ANNEX XV RESTRICTION REPORT

PROPOSAL FOR A RESTRICTION

SUBSTANCE NAME: METHANOL

IUPAC NAME: METHANOL

EC NUMBER: 200-659-6

CAS NUMBER: 67-56-1

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Contents

PROPOSAL FOR A RESTRICTION

A. Proposal

A.1 Proposed restriction(s)

Methanol CAS No 67-56-1 EC No 200-659-6	Shall not be placed on the market for supply to the general public: - as a constituent of windshield washing fluids in concentration equal to, or greater than 3.0% by weight, - as an additive to denaturated alcohol (*methylated spirit, brennspiritus*) in concentrations equal to, or greater than 3.0% by weight. Member State may maintain any existing and more stringent restrictions for methanol.

A.1.1 The identity of the substance

Substance name	Methanol
IUPAC name	Methanol
EC number	200-659-6
CAS number	67-56-1
Molecular formula	CH_4O
Purity and impurities	

A.1.2 Scope and conditions of restriction(s)

The proposed restriction covers the supplying to the general public of windshield washing fluids and denaturated alcohol (as reffered to Article 27(1)(a) and 27(1)(b) of the Council Directive 92/83/EECof 19 October 1992 on the harmonization of the structures of excise duties on alcohol and alcoholic beverages) containing methanol in concentration equal to, or greater than 3.0% by weight. Other mixtures containing methanol in concentration equal to or higher than 3.0%, for example glues or paints, supplying to the general public are not included in the scope of the restriction. Industrial use of methanol or methanol-based mixtures is not included in the scope of this restriction. Manufacturing methanol or mixtures containing methanol is either not included in the scope of the restriction.

The proposed restriction does not cover the supplying of methanol and mixtures containing methanol to professional users.

The proposed restriction does not cover the supplying to the general public:
- windshield washing fluids containing methanol in concentration less than 3.0% by weight,
- denaturated alcohol containing methanol in concentration less than 3.0% by weight.

A proposal for an Annex XVII entry is given below:

Methanol CAS No 67-56-1 EC No 200-659-6	Shall not be placed on the market for supply to the general public: – as a constituent of windshield washing fluids in concentration equal to, or greater than 3.0% by weight, – as an additive to denaturated alcohol (*methylated spirit, denaturated alcohol, brennspiritus*) in concentrations equal to, or greater than 3.0% by weight. Member State may maintain any existing and more stringent restrictions for methanol.

No derogations needed.

The proposed restriction should apply 3 months after the amendment of the REACH Annex XVII comes into force.

A.2 Targeting

Causes of poisonings with methanol:

1. Incidental consumption of methanol:
   a) consumption of winter windshield washing fluids, which apart from ethanol contain also methanol in high concentrations, by alcoholics is the most frequent cause of the poisonings, which in many cases are fatal (sources of methanol poisonings – Table D.1-5). Such poisonings take place in particular in the situation where a specific country previously applied a restriction of methanol content in such fluids or where both fluids without methanol and fluids containing methanol are placed on the market,
   b) consumption of methanol added to denaturated alcohol (methylated spirit) by alcoholics is another key cause of the poisonings (source of methanol poisonings – Table D.1-5). Similarly, as in the case of winter windshield washing fluids, the poisonings also take place in particular in the situation where previously there was a ban on adding methanol to denaturated alcohol or where both denaturated alcohol containing methanol and denaturated alcohol without methanol were placed on the market,
   c) fake consumable alcohol to which methanol has been added purchased at legally operating sales network, is another cause of the poisonings – a large number of poisonings in Poland, the Czech Republic and Slovakia in the years 2012 – 2013,
   d) methanol illegally obtained from such sources as chemical reagents or from industrial sources, also is a cause of the poisonings,
   e) methanol which has been inappropriately stored which is used by general public as a fuel in power-boat sports or in model-making activities can also contribute to the poisonings,
   f) winter windshield washing fluids, denaturated alcohol, and anti-freezing fluids can be consumed by children, particularly where they are stored inappropriately, although due to their unpalatable taste, in most cases the consumed quantities are very small and the poisonings are not severe.
2. Conscious consumption of methanol contained in any of the above-listed products for suicidal purposes.

3. Inhalation of methanol vapours or methanol absorption through skin under occupational exposure – OEL for methanol is 260 mg/m^3.

The proposed restriction is namely to eliminate poisonings caused by consumption of methanol contained in high concentrations in winter windshield washing fluids and in denatured alcohol by alcoholics. These products represent the most common cause of severe methanol poisonings, which in many cases turn fatal. Winter windshield washing fluids containing alcohol and denaturated alcohol, which are available in retail, are consumed as a surrogate of consumable alcohol by some alcoholics. This is encouraged by the difference in price between excisable consumable alcohol and the products in which alcohol is not excisable therefore the price of equivalent quantity of alcohol is considerably lower. In Poland for instance the price of half a litre of the cheapest 40% vodka reaches almost 5 EURO, while the price of 5 litres of the cheapest winter windshield washing fluid containing a similar concentration of ethanol, reaches 2 – 3 EURO. Half a litre of 70% denatured alcohol in Poland costs approx. 1 EURO. Similar price differences also occur in other countries. Additives to ethanol contained in such products, which make it unpalatable for a great majority of people, do not deter many alcoholics from their consumption. A relatively limited availability of consumable alcohol contributes to using this easealy available surrogate of ethanol in some countries, such as Finland. The restriction of methanol concentration in these products will eliminate incidental methanol poisonings due to consumption of these products.

The proposed restriction will also prevent some cases of methanol poisoning in children, who sometimes reach for inappropriately stored coloured winter windshield washing fluids, however this is not the main objective of the restriction as the unpalatable taste of these products contributes to the fact that in most cases the consumed quantities are very small and poisonings are not severe.

