COMMITTEE OF EXPERTS ON THE TRANSPORT OF DANGEROUS GOODS AND ON THE GLOBALLY HARMONIZED SYSTEM OF CLASSIFICATION AND LABELLING OF CHEMICALS

Sub-Committee of Experts on the Globally Harmonized System of Classification and Labelling of Chemicals

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DEVELOPMENT OF GUIDANCE ON THE APPLICATION OF GHS CRITERIA

Application of GHS criteria to UVCBs[1], in specific petroleum substances

Transmitted by the International Petroleum Industry Environmental Conservation Association (IPIECA)

Background

1. IPIECA has been working on guidance on the application of GHS criteria to petroleum substances according to the work plan presented at the thirteenth session of the Sub-Committee (UN/SCEGHS/13/INF.4). At the fourteenth session IPIECA listed issues that could result in divergent classification of petroleum substances (UN/SCEGHS/14/INF.10). These issues have been informally discussed at the fourteenth and fifteenth sessions, which resulted in useful feedback from the Sub-Committee.

Development of draft guidance

2. Additional feedback has been obtained by email and via two webcasts. For a summary of the feedback, see Annex 2. Using the feedback IPIECA revised the draft guidance on the application of GHS criteria to petroleum substances. Draft guidance has been developed with input from experienced technical experts on the field of petroleum substance toxicology.

3. The draft guidance may be found in Annex 1 to this document. The draft guidance addresses crude oil and petroleum substances produced from oil and gas operations and the process streams derived from petroleum substances in refinery operations. It should be noted that in response to the feedback received an addition to the guidance document is being developed, in which the principles of the guidance will be explained with examples using scientific literature.

[1] Substances of unknown or variable composition, complex reaction products or biological materials

Finding an appropriate location for the guidance

4. Feedback has been requested and obtained on the most appropriate location for the guidance. Some sub-committee members suggested including the guidance as an Annex to the 'Purple Book'. However, one of the concerns raised by the Sub-Committee is whether the 'Purple Book' itself is the appropriate home for this guidance in light of the likelihood that more industry sectors may develop guidance in the future.

5. IPIECA understands these concerns and wants to emphasize that the guidance should be used as a tool to achieve harmonised classifications without the intent to interfere with GHS implementation decisions within Member States. Therefore, IPIECA suggests creating a space at the UN GHS website (http://www.unece.org/trans/danger/publi/ghs/ghs_welcome_e.html) for sector-specific guidance to achieve globally harmonised classifications.

Benefits of Guidance

6. IPIECA believes that the guidance presented in Annex 1, if adopted by the Sub-Committee, will have benefits in the following areas:

(a) Greater global harmonization on products broadly traded in international commerce;

(b) Enhanced credibility of the GHS framework with regard to petroleum substances; and

(c) Improved certainty of classification, less complexity, and lower costs for industry and country authorities.

7. We acknowledge that achieving these benefits is dependent on the pursuit of a credible approach, which is well communicated and understood by the affected parties.

Review of draft guidance

8. IPIECA invites the Sub-Committee to review the draft guidance. Feedback can be communicated to Rob.Cox@ipieca.org. If you are interested in follow-up discussions and/or review of the documents, you can also communicate this to Rob Cox.

Next steps

9. IPIECA proposes to continue working on this guidance in the next biennium. IPIECA aims to provide revised draft guidance by July 2009 for formal consideration by the Sub-Committee.

Annex 1

DRAFT GUIDANCE

APPLICATION OF GHS CRITERIA TO UVCBS, IN SPECIFIC PETROLEUM SUBSTANCES

Background

1. This document provides supplemental guidance for the classification and labelling of petroleum substances, a class of UVCBs.

2. The consistent classification and labelling of petroleum substances is not straightforward due to the complex nature and chemistry of the substances. Hence, whilst the Globally Harmonized System of Classification and Labelling of Chemicals (GHS) provides a well structured approach that is readily applicable to most substances and mixtures, for certain substances, such as UVCBs and in particular petroleum substances, application of GHS principles may be subject to interpretation and therefore not be consistent. Potential inconsistencies in classification and labelling may result as GHS is being implemented due to:

(a) The complex nature (composition) of petroleum substances;

(b) Differences in interpretation of the experimental data, and

(c) Divergent application of the GHS criteria.

