and reasons they were added
· Clinical observations performed and frequency (clinical pathology, functional observations, etc.)
· Organs examined at necropsy (macroscopic and microscopic)

RESULTS

- **NOAEL (NOEL)**

- **LOAEL (LOEL)**
- **Actual dose received by dose level by sex, if known,**
- **Toxic response/effects by dose level**
- **Statistical results, as appropriate**

Remarks field for Results. Describe additional information that may be needed to adequately assess data for reliability and use include the following if available. Provide at a minimum qualitative descriptions of elements where dose effect related observations were seen.

- Body weight
- Food/water consumption
- Description, severity, time of onset and duration of clinical signs
- Ophthalmologic findings incidence and severity
- Hematological findings incidence and severity
- Clinical biochemistry findings incidence and severity
- Mortality and time to death
- Gross pathology incidence and severity
- Organ weight changes
- Histopathology incidence and severity

CONCLUSIONS

Remarks field with the ability to identify source of comment, i.e. author and/or submitter

DATA QUALITY

- **Reliabilities (Klimisch Code, if used, possibly a flag if 'key study')**

Remarks field for Data Reliability

REFERENCES (Free Text)

OTHER

- **Last changed (administrative field for updating)**
- **Order number for sorting (administrative field)**

Remarks field for General Remarks [Note - Use for any other comments necessary for clarification.]

17) TOXICITY TO REPRODUCTION

TEST SUBSTANCE

- **Identity**

Remarks field for Test Substance (Use for any pertinent, test substance-specific remarks.)

METHOD

- **Method/guideline followed**
- **Type (one generation, two generation, etc.)**
- **GLP (Y/N)**
- **Year (study performed)**
- **Species**
- **Strain**
- **Route of administration - oral (gavage, drinking water, feed), dermal, inhalation (aerosol, vapor, gas, particulate), other**
- **Doses/concentration levels**
- **Sex**
- **Control group and treatment**
- **Frequency of treatment**
- **Duration of test**
- **Premating exposure period for males (P and F1) as appropriate**
- **Premating exposure period for females (P and F1) as appropriate**
- **Statistical methods**

Remarks field for Test Conditions. Detail and discuss any significant protocol deviations and detail differences from the guideline followed including the following as appropriate:

- Test animals

· Number, age, sex per dose for P, F1 and F2, if appropriate

- Test design

· Vehicle
· Dosing schedules and pre and post dosing observations periods for P, F1 and F2, if appropriate

- Mating procedures (M/F ratios per cage, length of cohabitation, proof of pregnancy)
- Standardization of litters (yes/no and if yes, how and when)
- Parameters assessed during study P and F1 as appropriate

· Clinical observations performed and frequency (clinical pathology, functional observations, etc.)
· Estrous cycle length and pattern (number of days spent in each phase)
· Sperm examination (epididymal or vas sperm, concentration, motility, morphology)

- Parameters assessed during study F1 and F2, as appropriate

· Clinical observations performed and frequency (weight gain, growth rate, etc.)

· Others, for example anogenital distance, if performed
· Organs examined at necropsy (macroscopic and microscopic)

RESULTS

- NOAEL (NOEL) and LOAEL (LOEL) for P, F1 and F2, as appropriate
- Actual dose received by dose level by sex if known
- Parental data and F1 as appropriate (toxic response/effects with NOAEL value). Provide at a minimum qualitative descriptions of elements were dose related observations were seen
- Offspring toxicity F1 and F2, as appropriate (toxic response/effects with NOAEL value). Provide at a minimum qualitative descriptions of elements where dose related observations were seen.
- Statistical results, as appropriate

Remarks field for Results. Describe additional information that may be needed to adequately assess data for reliability and use include the following when there are dose related effects if available:

- Parental data and F1 as appropriate, provide at a minimum qualitative descriptions of elements were dose related observations were seen
- Body weight
- Food/water consumption
- Description, severity, time of onset and duration of clinical signs
- Fertility index (pregnancies/matings)
- Precoital interval (w/number of days until mating and number of estrous periods until mating)
- Duration of gestation (calculated from day 0 of pregnancy)
- Gestation index (live litters/pregnancies)
- Changes in lactation
- Changes in estrus cycles
- Effects on sperm
- Hematological findings incidence and severity
- Clinical biochemistry findings incidence and severity
- Mortality
- Gross pathology incidence and severity
- Number of implantations
- Number of corpora lutea (recommended)
- Ovarian primordial follicle counts
- Organ weight changes
· Histopathology incidence and severity
- Offspring toxicity F1 and F2, as appropriate, provide as a minimum qualitative descriptions of elements where dose related observations were seen
- Litter size and weights
- Sex and sex ratios
- Viability index (pups surviving 4 days/total births)
- post natal survival until weaning
- Effects on offspring (grossly visible abnormalities)
- Postnatal growth, growth rate
- Vaginal opening (F) or preputial separation (M)
- Other observations, for instance anogenital distance, if measured
- Organ weights

· Gross pathology

CONCLUSIONS

Remarks field with the ability to identify source of comment, i.e. author and/or submitter

DATA QUALITY

- Reliabilities (Klimisch Code, if used, possibly a flag if 'key study')

Remarks field for Data Reliability

REFERENCES (Free Text)

OTHER

- Last changed (administrative field for updating)
- Order number for sorting (administrative field)

Remarks field for General Remarks (Use for any other comments necessary for clarification.)

18) DEVELOPMENTAL TOXICITY/TERATOGENICITY

TEST SUBSTANCE

- Identity

Remarks field for Test Substance (Use for any pertinent, test substance-specific remarks.)

METHOD

- Method/guideline followed
- GLP (Y/N)
- Year (study performed)
- Species
- Strain
- Route of administration - oral (gavage, drinking water, feed), dermal, inhalation (aerosol, vapor, gas, particulate), other
- Doses/concentration levels
- Sex
- Exposure period
- Frequency of treatment
- Control group and treatment
- Duration of test

- **Statistical methods**

Remarks field for Test Conditions. Detail and discuss any significant protocol deviations and detail differences from the guideline followed including the following as appropriate:

- Age at study initiation
- Number of animals per dose per sex
- Vehicle
- Clinical observations performed and frequency
- Mating procedures (M/F ratios per cage, length of cohabitation, proof of pregnancy)
- Parameters assessed during study (maternal and fetal)
- Organs examined at necropsy (macroscopic and microscopic)

RESULTS

- **NOAEL (NOEL) and LOAEL (LOEL) maternal toxicity**
- **NOAEL (NOEL) and LOAEL (LOEL) developmental toxicity**
- **Actual dose received by dose level by sex if available**
- **Maternal data with dose level (with NOAEL value). Provide at a minimum qualitative descriptions of responses where dose related effects were seen.**
- **Fetal data with dose level (with NOAEL value). Provide at a minimum qualitative descriptions of responses where dose related effects were seen.**
- **Statistical results, as appropriate**

Remarks for Results. Describe additional information that may be needed to adequately assess data for reliability and use include the following when there are dose related effects if available: Maternal data, provide at a minimum qualitative descriptions of responses where dose related effects were seen.

- Mortality and day of death
- Number pregnant per dose level
- Number aborting
- Number of resorptions, early/late if available
- Number of implantations
- Pre and post implantation loss, if available
- Number of corpora lutea (recommended)
- Duration of Pregnancy
- Body weight
- Food/water consumption
- Description, severity, time of onset and duration of clinical signs
- Hematological findings incidence and severity
- Clinical biochemistry findings incidence and severity
- Gross pathology incidence and severity
- Organ weight changes, particularly effects on total uterine weight
- Histopathology incidence and severity
- Fetal data, provide at a minimum qualitative descriptions of responses where dose related effects were seen

· Litter size and weights
· Number viable (number alive and number dead)

· Sex ratio
· Postnatal growth (depending on protocol)
· Postnatal survival (depending on protocol)
· Grossly visible abnormalities, external, soft tissue and skeletal abnormalities

CONCLUSIONS

Remarks field with the ability to identify source of comment, i.e. author and/or submitter

DATA QUALITY

- **Reliabilities (Klimisch Code, if used, possibly a flag if 'key study')**

Remarks field for Data Reliability

REFERENCES (Free Text)

OTHER

- **Last changed (administrative field for updating)**
- **Order number for sorting (administrative field)**

Remarks field for General Remarks (Use for any other comments necessary for clarification.)