The restriction will not eliminate suicidal methanol poisonings, however it may partly limit their number. Methanol used as fuel in model-making activities, power-boat sports and in speedway, methanol used as an additive to bio-fuels and illegally obtained methanol can be used for suicidal purposes. The restriction will not eliminate nor most likely reduce the number of potential poisonings with fake consumable alcohol with added methanol and legally placed on the market.

The restriction’s aim is not to protect workers as they are protected by regulations concerning protection of workers against risk posed by effects caused by chemicals, including OEL, which for methanol is 260 mg/m^3.

The restriction’s aim is not to protect consumers using winter windshield washing fluids and denaturated alcohol in accordance with their purpose.

Summing up:

— Target group: the restriction is namely to protect people who chronically abuse alcohol, and who use (consume) winter windshield washing fluids and denaturated alcohol as a surrogate of consumable alcohol. The restriction is not applicable to persons who use these products in accordance with their purpose, nor its aim is to protect the groups that are specifically vulnerable to harmful effects of methanol.
— Scope: subject of the restriction covers the ban on placing on the market of winter windshield washing fluid and denaturated alcohol available to general public, containing methanol in concentration equal to, or greater than 3%.
— Exposure route: application concerns oral route exposure. Inhalation or dermal route exposure to methanol in case of using these products in accordance with their intended purpose is not the subject of the application and is not considered.

A.3 Summary of the justification

A.3.1 Identified hazard and risk

Targeted risks in this restriction dossier are acute poisonings (with high rate of fatal cases) occuring among alcoholics drinking winter windshield washing fluids and denaturated alcohol (methylated spirit) as a substitute of consumable alcohol. The population who faces the risk lives mainly in the northern and central parts of the EU, in the countries were people prefer strong alcohols, but those people do not quit their habits coming into other UE Member States and cases of acute poisonings with denaturated alcohol containing methanol were noted also in Italy among people from countries of Central Europe. No other Community-wide option was found to appropriately manage the targeted risk. The proposed restriction is expected to eliminate methanol poisonings in this population.

When there are no restrictions of methanol content in winter windshield washing fluids and in denaturated alcohol, poisonings with methanol contained in these products constitute the highest rate of methanol poisonings. This is demonstrated by data from Poland and Finland. In Poland, methanol restriction in consumer products ceased to be effective in June 2010. That resulted in a huge number of poisonings with methanol namely contained in winter windshield washing fluids and in denaturated alcohol, which started in December 2011. Reintroduction of the restriction in January 2014 considerably reduced the number of the poisonings, although the complete data will be available in the mid-2015. A similar situation was observed in Finland, where withdrawal of the restriction of methanol content in winter windshield washing fluids in 1994 was accompanied by a considerable increase in the number of poisonings with methanol contained in these fluids, starting in 1996.

A.3.2 Justification that action is required on a Union-wide basis

The justification for the proposed restriction is based on the following evidences:

1. Methanol contained in winter windshield washing fluids and in denaturated alcohol caused considerable number of poisonings in those countries where the concentration of methanol in these products was not restricted.
2. Winter windshield washing fluids are used in all those countries and regions of the EU where temperature at the winter falls below zero centigrade. Denaturated alcohol is widely used across the EU as a cleaning agent or a fuel for touristic cooking appliances.
3. Till the 1st of June 2015 a number of countries, namely Scandinavian countries (apart of Finland) and at least Germany, Austria and Lithuania will still have in place national legislation restricting the sale to general public substances and mixtures classified as toxic or very toxic, according to directive 67/548/EEC and directive 1999/45/EC. This legislation restricts the concentration of methanol in products intended for general public to 10% (T, R39/23/24/25). This restriction, especially as the products proposed to be restricted contain ethanol which protects against the toxic action of methanol, prevents severe poisonings with methanol, and at least prevents fatal poisonings. However this legislation will have to be repelled in June 1, 2015, when the CLP Regulation will be used for classification of

mixtures. Even if these national legislation is rearranged to fit CLP and the restriction will cover mixtures of category 1 – 3 considering the acute toxicity, mixtures containing methanol will be classified as Acute Tox. 3, H301/311/331 when the concentration of methanol will be equal or higher than 30%. Mixtures with so high concentration of methanol when drunk, cause severe poisonings with the high rate of fatal cases.

4. Although the problem of methanol poisonings namely concerns all the countries located in the northern and central parts of Europe and is strictly related to culture of strong alcohols drinking, the free movement of persons across the EU makes inappropriate adoption of restrictive measures concerning methanol only in single Member States. As it was mentioned earlier people drinking products proposed to be restricted do not quit this habit after coming to another country.

A.3.3 Justification that the proposed restriction is the most appropriate Union-wide measure

Existing legislation concerning methanol, namely the child resistant fastening, did not prevent the high number of severe poisonings with methanol in countries where the concentration of methanol in products available to general public was not restricted.

Methanol is not yet identified as a SVHC since it doesn't fulfill the criteria of art. 57 of REACH Regulation. Therefore at present the only way for a risk reduction under REACH is a restriction.

Methanol is not yet classified as CMR and currently no consumer restriction of methanol under article 68 (2) of REACH can be proposed (*article 68 (2) of REACH: For a substance on its own, in a mixture or in an article which meets the criteria for classification as carcinogenic, mutagenic or toxic to reproduction, category 1 or 2, and could be used by consumers and for which restrictions to consumer use are proposed by the Commission, Annex XVII shall be amended in accordance with the procedure referred to in Article 133(4). Articles 69 to 73 shall not apply*). Currently the only way to propose a restriction of methanol for consumers is preparing a restriction dossier which conforms to the requirements of Annex XV.