GHS would benefit from more detailed guidance on classification of petroleum substances, based on the industry's experience in characterizing their hazards.

3. The purpose of this document is to provide supplemental guidance to facilitate a consistent approach to the classification and labelling of petroleum substances. The approach identified has been developed independent of specific regulatory approaches that exist or may be proposed and represents the global oil industry’s recommended approach under GHS.

The nature of petroleum substances

4. Petroleum substances are chemicals derived from crude oil by physical separation (distillation), which may be followed by chemical modification (e.g. hydrogenation, cracking, etc). There are many different types of crude oil and each consists of many thousands of chemicals, predominantly hydrocarbons. Furthermore, no two crude oils are compositionally the same. Thus, since the composition of any distillation fractions derived from crude oil will be dependent on the source crude oil itself, and the distillate fractions may be subject to a variety of chemical modifications, it follows that petroleum substances will be of variable chemical composition. Petroleum substances are, therefore, classed as “Unknown or Variable composition, Complex reaction products and Biological substances” (UVCB substances). For this reason petroleum substances cannot be produced to meet specific chemical specifications. Rather, specifications for petroleum substances are normally related to several physical chemical specifications (such as boiling range, flash point, viscosity) that establish specification limits related to the intended use of the material.

CAS descriptions of petroleum substances

5. According to the definitions in Chapter 1.3.3.1 of the GHS (second revised edition), substances are defined as: “*Chemical elements and their compounds in the natural state or obtained by any production*

process, including any additive necessary to preserve the stability of the product and any impurities deriving from the process used, but excluding any solvent which may be separated without affecting the stability of the substance or changing its composition." Petroleum streams meet the GHS definition of substance and are hence considered to be substances, not mixtures.

6. Although petroleum substances are of complex composition they are defined as substances and each has a CAS number and associated CAS definition. The CAS definition typically identifies the starting material and the last process step that a substance will have undergone during its production. In many cases an indication of important physico-chemical parameters such as either a boiling range or a carbon number range or both will be included in the CAS definition. An example of a typical CAS definition for a petroleum substance follows:

> *Gas oils (petroleum), straight run*
>
> *A complex combination of hydrocarbons produced by the distillation of crude oil. It consists of hydrocarbons having carbon numbers predominantly in the range of C11 through C25 and boiling in the range of approximately 205 °C to 400 °C (410 °F to 752 °F).*

7. Although the CAS definition is imprecise, it nevertheless does limit wide variation of composition for a given petroleum substance.

8. Regulatory authorities have included petroleum substances and other UVCBs on their chemical control inventories despite their complex and variable composition. Chemical inventories that include petroleum substances exist in Australia, Canada, China, the European Union, Japan, Korea, New Zealand, Philippines and the United States of America.

Grouping of petroleum substances for classification purposes

9. Petroleum substances are usually described in terms of starting material, production process and ranges of e.g. boiling point or carbon number. In order to maximise the use of available information and minimise animal testing, petroleum substances can be arranged into groups of "similar" substances.

10. The rationale for such groupings is that since they are all derived from similar starting materials and have similar physico-chemical properties and broadly similar chemical composition, they exhibit broadly similar hazard properties. Classification may then be addressed on a group rather than single substance basis.

11. Such grouping schemes have been devised by CONCAWE (Conservation of Clean Air and Water in Europe, the oil companies' European association for environment, health and safety in refining and distribution) and subsequently adopted in the EU in the Existing Substances Regulation (1993) and the Dangerous Substances Directive (1993) and also by the American Petroleum Institute in their activities to fulfil the requirements of the United States High Production Volume (HPV) Challenge program of the United States Environmental Protection Agency (2007).

12. Toxicity and environmental information is available on some members of each of the groups of petroleum substances and these data can be 'read-across' to all members of the petroleum substance group. These data have been summarized by the American Petroleum Institute (Ref to API Robust summaries) and CONCAWE (Ref to HEDSETs and Product dossiers; Classification guidance report; Environmental data report) and should be used as the prime sources of information.

