

Category M 'Xylenes' - Chemical Category Justification

Category definition and its members															
1.1.	Category Definition														
1.1.a.	Category Hypothesis														
<p>The Xylenes category covers streams that have a carbon number distribution that is predominantly C8. All of the streams in this category are almost entirely aromatic, and contain <1% benzene and toluene. Companies importing streams will need to confirm that such streams meet the chemical description and are in domain.</p> <p>It is reasonable to assume that the phys-chem and environmental fate properties of the category members will be very similar due to the small spread of carbon numbers. Environmental effects will behave in a similar manner, acting via narcosis. With regard to mammalian endpoints, category members are liquids of moderate volatility. Inhalation and skin contact therefore represent the primary route of exposure. Xylene isomers and ethylbenzene account for >95% of the total aromatics present and are the key drivers in establishing and assessing health effects. It can therefore be assumed that streams meeting the applicability domain will behave in a similar manner and that use of read-across is valid.</p> <p>For mammalian endpoints, the classification of these streams will be driven by the content of xylene isomers and ethylbenzene, which together account for >95% of the total for all category members. A nota will be developed for member of the category which contain >0.1% of benzene.</p>															
1.1.b.	Applicability domain (AD) of the category														
<p>The category applies to streams with the following PIONA* analysis: > 95% aromatics and a carbon number distribution which is >95% C8. The streams are typically composed of varying percentages of o-xylene, m-xylene, p-xylene and ethyl benzene</p> <p><i>Boiling Point –the streams in this category will boil predominantly in the range of 130-150°C</i></p> <p>Components</p> <p><i>o-xylene, m-xylene and p-xylene : ≥45%</i></p> <p><i>ethylbenzene : ≤55%</i></p> <p><i>styrene : ≤ 25% (dependent on manufacturer)</i></p> <p><i>Benzene: <0.1 - 1% (dependent on manufacturer)</i></p> <p><i>Toluene: <0.1 - 5% (dependent on manufacturer)</i></p> <p><i>*: PIONA refers to a description of the type of hydrocarbons present, paraffins, isoparaffins, olefins, naphthenics and aromatics. It does not refer to a specific type of analysis or determination.</i></p>															
1.2.	Category Members														
<table border="1" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th style="width: 20%; padding: 5px;">CAS Number</th> <th style="width: 30%; padding: 5px;">CAS Description</th> <th style="width: 50%; padding: 5px;">Registered Substance Name</th> </tr> </thead> <tbody> <tr> <td rowspan="5" style="text-align: center; vertical-align: middle; padding: 5px;">1330-20-7</td> <td rowspan="5" style="text-align: center; vertical-align: middle; padding: 5px;">Xylene</td> <td style="text-align: center; padding: 5px;">Xylene</td> </tr> <tr> <td style="text-align: center; padding: 5px;">Xylenes</td> </tr> <tr> <td style="text-align: center; padding: 5px;">Xylenes (incl. META PARA-XYLENE)</td> </tr> <tr> <td style="text-align: center; padding: 5px;">Xylene mixture</td> </tr> <tr> <td style="text-align: center; padding: 5px;">Mixed xylenes</td> </tr> <tr> <td style="text-align: center; vertical-align: middle; padding: 5px;">85536-20-5</td> <td style="text-align: center; vertical-align: middle; padding: 5px;">Solvent naphtha (coal), xylene-styrene cut</td> <td style="text-align: center; vertical-align: middle; padding: 5px;">Solvent naphtha (coal), xylene-styrene cut</td> </tr> </tbody> </table>			CAS Number	CAS Description	Registered Substance Name	1330-20-7	Xylene	Xylene	Xylenes	Xylenes (incl. META PARA-XYLENE)	Xylene mixture	Mixed xylenes	85536-20-5	Solvent naphtha (coal), xylene-styrene cut	Solvent naphtha (coal), xylene-styrene cut
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1330-20-7	Xylene	Xylene													
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85536-20-5	Solvent naphtha (coal), xylene-styrene cut	Solvent naphtha (coal), xylene-styrene cut													