Without any restriction of concentration of methanol in winter windshield washing fluids and denaturated alcohol available for consumers it must be expected that the number of new incidences of poisoning caused by ingestion of mixtures containing high concentration of methanol in some EU Member States will remain at the high level seen today. The change in classification of mixtures containing methanol introduced by CLP Regulation since June 1, 2015 may cause incidents of methanol poisonings also in countries where severe poisonings were not noted so far.

Diminishing the concentration of methanol in the products proposed to be restricted and its replacement by other alternatives (ethanol) seems to be economically and technically feasible. Consequently, the actors should be capable in practice to comply with the restriction proposal.

The proposed restriction is understandable to all affected parties.

Given the fact that analytical methods to measure methanol concentration in mixtures or as a constituents of another substances are already available, this restriction is also expected to be manageable for the enforcement.

Results of the implementation of this restriction may be monitored by collecting information about accidents/incidents occurring to consumers as a result of exposure to windshield washing fluids and denaturated alcohol containing methanol from poison control centers and by measuring the methanol concentration in the above mentioned mixtures which are available for consumers. Indicators such as number of mixtures (windshield washing fluids and denaturated alcohol) available for consumers which have a methanol concentration above 3.0% w/w" or "number of notifications to poison control centers about accidents/incidents occurring to consumers as a result of exposure to windshield washing fluids and denaturated alcohol containing methanol" can be used to assess the effects of the restriction proposal.

B. Information on hazard and risk

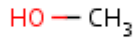
B.1 Identity of the substance(s) and physical and chemical properties

The information provided under this section is taken from registration dossiers.
Registration number of methanol: 01-2119433307-44-XXXX.

B.1.1 Name and other identifiers of the substance

Table B.1-1 Name and other identifiers of methanol

Identifier	Value
EC number	200-659-6
EC name	methanol
CAS number	67-56-1
CAS name	Methanol
Synonyms	Methanol Methanol (8CI, 9CI) Methyl alcohol Methyl hydroxide Monohydroxymethane Carbinol MeOH Methanol (8Cl, 9Cl) methanol Methyl Alcohol Renewable Methanol methyl alcohol EUROALIMENT 40 Methanol for technical use AZEOsolve technical methanol industrial methanol 12120490 Methanol Methanol technical Phase I REACH Kandidat CHINT: Methanol methanol, bio- methanol Methanol Stripping CR12 Phase II REACH Kandidat Dow Corning Raw Material No. 2237296 METHYL ALCOHOL 99.85%, METHANOL (EUROPE)
Trade names	
index number in Annex VI of CLP	603-001-00-X
Molecular formula	CH_4O
Molecular weight	32.0419

Structural formula	

B.1.2 Composition of the substance

Name: methanol

Degree of purity: > 80.0 — 100.0 % (w/w)

Table B.1-1. Constituents

Constituent	Typical concentration	Concentration range
methanol EC no.: 200-659-6	99.0% (w/w)	80.0 — 100.0% (w/w)

B.1.3 Physicochemical properties

Methanol is the simplest alcohol. It is a light, volatile, colorless, flammable liquid with a distinctive odour very similar to, but slightly sweeter than, ethanol (drinking alcohol). At a room temperature, it is a polar liquid.

Table B.1-2 Physicochemical properties

Property	Value	Remarks
Physical state at 20°C and 101.3 kPa	Methanol is a clear, colourless liquid that has an alcoholic odour	Discussion and the value used for Chemical Safety Assessment (CSA) reported in the endpoint summary
Melting/freezing point	-97.8 °C	
Boiling point	64.7 °C	
Vapour pressure	169.27 hPa at 25°C	
Surface tension	-	Based on chemical structure, no surface activity is predicted.
Water solubility	>= 1000 g/L	Completly miscible in water at 20°C.
Partition coefficient n-octanol/water (log value)	log Kow=-0.77	
Flash point	9.7 °C at 101325 Pa	
Flammability	highly flammable	The flammability is deduced from flash point and boiling point, so the substance is a highly flammable liquid. Based on chemical structure pyrophoric properties and flammability in contact with

		water are not to be expected.
Explosive properties	non explosive	There are no chemical groups associated with explosive properties present in the molecule.
Explosive limits in air (% by volume)	Lower 5.5 Upper 44	
Self ignition temperature	455°C at 101325 Pa	
Oxidising properties	no oxidising properties	Substance is incapable of reacting exothermically with combustible materials.
Granulometry	not applicable	Substance is marketed or used in a non solid or granular form.
Stability in organic solvents and identity of relevant degradation products	-	The stability of the substance is not considered as critical.
Dissociation constant	-	The substance does not contain any ionic structure under enviromental conditions.
Viscosity	0.54 mPa · s (dynamic)	
Auto flammability	455 °C at 101325 Pa	
Reactivity towards container material	-	-
Thermal stability	-	-
Methanol volatilization half-life (model river)	5.3 days	
Methanol atmospheric half-life	8.4 days	

B.1.4 Justification for grouping

Grouping is not relevant for this proposal.

B.2 Manufacture and uses

B.2.1 Manufacture, import and export of a substance

According to information provided by ECHA, methanol is manufactured/imported in the total tonnage band of 10 000 000 - 100 000 000 tonnes per annum. According to Methanol Institute (2012) the world-wide yearly use of methanol exceeds 90 000 000 tonnes. The consumption of methanol is not expected to increase significantly in Europe, however, a massive increase in production and consumption of methanol is expected to happen in China (increase of approximately 220% from 2010 – 2017) (Survey of methanol; Danish Ministry of Environment). The Chinese growth is particularly in new areas like fuel (as blending or as DME) and MTO (methanol to olefins).

The methanol production process converts a gaseous mixture of carbon oxides and hydrogen, derived in a steam reforming of a hydrocarbon feedstock, typically natural gas, into methanol. This mixture is compressed and then reacted over a metal oxide catalyst to give methanol and by-products, according to the following reactions.