13. The petroleum substance groups for which data exist and/or for which read-across is possible are:

(a) Crude oil
(b) Petroleum gases
(c) Naphthas/gasolines
(d) Kerosines
(e) Gas oils
(f) Heavy fuel oils
(g) Residual aromatic extracts
(h) Distillate aromatic extracts
(i) Treated distillate aromatic extracts
(j) Lubricant base oils
(k) Petroleum waxes
(l) Petrolatums
(m) Foots oils
(n) Slack waxes
(o) Bitumens (asphalts) and vacuum residues
(p) Petroleum cokes

14. By using the grouping system of petroleum substances and a tiered approach to the classification of petroleum substances, the potential hazards of petroleum substances can be accurately identified and communicated on a consistent basis.

15. Some petroleum substances may contain specific constituents which may be classified as hazardous, e.g., as acutely toxic or as carcinogens, mutagens, specific target organ toxicants (e.g. neurotoxicants), or reproductive toxicants. However, tests may show that the full petroleum substance may not in itself be hazardous. In addition, hazardous constituents may not be present in toxicologically significant amounts. In some regions of the world, there are lists of hazardous substances with mandatory classifications. These lists and mandatory classifications vary however by region. By considering data available on the petroleum substance as a whole and not simply as a mixture of its constituents, the actual hazard of the petroleum substance should globally be similar regardless of regional differences in the classification of individual constituents.

Classifying petroleum substances under GHS

16. GHS establishes the principle (section 1.3.2.2) that where test data are available for a complete substance or mixture, then the classification of the substance or mixture should be based on these data. Such a principle is generally applied to petroleum substances. In the absence of test data on the specific petroleum substance itself, read-across from a similar petroleum substance should be applied.

17. The petroleum substances in each of the groups have similar physico-chemical properties (i.e. a similar boiling point range and similar carbon number range) and have therefore a comparable composition and similar hazard properties. In certain specific cases read-across between groups is also possible provided the groups have a similarity of composition. This may occur because the manufacturing processes may result in some overlap in chemical composition between groups.

18. In some cases data may not be available for the petroleum substance per-se and reliable read-across may not be possible. As stated, petroleum substances are of a complex nature and may contain specific constituents which may themselves be classified as hazardous. Consideration of the amount and significance of such hazardous constituents may be then of assistance for the classification of the whole petroleum substance.

19. This concept is described within GHS as “bridging” where there are data on ingredients and similar substances that can be used to adequately characterize the hazards. Each hazard class has its own specific rules on bridging, as to the concentration limits that impact the final hazard classification. This provides a logical approach to enable consistent classification in the absence of test data or reliable read across data.

20. The first principle (i.e., Tier 1) is that data derived from actual testing on the substance or from read-across from similar substances (petroleum substances from the same group) that have been tested, should inform the classification of any petroleum substance for each hazard class. This principle is laid out in section 1.3.2.2 of the GHS (second revised edition). Information that is used as the basis for the classification decision should be of an adequate standard so that it is fit for purpose, or in the case where there is a sufficient weight of evidence to underpin the decision made. This is in line with the GHS principle that data can override decisions on classification based on the concentrations of constituents. For physico-chemical hazard classes, use of data is the only acceptable approach to classification.

21. For health and environmental hazard classes, in the absence of actual data derived from testing or read-across, the next tier (i.e. Tier 2) is classification based on the presence of specific hazardous constituents. This principle is laid out in section 1.3.3.1.3 of the GHS (second revised edition). If the concentration of suspected hazardous constituents is less than the thresholds defined by GHS for classification for specific hazards, then classification of the full petroleum substance is not required. However, if there are no data or read-across for the petroleum substance (Tier 1 is not fulfilled) and the concentration of suspected hazardous constituents is greater than the thresholds defined by GHS, then the final tier (Tier 3) is to recommend classification.

Table 1: Tiered approach

Tier	Information available	Hazard classification
1	Data available on petroleum substance or there is read-across from similar substances (petroleum substances from the same group) that have been tested	Based on the results of the specific study(ies)
2	Content of individual component is below specified concentration limits [a]	No classification
3	Content of individual constituent is above specified concentration limits [a]	Classification recommendation

[a] *Limits specified by GHS for specific hazard classes*

22. Some petroleum substances may contain specific constituents which may be classified as hazardous. The presence of these constituents in the different groups of petroleum substances depends on the average boiling point range of the group and of the specific constituent. Potential presence of specific (potentially hazardous) constituents in the different groups of petroleum substances is indicated in Table 2.