90989-38-1	Aromatic hydrocarbons, C-8	Aromatic hydrocarbons, C8
1.3.	Purity / Impurities	
<p>The substances in this category are UVCB multi-component substances, each containing various proportions of the three xylene isomers and ethylbenzene, and as such are considered to be 100% pure. The term impurity is not relevant to UVCB categories, however, substances will be described using the following:</p> <ul style="list-style-type: none"> ○ <u>Known</u> constituents present at 10% or greater (if any), identified by IUPAC name and EC number/CAS number, indicating typical concentrations and/or concentration ranges; ○ Constituents relevant for hazard classification (if any); ○ Constituents relevant for PBT assessment (if any); <p>Primary marker</p> <p><u>Xylenes</u> (CAS# ortho, 95-47-6; meta, 108-38-3; para, 106-42-3) R 20/21, R36/37/38, R65; R43 and R48/20 possible (reflects current state of LOA self-classification discussion)</p> <p><u>Ethylbenzene</u> (CAS# 100-41-4) R36/37/38, R48/20, R65 (proposed in Annex XV dossier)</p> <p>Tox statements:</p> <p><u>Xylenes</u> are acutely harmful by inhalation and skin contact and present an aspiration hazard. They are also irritating by all routes of exposure. LOA discussion continues with regard to their potential to cause ototoxicity and skin sensitisation.</p> <p><u>Ethylbenzene</u> has a potential to cause ototoxicity, with a proposal (Annex XV dossier) that it be regulated as harmful by inhalation. It is irritating by all routes of exposure and presents an aspiration hazard.</p>		
2.	Category justification	
<p><u>Xylenes</u> is a UVCB category and therefore identification of trends between category members is not appropriate. The stream members are very homogenous with respect to carbon number and hydrocarbon class and the data across the xylenes category is also very homogenous. The physico-chemical properties associated with these types of UVCBs indicated that they comprise a category based on the range of boiling points (from 130°C to 150°C) and will have similar behaviour in the environment. The log Kow ranges from 3.12 to 3.2 and the streams in this category are not considered to be readily biodegradable. The mammalian toxicity information and environmental assessment also indicated that the streams in this category exert similar effects.</p>		
3.	Data matrix	
<p><u>Xylenes</u> is a UVCB category and therefore identification of trends between category members is not appropriate and therefore, according to the ECHA Guidance on information requirements and chemical assessment Chapter R.6, it is not feasible to establish a full data matrix for this category. Consequently, a data set that applies to all members of this category has been developed.</p>		

4. Conclusions per endpoint for C&L, PBT/vPvB and dose descriptor
CLASSIFICATION AND LABELLING
Physico-chemical Hazard Assessment

- **Boiling point** - The measured boiling point of streams in this category ranged from 130°C to 150°C.
- **Partition coefficient** - The streams in this category have partition coefficients ranges from log Kow 3.12 to 3.2.
- **Flash point** - The flash point of streams in this category is 27°C to 32°C. Some streams will have the following classification.

Flashpoint of ≥ 23 °C and initial boiling point > 60 °C.

Flam. Liquid 3 (Hazard statement: H226: Flammable liquid and vapour).