$CO + 2\ H_2$ <-> CH_3OH

$CO_2 + 3\ H_2$ <-> $CH_3OH + H_2O$.

The pure product is obtained by fractional distillation. All process steps are performed in closed systems.

According to registration dossiers methanol is also produced as by-product from the manufacture of polymers and other substances.
On the basis of submitted for the first REACH registration deadline dossiers more than 35 production sites were identified in Europe.

B.2.2 Uses

According to the Methanol Institute (2012) methanol has been one of the world's most widely used industrial chemicals since 1800's. From paints and plastic, furniture and carpenting, to car parts and windshield washing fluid, methanol is a chemical building block used in making hundreds of products used in daily life. Methanol is also an emerging energy fuel for running cars, trucks, buses and electric power turbines. According to SPIN (the Nordic Database on Substances in Preparations in the Nordic Countries) methanol is also categorized under the label "very wide range of applications".

Technical function of the substance during formulation of chemical products:

- Solvents
- Intermediates
- Anti-freezing agents
- Laboratory chemicals
- Fuels and fuel additives
- Process regulators, other than polymerisation or vulcanisation processes
- Process regulators, used in vulcanisation or polymerisation processes
- Washing agent
- Stabilisers
- Corrosion inhibitors and anti-scaling agents
- Processing aid, not otherwise listed

B.2.3 Uses advised against by the registrants

No information available

B.3 Classification and labelling

B.3.1 Classification and labelling in Annex VI of Regulation (EC) No 1272/2008 (CLP Regulation)

Methanol is listed by Index number 603-001-00-X in Annex VI, Part 3, Table 3.1 and Table 3.2 (list of harmonised classification and labelling of hazardous substances) of Regulation (EC) No 1272/2008 as follows:

Table B.3-1 Classification and labelling according to CLP

Index No	International Chemical Identification	Classification		Labelling			Specific Conc. Limits, M-factors
		Hazard Class and Category Code	Hazard statement Codes	Pictogram, Signal Word Code	Hazard statement Codes	Suppl. Hazard statement Code(s)	
603-001-00-X	Methanol	Flam. Liq. 2 Acute Tox. 3* Acute Tox. 3* Acute Tox. 3* STOT SE 1	H225 H301 H311 H331 H370**	GHS02 GHS06 GHS08 Dgr	H225 H301 H311 H331 H370		STOT SE 1; H370: C ≥ 10% STOT SE 2; H371: 3% ≤ C < 10%

* For certain hazard classes, including acute toxicity and STOT repeated exposure, the classification according to the criteria in Directive 67/548/EEC does not correspond directly to the classification in a hazard class and category under this Regulation. In these cases the classification in this Annex shall be considered as a minimum classification.
** The classification under 67/548/EEC indicating the route of exposure has been translated into the corresponding class and category according to this Regulation, but with a general hazard statement not specifying the route of exposure as the necessary information is not available.

Table B.3-2 Classification and labelling according to Directive 67/548/EEC.

Index No	International Chemical Identification	Classification	Labelling	Concentration limits
603-001-00-X	Methanol	F; R11 T; R23/24/25-39/23/ 24/25	F; T R: 11-23/24/25-39/23/24/25 S: (1/2-)7-16-36/37-45	T; R23/24/25: C ≥ 20 % Xn; R20/21/22: 3 % ≤ C < 20 % T; R39/23/24/25: C ≥ 10 % Xn; R68/20/21/22: 3 % ≤ C < 10 %

The special rules on packaging defined in Annex II, part 3, section 3.1.1.3 of the CLP Regulation apply to methanol. The packaging of whatever capacity supplied to general public must be fitted with a child-resistant fastening if the concentration of methanol in a substance or a mixture is ≥ 3.0%.
In the homepage of ECHA (http://echa.europa.eu/registry-of-submitted-harmonised-classification-and-labelling-intentions/-/substance/753/search/+/del/20/col/SUBMISSIONDATEROI/type/desc/pre/2/view)
it can be seen, that Italy has recently proposed the following additional classification of methanol:
- proposed classification according to Regulation (EC) No 1272/2008 (CLP): Reproductive toxicity (Repr. 1B – H360D).

B.3.2 Classification and labelling in classification and labelling inventory/

Industry's self classification(s) and labelling

Methanol was notified in the C&L Inventory by a total of 4129 notifiers by 7th of January, 2015 (Source: http://echa.europa.eu/information-on-chemicals/cl-inventory-database). The existing harmonised classification was notified by the majority of the notifiers. However, many of the notified harmonised classifications (1527) did not include the SCLs for STOT SE 1; H370. This might be due to the fact that the SCL given according to the Dangerous Substance Directive (DSD) for T; R39/23/24/25 is in fact the general concentration limit (GCL) for STOT SE 1 in CLP. However for STOT SE 2 the situation is slightly different: in the DSD the SCLs for Xn; R68/20/21/22 were 3% ≤ C < 10% which do not exactly correspond with the GCLs of CLP (1% ≤ C < 10 %). Furthermore, many notifiers had included affected organs in the hazard statement H370. The organs mentioned were

- optic nerve
- central nervous system
- eyes
- skin
- kidneys
- liver
- heart
- respiratory tract
- lungs
- GI tract
- visual organs
- brain

In addition to the harmonized classification, methanol was also classified as Eye Irrit. 2; H319 (441 notifiers), as Skin Corr. 1A; H314 (1 notifier); as Skin Irrit. 2; H315 (4 notifiers), as Repr. 1B; H360 (3 notifiers), as Repr. 2; H361 (1 notifier), as Carc. 2; H351 (2 notifiers), as STOT SE 3; H335 (1 notifier), as STOT SE 3; H336 (1 notifier), as Aquatic Acute 1; H400 (1 notifier), as Aquatic Chronic 1; H410 (1 notifier) and as Ox. Liq. 1; H271 (1 notifier).