Table 2: Petroleum substance groups and their specific (potentially hazardous) constituents

Petroleum substance groups	Toxicity/Classification concerns	Components
Crude oil	Carcinogenicity, mutagenicity, acute toxicity	H_2S[a], Benzene[b], PAH[c]
Petroleum Gases	Carcinogenicity/mutagenicity, acute toxicity	1,3-Butadiene[d], H_2S[a]
Naphtha's/Gasoline's	Carcinogenicity/mutagenicity	Benzene[b]
	Specific target organ toxicity	May contain specific components which may be classified for this hazard class in some regions (e.g. n-hexane, toluene, benzene).
	Reproductive effects	May contain specific components which may be classified for this hazard class in some regions (e.g. n-hexane, toluene, xylenes).
Kerosines	------	------
Gasoils	Carcinogenicity	PAH[c]
Heavy fuel oil	Carcinogenicity, acute toxicity	PAH[c], H_2S[a]
Residual aromatic extracts	------	------
Distillate aromatic extracts	Carcinogenicity	PAH[c]
Treated distillate aromatic extracts	Carcinogenicity	PAH[c]
Lubricant base oils	Carcinogenicity	PAH[c]
Petroleum waxes	------	------
Petrolatums	Carcinogenicity	PAH[c]
Foots oils	Carcinogenicity	PAH[c]
Slack waxes	Carcinogenicity	PAH[c]
Bitumens (asphalts) and vacuum residues	------	------
Petroleum cokes	------	------

[a] *Hydrogen sulphide is an acutely toxic gas, commonly found in some groups of petroleum substances. Hydrogen sulphide may collect in the headspace during storage and transport and may therefore present an acute inhalation hazard.*

[b] *Benzene is classified by IARC as a Group 1 carcinogen ("Carcinogenic to humans").*

[c] *Individual polycyclic aromatic hydrocarbons (PAH) are assessed by IARC. Several 3-7 fused-ring PAH are classified to be Group 1 or 2 carcinogens ('Carcinogenic to humans' or 'Probably/possibly carcinogenic to humans').*

[d] *1,3-Butadiene is classified by IARC as a Group 1 carcinogen ('Carcinogenic to humans').*

Classification approach per hazard class

Acute toxicity

23. For the classification for the acute toxicity hazard class, the general principles laid out in Chapter 3.1 of the GHS can be followed. Note that some groups of petroleum substances may contain hydrogen sulphide (for example crude oil, petroleum gases, heavy fuel oil streams, etc.). The levels of hydrogen sulphide are generally below the specified concentration limits that warrant classification. However, hydrogen sulphide may collect in the headspace during storage and transport and adequate warning for this should be in place (see transport regulations).

24. For good product stewardship, if headspace accumulation of hydrogen sulphide is possible, regardless of measured concentrations of hydrogen sulphide in the petroleum substance, it is advised to include appropriate warnings on the Safety Data Sheet (SDS).

Skin irritation

25. For skin irritation the principles laid out in Chapter 3.2 of the GHS can be applied to petroleum substances.

26. Note that petroleum substances (hydrocarbons in general) may cause defatting of the skin, leading to skin dryness and cracking. Although GHS currently does not provide guidance on this specific hazard class, it is advised to include appropriate warnings on the SDS.

Eye irritation

27. For eye irritation the principles laid out in Chapter 3.3 of the GHS can be applied to petroleum substances.

Sensitization

28. For sensitization the principles laid out in Chapter 3.4 of the GHS can be applied to petroleum substances.

Germ cell mutagenicity

29. The first Tier is that data derived from actual testing on the substance or from read-across from similar substances that have been tested, should inform the classification of any substance for germ cell mutagenicity.