Human Health Hazard Assessment

- **Toxicokinetics** – The marker substances, in their pure form, have well-defined toxicokinetic parameters that have been taken into account during the derivation of their respective DNEL's. The overall DNEL of this category is driven by the DN(M)EL for ethylbenzene.
- **Acute toxicity** – In animal studies xylene isomers, ethylbenzene and mixed xylenes exhibit low acute toxicity by the oral route. Mixed xylene is classified under DSD as harmful by inhalation and the dermal route, although it is not clear why this is the case as the available data indicates that classification is not warranted. In humans critical effects of xylenes are irritation and CNS effects, with the overall NOAEC inhalation for the latter effect being 300 mg/m³.
- **Irritation** – The available data indicate that mixed xylenes (comprising mixed xylene isomers and ethylbenzene) should be considered to be irritating to skin, eyes and the respiratory tract.
- **Sensitisation** – No evidence of sensitisation reported from worker exposure to mixed xylenes (xylene isomers or ethylbenzene).
- **Repeat dose toxicity** – In repeated dose studies, the principle effects of xylenes were adaptive changes in the liver, changes in kidney and liver weights, body weight changes and minimal nephropathy in females.
- **Genetic toxicity** – Available data from both *in vitro* and *in vivo* studies indicate that the individual xylene isomers, ethylbenzene and mixed xylene have no significant genotoxicity. Since a number of negative studies have been reported covering both mutation and cytogenetic endpoints, additional *in vivo* or *in vitro* assays of the genotoxicity potential of xylenes are considered unnecessary.
- **Carcinogenicity** – There is no evidence of carcinogenicity of mixed xylenes following oral administration. No classification of xylene isomers or ethylbenzene is warranted under DSD or CLP.
- **Toxic to reproduction** – Available animal data does not provide clear evidence of an adverse effect on sexual function, fertility or development.

Environmental Hazard Assessment

- **Biodegradation** - Information is available for the xylene isomers the streams in this category are considered to be readily biodegradable.
- **Bioaccumulation** - These streams are also expected to have low potential for bioaccumulation based on a measured BCF of 29 in fish for mixed xylene.
- **Ecotoxicity** – The lowest 96hr LC50 for fish is 2.6mg/l. The lowest 48hr EC50 for Daphnia magna is 3.62mg/l. The lowest 72 or 96hr ErC50 for algae is 3.2mg/l. However, a 24hr EC50 for Daphnia magna of 1mg/l is reported for o-xylene. A second study with o-xylene reports a 48hr EC50 of 3.82mg/l for Daphnia magna. Both these studies with the same test organism are considered valid. None of the LC or EC50 from the acute ecotoxicity tests conducted with the xylene isomers are less than 1mg/L.

Based on the available experimental data and weight of evidence this category should not be classified under the DSD and the CLP regulations.

CONCLUSION FOR PBT

The screening assessment of the available data indicates that the properties of the members of this category do not meet the specific criteria detailed in Annex XIII or do not allow a direct comparison with all the criteria in Annex XIII but nevertheless indicate that the substance would not have these properties and therefore are not considered PBT/vPvB.

CONCLUSION FOR DOSE DESCRIPTOR

Environment: Members of this category are not classified for the environment and are not PBT or vPvB. Therefore derivation of PNECs is not required.

Human Health:

Risk characterization will be based on the premise that a marker substance with a low DN(M)EL present at high concentration in a stream will possess a greater relative hazard potential than a marker substance with a higher DN(M)EL present at the same or lower concentration.

The most hazardous marker substances present are highlighted in the following table:

Marker substance	Indicative concentration (%)	Worker Short-term inhalation		General population inhalation	
		DN(M)EL mg/m ³	Relative hazard potential (max % ÷ DN(M)EL)	DN(M)EL mg/m ³	Relative hazard potential (max % ÷ DN(M)EL)
xylene isomers	≥45	442	0.10	260	0.17
ethylbenzene	<55	289	0.19	174	0.32

Marker substance	Indicative concentration (%)	Inhalation		Dermal		Oral	
		DN(M)EL mg/m ³	Relative hazard potential (max % ÷ DN(M)EL)	DN(M)EL mg/kg bw/d	Relative hazard potential (max % ÷ DN(M)EL)	DN(M)EL mg/kg bw/d	Relative hazard potential (max % ÷ DN(M)EL)
<u>Workers</u>							
ethylbenzene	≤ 55	77	0.71	180	0.31	-	-
xylene isomers	≥ 45	221	0.20	3182	0.014	-	-
<u>General population</u>							
ethylbenzene	≤ 55	14.8	3.72	108	0.51	1.60	34.4
xylene isomers	≥ 45	65.3	0.69	1872	0.024	12.5	3.6

Based on this analysis, demonstration of “safe use” for hazards associated with inhalation, dermal and oral exposure to ethylbenzene will also provide adequate protection for workers against hazards arising from other marker substances.