B.4 Environmental fate properties

Not relevant for this proposal.

B.5 Human health hazard assessment

B.5.1 Toxicokinetics (absorption, metabolism, distribution and elimination)

B.5.1.1. Non-human information

The results of studies on absorption, metabolism, distribution and elimination are summarised in the following table:

Table B.5-1. Studies on absorption, metabolism, distribution and elimination

Method	Results	Remarks	Reference
mouse (CB6F1) male/female intraperitoneal Exposure regime: single ip injection Doses/conc.: 5, 100 mg/kg bw (specific activities 0.06 and 0.002 µCi/µmol, respectively) Comparison of formate elimination in wildtype and FDH-deficient (NEUT2) mice after formate application. Determination of LD_{50} for methanol in wildtype, heterozygous and homozygous NEUT2 mice.	Metabolites identified: yes Details on metabolites: formate	2 (reliable with restrictions) supporting study experimental result **Test material (EC name): methanol**	Cook, R.J. et al. (2001)
rat (Long-Evans) female inhalation: vapour Exposure regime: 1.) 3 consecutive days, 6 h/d 2.) GD6 to PND 21 (dams and offspring) Doses/conc.: 5.98 mg/l (corresponding to 4500 ppm) Non-pregnant rats were exposed to methanol vapors for three consecutive days and their blood methanol levels were determined. Pregnant rats were exposed to methanol vapors from GD6 to PND 21 and methanol blood levels in dams and offspring were determined.	Metabolites identified: no Details on metabolites: not determined	1 (reliable without restriction) supporting study experimental result **Test material (EC name): methanol**	Stern, S. et al. (1996a)
mouse (C57BL/6Csa (catalase wildtype) and C57BL/6Csb (catalase deficient)) male oral: gavage Exposure regime: single application Doses/conc.: 2000, 4000,	Metabolites identified: yes Details on metabolites: Formate levels in blood and urine were found to be elevated.	2 (reliable with restrictions) supporting study experimental result **Test material (EC name): methanol**	Smith, E.N. and Taylor, R.T. (1982)

5000, 6000, 7000, 8000, 9000, 10000 mg/kg bw Comparative toxicity and metabolic study in folate-deficient and -sufficient wildtype and respective catalase-deficient mice.			
rat (Fischer 344) male intraperitoneal Exposure regime: single application Doses/conc.: 25, 125, 600, 3000 mg/kg bw (unlabeled and 14C-labeled methanol, respectively) Male rats received unlabeled and 14C-labeled methanol per i.p. injection, respectively, to investigate metabolism and absorption/excretion. Blood was collected after various time points and investigated for biochemical parameters; for determination of absorption/excretion radioactivity in blood, urine, feces and exhaled air was determined.	Metabolites identified: yes Details on metabolites: Formic acid	2 (reliable with restrictions) supporting study experimental result **Test material (EC name): methanol**	New Energy Development Organization (1987)
monkey (Macaca fascicularis) male intraperitoneal Exposure regime: single application Doses/conc.: 25, 125, 600, 3000 mg/kg bw (unlabeled and 14C-labeled methanol, respectively) Male monkeys received unlabeled and 14C-labeled methanol per i.p. injection, respectively, to investigate metabolism and absorption/excretion. Blood was collected after various time points and investigated for biochemical parameters;	Metabolites identified: yes Details on metabolites: Formic acid	2 (reliable with restrictions) supporting study experimental result **Test material (EC name): methanol**	New Energy Development Organization (1987)

for determination of absorption/excretion radioactivity in blood, urine, feces and exhaled air was determined.			
monkey (Macaca fascicularis) male/female nasogastric tube Exposure regime: single treatment Doses/conc.: 2000 mg/kg bw: folate-deficient; 3000 mg/kg bw: normal folate status Analysis of metabolite concentrations in various body fluids and organs after methanol intoxication of monkeys. The metabolite concentrations in normal animals were compared to folate-deficient animals.	Metabolites identified: yes Details on metabolites: formaldehyde, formate	2 (reliable with restrictions) supporting study experimental result **Test material (EC name): methanol**	McMartin, K. et al. (1979)
monkey (Macaca fascicularis) male/female methanol via nasogastric tube, formate via intravenous infusion Exposure regime: single administrationof either formate or ethanol Doses/conc.: formate: 1, 2.5, 5, 10 mmol/kg; methanol: 3000 mg/kg folate-deficiency: formate: 2.5 mmol/kg; methanol: 500 mg/kg Clay et al.: 50, 72, 200, 255, 470 mg/kg formate i.v. The metabolism of formate and methanol was studied in monkeys after i.v infusion of radiolabeled formate or gavage of radiolabeled methanol via a nasogastric tube. Additionally, the influence of folate-deficiency on their metabolism was	Metabolites identified: yes Details on metabolites: formate	2 (reliable with restrictions) weight of evidence experimental result **Test material (EC name): methanol**	McMartin, K.E. et al. (1977) Clay, K.L. et al. (1975)

investigated.			