30. In the absence of actual data derived from testing or read-across, the next tier (Tier 2) is classification based on specific constituents. Constituents generally accepted as mutagenic in petroleum substances are 1,3-butadiene and benzene. Thus, under Tier 2, if 1,3-butadiene or benzene is present at $< 0.1\%$, no classification for mutagenicity is warranted. However, if 1,3-butadiene or benzene is present at $\geq 0.1\%$, under Tier 3 classification for mutagenicity is advised.

31. Classification as mutagen category 1B is recommended, where:

(a) This is consistent with the GHS bridging principles for Category 1 mutagens (such as benzene and 1,3-butadiene) as laid out in section 3.5.3.3 of the GHS;

(b) There is no evidence from human epidemiology studies that warrant classification as a Category 1A mutagen

Table 3: Germ cell mutagenicity

Tier	Information available	Germ cell mutagenicity classification
1	Genotoxicity data available on stream or there is appropriate read across	Based on the results of the specific study(ies) or read-across
2a	Content of individual Category 1 genotoxicant is < 0.1% [a] and	No classification
2b	Content of individual Category 2 genotoxicant is < 1%	No classification
3a	Content of individual Category 1 genotoxicant is ≥ 0.1% [a]	Category 1B
3b	Content of individual Category 2 genotoxicant is ≥ 1%	Category 2

[a] *For components benzene and butadiene.*

Carcinogenicity

32. The first Tier is that data derived from actual testing on the substance or from read-across from similar substances that have been tested, should inform the classification of any substance for carcinogenicity.

33. In the absence of actual data derived from testing or read-across, the next tier (Tier 2) is classification based on specific constituents. Constituents generally accepted as carcinogenic in petroleum substances are 1,3-butadiene, benzene and 3-7 ring PAHs. For 1,3-butadiene and benzene the bridging principle as laid out in section 3.6.3.3 should be applied. Thus, under Tier 2 if 1,3-butadiene or benzene is present at < 0.1%, no classification for carcinogenicity is warranted. However, if 1,3-butadiene or benzene is present at ≥ 0.1%, under Tier 3 classification for carcinogenicity is advised.

34. For petroleum substances containing PAHs, the carcinogenic potential has been thoroughly investigated. The skin carcinogenic potential is directly related to the level of 3-7 fused-ring PAHs. Examples of tests widely accepted to determine the carcinogenic potential of petroleum substances containing 3-7 fused-ring PAHs are:

(a) skin painting studies in mice (Freeman and McKee, 1993)

(b) modified Ames test E-1687 (Blackburn et al., 1986; ASTM, 2004)

(c) DMSO extractables as determined by IP 346 (Energy Institute, 1992)

35. Note that these tests are limited in their applicability: they should only be used within their domain of validity. For example, IP 346 specifies the determination of polycyclic aromatics (PCA) over the concentration range 1-15 mass% in unused additive free lubricating base oils having an atmospheric boiling point of 300 °C minimum at 5% recovered sample. ASTM E-1687 is applicable to virgin base oils with viscosities of 18 cSt (90 SUS) or greater at 40°C.

36. For an overview of the approach to classify petroleum substances for carcinogenicity, see Table 4.

37. If there are no data or read-across for the petroleum substance (first Tier is not fulfilled) and the concentration of suspected hazardous constituents is greater than the thresholds defined by GHS, then the final tier (Tier 3) is the recommend classification.

38. Classification as carcinogen category 1B is recommended, where:

(a) This is consistent with the GHS bridging principles for Category 1 carcinogens as laid out in section 3.6.3.3 of the GHS, and

(b) There is no evidence from human epidemiology studies that warrant classification as a Category 1A mutagen.

Table 4: Carcinogenicity

Tier	Information available	Carcinogenicity classification
1	Carcinogenicity study available on stream or there is appropriate read-across	Based on the results of the specific study(ies) or read-across
2a	Content of individual Category 1 carcinogens is < 0.1% [a] or Negative results from appropriate test for skin carcinogenic potential	No classification
2b	Content of individual Category 2 carcinogens is < 1%	No classification
3a	Content of individual carcinogens is ≥ 0.1% [1] or Positive results from appropriate test for skin carcinogenic potential	Category 1B
3b	Content of individual Category 2 carcinogens is ≥ 1%	Category 2

[a] *For components benzene and butadiene*

Reprotoxicity

39. The first Tier is that data derived from actual testing on the substance or from read-across from similar substances that have been tested, should inform the classification of any substance for reprotoxicity.

40. In the absence of actual data derived from testing or read-across, the next tier is classification based on the presence of specific constituents. Constituents that may be present in some groups of petroleum substances that are classified as reprotoxicant Category 2 by some regions are for example n-hexane, toluene, and xylenes. Bridging principles as laid out in section 3.7.3.3 apply.

41. If there are no data or read-across for the petroleum substance (first Tier is not fulfilled) and the concentration of suspected hazardous constituents is greater than the thresholds defined by GHS, then the final tier (Tier 3) is to recommend classification.

42. Classification as reprotoxicant Category 2 is recommended, where this is consistent with the GHS bridging principles for Category 2 reprotoxicants as laid out in section 3.7.3.3. of the GHS

Table 5: Toxic to reproduction

Tier	Information available	Reproductive toxicity classification
1	Reproductive toxicity study available on stream or there is appropriate read across	Based on the results of the specific study (ies) or read across
2a	Category 1 reprotoxicant content is < 0.1 %	No classification
2b	Category 2 reprotoxicant content is < 3 %	No classification
3a	Category 1 reprotoxicant content is ≥ 0.1 %	Category 1
3b	Category 2 reprotoxicant content is ≥ 3 %	Category 2

Specific target organ toxicity following single exposure

43. For specific target organ toxicity (STOT) following single exposure the principles as laid out in Chapter 3.8 of the GHS can be applied to petroleum substances. It should be noted that exposure to high levels of certain low boiling point hydrocarbons may cause narcotic effects (included in Category 3: Transient target organ effects). These narcotic effects may occur when exposed to high concentrations of petroleum substances with a relatively low boiling point, for example petroleum gases and naphthas/gasolines.

Specific target organ toxicity following repeated exposure

44. The first Tier is that data derived from actual testing on the substance or from read-across from similar substances that have been tested, should inform the classification of any substance for specific target organ toxicity following repeated exposure.

45. In the absence of actual data derived from testing or read-across, the next tier is classification based on the presence of specific constituents. Constituents that may be present in some groups of petroleum substances that are classified as STOT by some regions are for example n-hexane, toluene, and benzene.

46. The bridging principles are stated in section 3.9.3.3. Based on data for several petroleum substance groups and considering the constituents potentially classified for STOT, it should be noted that the levels at which the STOT effects occur are usually above the levels in which they are found in gasoline. Based on experience the 10% cut-off applies.

47. If there are no data or read-across for the petroleum substance and the concentration of suspected hazardous constituents is greater than the 10% threshold, then Tier 3 is to recommend classification.

48. Classification as specific target organ toxicity following repeated exposure Category 2 is recommended, where this is consistent with the GHS bridging principles for Category 2 STOT following repeated exposure as laid out in section 3.9.3.4 of the GHS

Table 6: Specific target organ toxicity following repeated exposure

Tier	Information available	STOT classification
1	Repeat dose toxicity study available on stream or there is appropriate read-across	Based on the results of the specific study (ies) or read across
2	Target organ toxicant content is < 10 %	No classification
3	Target organ toxicant content is ≥ 10 %	Category 2

Aspiration

49. Petroleum substances may present an aspiration hazard, depending on their viscosity. Clear guidance on classification for this hazard class is laid out in chapter 3.10 of GHS.

Environmental hazards

50. For environmental classification, the principles laid out in section 4.1.2 of GHS can be applied using either test data for the overall substance or read-across to a similar substance. Unlike the approach for classification of several health hazard classes, the use of data on constituents is not appropriate to derive the environmental classification of a petroleum substance. As petroleum substances are complex substances, specific test methods may be required. Specific guidance on environmental tests with complex substances is laid out in Annex 9 of the GHS (A9.1.10 (d) and A9.3.5.10).

Animal testing and animal welfare

51. IPIECA shares the concerns on welfare of experimental animals as described in section 1.3.2.4.6 of the GHS. Therefore this guidance is designed to maximize the use of existing health and environmental data while significantly reducing the overall number of tests needed. The similarity of many petroleum substances allows for their grouping into categories based on chemical composition. Petroleum substances representative of each category are used as test materials to develop health and environmental effects information which can be extrapolated to all the substances in their category. This will avoid unnecessarily testing similar complex substances.