B.5.1.2. Human information

The exposure-related observations in humans are summarised in the following table:

Table B.5-2. Exposure-related observations on basic toxicokinetics and/or dermal absorption in humans

Method	Results	Remarks	Reference
Study type: cohort study (prospective) Details on study design: HYPOTHESIS TESTED (if cohort or case control study): exposure-excretion relationship and possible health effects of exposure to methanol vapour were studied STUDY POPULATION 33 exposed workers during the second half of 2 working weeks COMPARISON POPULATION Urinary methanol concentrations were also determined in 91 nonexposed subjects (Kawai et al., 1991). The geometric mean value for methanol in urine samples from the latter was < 2 mg/L. HEALTH EFFECTS STUDIED - photophobia; eye examination (retinal changes; pupil reflex; mydriasis); blurred vision; headache; nasal irritation OTHER DESCRIPTIVE INFORMATION ABOUT STUDY: - methanol levels in urine samples; formate excretion in urine samples Endpoint addressed: repeated dose toxicity: inhalation Endpoint addressed: basic toxicokinetics	OBSERVATIONS: - blurred vision and headache during or after work - no photophobia - retinal changes - retarded pupil reflex and one mild mydriasis - dimmed vision and nasal irritation were the most frequent symptoms complained during work	2 (reliable with restrictions) weight of evidence **Test material (EC name): methanol**	Kawai, T. et al. (1991) Yasugi, T. et al. (1992)
Study type: Experimental study of dermal exposure to methanol in human volunteers estimating percutaneous absorption. Details on study design:	The pre-exposure methanol concentration in blood was 1.7 mg/L, and subjects had statistically different mean concentrations. The maximum methanol concentration in blood was reached 1.9 h after exposure; this is comparable to that	2 (reliable with restrictions) supporting study **Test material**	Batterman, S.A. and Franzblau, A. (1997) Franzblau, A. and Batterman,

Method	Results	Remarks	Reference
Experimental study of dermal exposure to methanol in human volunteers estimating percutaneous absorption. 12 volunteers were exposed to methanol via one hand for durations of 0 to 16 min in a total of 65 sessions. The concentration in blood was measured and delivery rate from skin to blood was determined. Endpoint addressed: dermal absorption Endpoint addressed: basic toxicokinetics	reached following inhalational exposure at a methanol concentration of 200 ppm. Delivery rate from skin into blood lagged exposure by 0.5 h, and methanol continued to enter the systemic circulation for 4 h following exposure. The mean derived absorption rate was 8.1 ± 3.7 mg/cm²/h (corresponding to 0.135 ± 0.062 mg/cm²/min). Full exposure of one hand for 16 min resulted in a blood level equivalent to that reached after inhalation of 400 ml/m³ for one 8-h working shift with a maximal blood level of some 11 mg/L (corrected for background value).	**(EC name): methanol**	S.A (1995) DFG Commission for the Investigation of Health Hazards of Chemical (1999)
Study type: Two patients with extremely high blood methanol concentrations (260 and 282 mg/dl) were successfully treated using pharmacokinetic dosing of ethanol, hemodialysis and supportive measures. A few details on dosage regimen were reported. Details on study design: Two patients with extremely high blood methanol concentrations (260 and 282 mg/dl) were successfully treated using pharmacokinetic dosing of ethanol, hemodialysis and supportive measures. Endpoint addressed: basic toxicokinetics	Both patients recovered completely without residual ophthalmologic deficits. Early hemodialysis and inhibition of methanol metabolism with effective ethanol concentrations were attributed to the patients' full recovery. Methanol elimination was enhanced by hemodialysis as evidenced by a decrease in half-life from eight to two and a half hours. Methanol dialysance was 98 mL/min. A dosage regimen for ethanol was devised, utilizing dose-dependent pharmacokinetic parameters and the ethanol dialysance (100 to 120 mL/min) from these two patients. An ethanol loading dose of 0.6 g/kg should be administered to an adult with an acute methanol ingestion. This dose will produce a blood ethanol concentration of approximately 100 mg/dL which can be maintained by an ethanol infusion of 66 mg/kg/hour for nondrinkers to 154 mg/kg/hour for chronic ethanol drinkers. Hemodialysis should be initiated if the blood methanol concentration is greater than 50 mg/dL. If hemodialysis is initiated, the ethanol infusion should be increased by 7.2 g/hour.	2 (reliable with restrictions) supporting study **Test material (EC name): methanol**	McCoy, H.C. et al. (1979)
Study type: Investigation of methanol blood and urine concentration in 4 volunteers who had ingested small amounts of methanol. Details on study design: Methanol blood and urine concentrations were investigated in 4 volunteers who had ingested small amounts of methanol (0.2 ml hourly for 6 hours, 0.5 ml hourly in one of	The methanol urine concentration did not exceed 8.0 µg/ml. It was estimated, that at a MAC value of 200 ppm with a total 8 h ventilatory volume of 10 m^3 and assuming complete absorption and no exhalation 2.6 g methanol would be absorbed. The highest urinary concentration attained by oral ingestion of this amount of methanol at a rate of 0.5 ml hourly in one of the subjects was 17.6 µg/ml.	2 (reliable with restrictions) supporting study **Test material (EC name): methanol**	Ferry, D. et al. (1980)

Method	Results	Remarks	Reference
the volunteers). Endpoint addressed: basic toxicokinetics			
Study type: Comparison of toxikokinetic of methanol formation from aspartame in adults and infants. Details on study design: Blood methanol concentrations were measured in 24 1-year-old infants administered aspartame, a dipeptide methyl ester sweetener. The doses studied included a dose projected to be the 99th percentile of daily ingestion for adults (34 mg/kg body weight), a very high use dose (50 mg/kg body weight) and a dose considered to be in the abuse range (100 mg/kg body weight). Blood methanol values in infants were compared to values observed previously in adults administered equivalent doses of aspartame. Endpoint addressed: basic toxicokinetics	Methanol concentrations were below the level of detection (0.35 mg/dL) in the blood of 10 infants administered aspartame at 34 mg/kg body weight, but were significantly elevated (P less than or equal to 0.05) after ingestion of aspartame at 50 and 100 mg/kg body weight. At the latter doses, mean peak blood methanol concentrations and the area under the blood methanol concentration-time curve increased in proportion to dose. Mean (± SEM) peak blood methanol concentration was 0.30 ± 0.10 mg/100 mL at a 50 mg/kg body weight aspartame dose (n = 6) and 1.02 ± 0.28 mg/mL at the 100 mg/kg body weight dose (n = 8). Blood methanol values in infants were similar to those observed in normal adults	2 (reliable with restrictions) supporting study **Test material (Common name): aspartame**	Stegink, L.D. et al. (1983)
Study type: Information on methanol concentrations in human blood after aspartame consumption. Details on study design: Aspartame was administered to humans at a single dose of 500 mg per individual in 100 ml tap water. Four adult volunteers fasted for 8 h and avoided alcohol, fruits, fruit drinks or vegetable for 24 h. Blood methanol was measured at 0, 30, 45, 60, 90, 120, and 180 min following ingestion. The dose of aspartame was representative of the daily average sugar consumption and corresonded to about 50 mg methanol = 0.7 - 0.8 mg/kg. Endpoint addressed: basic toxicokinetics	Baseline blood methanol: 1.4 - 2.6 mg/L. Mean incremental increase (maximum after 45 min): ≤ 1 mg/L Aspartame consumption by adults at a dose equivalent to the daily intake of sugar results in methanol blood levels similar to endogenous levels, in particular when divided in smaller fractions over the day.	4 (not assignable) supporting study **Test material (Common name): aspartame**	Davoli, E. et al. (1986) National Toxicology Program (2003)
Study type: Absorption of inhaled methanol was analysed. Details on study design: During	Methanol was rapidly absorbed by inhalation. Serum methanol conc. were increased by more than fourfold at the end of exposure period, as were urinary	2 (reliable with restrictions) supporting study	Osterloh, J. D. et al. (1996)

Method	Results	Remarks	Reference
a randomized double-blind study of the potential neurobehavioral effects of inhaled methanol at 0.27 mg/L (corresponding to 200 ppm) for 4 hours, methanol analysis was performed. Endpoint addressed: basic toxicokinetics	methanol excretion rates, although formate concentration were not increased over background concentration. The overall elimation half-life was 3.2 + 2.3 h.	**Test material (EC name): methanol**	
Study type: Methanol absorption rate through the human skin has been examined by the use of a modified direct method. The excretion of unchanged methanol with urine and exhaled air, after the absorption through the skin and administration "per os" of identical doses, were also examined . Details on study design: The experiments were carried out on volunteers. A modification of the direct method has been applied to estimate liquid methanol absorption through the skin. The absorbed dose was calculated from the difference between the amount applied to the surface of the skin and the amount left after the exposure time (15 to 60 min). The amounts of methanol, 0.19 -0.21 cm^3, applied on the surface of the skin equal to the area of the applicator (11.2cm^2) were the smallest possible. A total of 22 experiments in six subjects have been carried out and the absorption rate was calculated in mg/cm^2/min. In two subsequent experiments the absorbed amount of methanol was calculated on the basis of the known surface on the skin of the hand (435-445 cm^2) immersed in liquid methanol and at a known absorption rate determined previously. The exposure time was always 20 min. The quantities ranged from 1.67-1.71 g making possible the quantitative determination of methanol in urine and in exhaled air after exposure.	Methanol absorption rate values through human skin (foremarm, 15-60 min.) range from 0.131 to 0.241 mg/cm^2/min, with an average value of 0.192 mg/cm^2/min. The absorbed amounts were 22 mg after 15 min exposure and ranged to 130 mg after 60 min of exposure. The excretion of unchanged methanol exhaled air, after absorption through skin and administration "per os" amounted to 271 mg (16.2 %) and 360 mg (21.6 %) of the absorbed dose (1.67 g), respectively. The amounts excreted with urine amounted to 2 and 5.73 mg, respectively. It was estimated, that exposure of one hand to liquid methanol for only 2 min. would lead to the absorption of as much methanol (170 mg), as would be taken up by the lungs from an 8 h exposure to MAC of 50 mg/m^3 (38 ml/m^3).	2 (reliable with restrictions) supporting study **Test material (EC name): methanol**	Dutkiewicz, B. et al. (1980) DFG Commission for the Investigation of Health Hazards of Chemical (1999)

Method	Results	Remarks	Reference
The exhaled air samples were collected in amounts of 5-10 dm^3, in the periods of time: 0, 0.5, 1.0, 1.5, 2.0, 2.5, 4.0 and 5.0 h after the termination of exposure. Urine samples were collected every hour for 8 h after the termination of exposure. Six experiments (3 subjects) were carried out on oral methanol administration, and collection of exhaled air and urine samples were performed as given above. The applied doses were always 1.67 g. A spectrophotometric method was employed for quantitative determination of methanol in water solutions and urine destillates. The background concentrations found in urine before exposure amounted to 1.9-2.3 mg/dm^3. Endpoint addressed: dermal absorption Endpoint addressed: basic toxicokinetics			
Study type: Toxikokinetics of blood methanol formation from aspartame in adults. Details on study design: Blood methanol concentrations were measured in 30 normal adult subjects administered aspartame, a dipeptide methyl ester. The doses studied included the 99th percentile of projected daily ingestion (34 mg/kg body weight) and three doses considered to be in the abuse range (100, 150, and 200 mg/kg body weight). Additionally, blood formate analyses were carried out in the 6 subjects who ingested aspartame at 200 mg/kg, since recent studies indicate that the toxic effects of methanol are due to formate accumulation. Endpoint addressed: basic toxicokinetics	Methanol concentrations were below the level of detection (0.4 mg/dL) in the blood of the 12 normal subjects who ingested aspartame at 34 mg/kg. They were significantly elevated (p less than or equal to 0.001) after ingestion of each abuse dose, with the mean peak blood methanol concentrations and the areas under the blood methanol concentration-time curve increasing in proportion to dose. Mean (±SD) peak blood methanol concentrations were 1.27 ± 0.48 mg/dL at the 100 mg/kg dose, 2.14 ± 0.35 mg/dL at the 150 mg/kg dose, and 2.58 ± 0.78 mg/dL at the 200 mg/kg dose. Blood methanol concentrations returned to predosing levels by 8 h after administration of the 100 mg/kg dose. Methanol was still detected in the blood 8 h after the subjects had ingested aspartame at 150 or 200 mg/kg. Blood formate analyses carried out in the 6 subjects who ingested aspartame at 200 mg/kg showed no significant increase over predosing concentrations. No changes were noted in any of the blood chemistry profile parameters measured 24 h after aspartame ingestion, compared to values noted before administration.	2 (reliable with restrictions) supporting study **Test material (Common name): aspartame**	Stegink, L.D. et al. (1981)