52. In addition, when testing is necessary, IPIECA strongly recommends that the number of laboratory animals used be minimized to the greatest extent possible within the constraints of the regulatory requirements and that studies be conducted according to component authority and OECD guidelines. In addition, where possible laboratories accredited by the Association for Assessment and Accreditation of Laboratory Animal Care (AAALAC) for excellence in animal care should be used.

Information requirements

53. To be able to use the above schemes it requires that the person making the classification has access to the required data for each tier.

54. It is recommended that they also:

(a) Maintain records on the level of substance drivers – when they are used as a basis for classification.

(b) Ensure that the studies used to derive a classification are of a consistent and reliable quality

(c) Have access to the documentation that provides the read across argumentation.

Advantages of the proposed approach

(a) Allows full GHS criteria to be explored.

(b) Full use of available data

(c) Consistent with bridging principles.

(d) Consistent with GHS and represents a consistent industry view

(e) By considering the petroleum substance as a whole and not as a mixture of its constituents, the actual hazard of the petroleum substance should globally be similar regardless of regional differences in the classification of the constituents

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Annex 2

RESPONSES RECEIVED DURING IPIECA WEBCASTS ON THE IPIECA GUIDANCE DOCUMENT

1. Background

IPIECA organised two webcasts in August to provide the Sub-Committee the opportunity to discuss and comment on the Guidance document.

The comments received (both by email as well as verbally) are summarised below. IPIECA has carefully considered all comments received. Below is IPIECA's reply to the comments.

2. Response and IPIECA reply

Comment 1:

At several points in the paper the industry refers to the principle in section 1.3.2.3 of the 'Purple Book'. However, this text refers to the classification of mixtures, not of substances. An alternative approach could be based on section 1.3.3.1.3 of the 'Purple Book', which states: "These definitions [including those of substances and mixtures] should be used to maintain consistency when classifying substances and mixtures in the GHS.

Reply 1:

It is agreed that reference to section 1.3.2.3 is confusing. Reference to section 1.3.2.3 is replaced by reference to section 1.3.2.2, which refers to the classification of substances and mixtures. In addition, reference is made to section 1.2.2.1.2. and the guidance document now includes the definition of 'substance', which applies to petroleum substances.
In the classification approach subsequently reference is made to section 1.3.3.1.3 when no data or read across are available and the classification is based on the constituents.

Comment 2:

The IPIECA approach relies on test data for a sample of a petroleum substance to classify all petroleum substances with that description. However, how does the industry know that their test data can be taken as representative of all petroleum substances meeting that description supplied worldwide, given the inherent variable composition of petroleum substances emphasised in the introductory paras. of the guidance.

Reply 2:

The grouping of petroleum substances has been developed based on the rationale that petroleum substances in one group have similar physico-chemical properties and similar hazards. This grouping has been developed based on available scientific data and has been used for classification purposes in the EU, the EU REACH program, and for the U.S. High Production Volume (HPV) Chemicals Challenge program. After development of the grouping several data gaps have been filled by testing 'worst case' examples from each group. The selection of the substance samples was based on the extremes in a group and on composition (percentage of alkanes, cycloalkanes, alkenes and aromatics). Remaining data gaps

have been identified under HPV and REACH and test proposals have been formulated. The result is a complete and scientifically reliable data set that can be used for classification purposes.

Comment 3:

Following the points above, how can the industry be confident that negative data on a complex substance should override positive test data on ingredients known to be present in the complex substance at concentrations recognised to be significant for the purposes of classification of mixtures containing such ingredients?

Reply 3:

In past years a large database on petroleum substances has been generated. Specific attention has been given to substances that may contain constituents which are classified as hazardous. Overall, the toxicity generally observed with the constituents is not observed in test data on the petroleum stream. Also, most current regulatory frameworks are consistent with the approach to classify substances based on their overall properties rather than upon the presence of specific constituents. Specific examples and/or information will be given in an Annex, with reference to scientific literature. This Annex is under development and will be submitted to the Sub-Committee.

Comment 4:

What are the implications of the industry's proposed approach in terms of additional animal testing and so for animal welfare?

Reply 4:

Animal welfare is an important issue for petroleum industry and was one of the main drivers for the development of the grouping of petroleum substances. By grouping similar petroleum substances and by reading across, animal testing has been kept to a minimum.

In addition, several analytical and in vitro tests have been validated and approved for use in the EU for the classification of petroleum substances for the hazard classes carcinogenicity and mutagenicity. Examples are the analytical method IP 346 and the Modified Ames test.

The industry position towards animal testing and welfare is now included in the guidance document.

Comment 5:

In line with section 1.3.3.2 of the 'Purple Book' we suggest changes need to be made in each relevant section under "Classification approach by endpoint" (paragraphs 23ff) to take into account the possibility that there may be information indicating that lower concentration limits than the default values should be used. This section also allows the option of higher concentration limits than the default values "on occasion" and where there is "conclusive data" demonstrating that the hazard is not evident at this higher level. The industry may wish to consider whether it would ever want to use this option.

Reply 5:

As discussed in the reply to question 3 (vide supra), a large database on petroleum substances exists. Specific attention has been given to substances that may contain constituents which are classified as hazardous. Overall, the toxicity generally observed with the constituents is not observed in test data on

the petroleum stream. Of the tested samples a chemical analysis is available, indicating the level of hazardous constituents in the test sample. This information has been used to set the default values in the guidance document. Specific examples and/or information will be given in an Annex, with reference to scientific literature.

Comment 6:

On a related point of terminology, the heading may be better expressed as "Classification approach by hazard class", as 'endpoint' is not a defined GHS term.

Reply 6:

For consistency with the language used in the 'Purple Book' the terms 'constituent' and 'hazard class' are now used throughout the document.

Comment 7:

Perhaps para 31 should read "Classification as mutagen category 1B is recommended where:" [i.e. 'where' not 'since'] as the subparagraphs (a) and (b) that follow are really criteria which, if met, would lead to such a classification. In any event, data available in the future may not be the same as that available now, so such a change would help to 'future proof' the guidance.

Reply 7:

'Since' has been replaced by 'where'.

Comment 8:

Reference to specific tests which are not specifically adopted by the EPA may cause a scientific review process in the US.

Reply 8:

Analogous to text in the 'Purple Book' reference is now made to 'Examples of tests…'. In addition it should be noted that the tests which are mentioned as examples are adopted by EU regulations and have been used for classification purposes for the past decade.

Comment 9:

In the classification table for carcinogenicity the use of 'and/or' is not clear.

Reply 9:

The text in the table has been rephrased and the 'and/or' has been removed.

Comment 10

Is the testing data globally available?

Reply 10:

Testing data have been summarized by the American Petroleum Institute (Refer to API Robust summaries developed in support of the U.S. HPV Chemicals Challenge program) and CONCAWE (Refer to HEDSETs and Product dossiers; Classification guidance report; Environmental data report) and should be used as the prime sources of information.

Comment 11:

What process is envisioned to keep the tables and recommendations up to date?

Reply 11:

The proposed guidance and recommendations are developed based on a large database. If testing (which is currently summarised in testing proposals for the U.S. HPV Chemicals Challenge program and the EU REACH program) will result in new information requiring the guidance to be updated, IPIECA will update the guidance according to the revision schedule of the 'Purple Book'.

Comment 12:

What quality of data is required on substance composition?

Reply 12:

With respect to data quality, IPIECA would like to refer to section 1.3.2.4 of the 'Purple Book'. This section defines the level of data quality expected; this is also applicable to petroleum substances.

Comment 13:

When would you recommend actual testing rather than read across?

Reply 13:

Reference is made to section 1.3.2.4. of the 'Purple Book'. This section clearly states that GHS itself does not include requirements for testing of substances or mixtures. In addition, for each group of petroleum substances data is available. Evident data gaps are identified under the U.S. HPV Chemicals Challenge program and will be identified under the EU REACH program and testing proposals have been developed to fill remaining gaps. To minimise animal testing, in absence of test data IPIECA recommends to classify the substance based on information on the constituents. In line with the GHS, the IPIECA guidance does not recommend actual testing.