Method	Results	Remarks	Reference
	Similarly, no differences were noted in ophthalmologic examinations carried out before and after aspartame loading.		
Study type: Information on methanol and formate blood concentration in humans after methanol exposure via inhalation. Details on study design: Six human volunteers (from 29 - 55 years) were subjected to a controled diet-regimen (without obvious methanol-delivering nutrition and additives) throughout the study and exposed to 0.27 mg/L (corresponding to 200 ppm) methanol for 6 hours. Five individuals were each tested at rest or at light exercise [Lee et al., 1992]. Endpoint addressed: basic toxicokinetics	Blood methanol concentrations increased from 1.8 µg/mL (mean endogenous level) to 7.0 µg/mL at rest and to 8.1 µg/mL under light exercise (increase in mean pulmonary ventilation at a factor of about 2.7 from average 10.5 to 26.6 L/min and increase in respiratory rate at a factor of about 1.7 from 11.2 to 18.6 breathes/min) [Lee et al., 1992]. Blood formate levels did not increase.	2 (reliable with restrictions) supporting study **Test material (EC name): methanol**	D´Alessandro, A. et al. (1994) Lee, E.W. et al. (1992) Medinsky, M.A. and Dorman, D.C. (1995)
Study type: Twenty persons occupationally exposed to methanol were examined according to their methanol levels in blood and urine and their formic acid excretion. Details on study design: The methanol concentration in blood and urine and and the concentration of its metabolite formic acid were examined in a group of 20 male workers (age 24 to 62 years, mean 46 years) occupationally exposed to methanol. 26 males who had no occupational contact with any chemicals, especially not methanol, served as controls. Parallel to the collection of bloood and urine samples air samples were taken every 30 min at a representative place. Methanol concentrations in air, blood and urine, and formic acid concentrations in blood were determined by gas chromatography. Endpoint addressed: basic toxicokinetics	The geometric mean of methanol concentrations in the air at the working area was 93 mL/m³ over an 8-h shift (arithmetic mean value 111±68 mL/m³). Exposure to this methanol concentration over 8 h increased blood methanol concentrations up to a mean value of 8.9±14.7 mg/L, in contrast to unexposed persons, whose methanol blood levels did not exceed the detection limit. Individual concentrations scattered within a broad range (<0.6-60.1 mg/L). Methanol concentrations in the urinary samples reached an average level of 21.8±20.0 mg/L during the second half of the exposure, urinary formic acid levels scattered in a broad range for both groups. In contrast to unexposed persons (nearly 40 % of their levels were below 6.5 mg/L and all of them below 15 mg/L), the concentrations in the exposed group ranged up to 121 mg/L (mean controls 12.7±11.7 vs. 29.9±28.6 mg/L exposed). The urinary methanol concentrations of the exposed persons correlated significantly with their methanol blood levels. Compared to methanol urinary level, the sensitivity of formic acid concentrations in urine as a parameter for biological monitoring is substantially reduced. Only 15% of of the urinary	2 (reliable with restrictions) supporting study **Test material (EC name): methanol**	Heinrich, R. and Angerer, J. (1982)

Method	Results	Remarks	Reference
	levels of the exposed persons lie above the upper limit of the normal level. Based on these results, a rough estimate of about 40 mg/L methanol content in urine for a corresponding 8-h exposure at 200 mL/m³ can be made.		
Study type: Determination of the correlation between occupational methanol exposure and formation of urinary formic acid. Details on study design: Fourteen workers exposed to methanol (1 female and 13 males), 41±10 (±SD) years of age, with 10±5 (±SD) years in their current occupation, participated in the study. They worked in 3 different plants. In order to have a reliable estimation of exposure to methanol, for 3 days the frequency and length of every task were recorded, personal exposures were evaluated by air samples collected from the breathing zone during every task on Wednesday and Thursday and calculated as time-weighted average concentrations for an 8-h workday. Urine specimens of the exposed workers were taken immediately after the work shift on Thursdays and 16 h later on Friday mornings. Urine samples were also taken from a control group consisting of 6 females and 12 males, 38±5 years old (±SD). The urinary formic acid concentrations were corrected for the excretion of creatinine. Endpoint addressed: basic toxicokinetics	Time-weighted average exposure to methanol ranged from 58 µg/L (40 ppm) to 227 µg/L (160 ppm). The highest concentrations of urinary formic acid were measured in the samples taken on Friday mornigs and ranged from 26 mg/g creatinine to 98 mg/g creatinine. The output of urinary formic acid 16 h after the exposure was found to be linearly proportional (r=0.81) to the methanol concentration in the air. No correlations were found between methanol exposure and urinary formic acid concentrations in samples taken immediately after the workshift. The urinary formic acid concentrations in the morning samples taken from the non-exposed control group were 15.1±6.1 mg/g creatinine (N=18, ±SD). Based on the concentrations measured in the study, a urinary formic acid concentration of 80 mg/g creatinine after exposure to 260 µg/L (200 ppm) methanol vapor, the current Finnish limit for methanol vapor in the air, can be anticipated.	2 (reliable with restrictions) supporting study **Test material (EC name): methanol**	Liesivuori, J. and Savolainen, H. (1987)
Study type: Information on 4-methylpyrazole as inhibitor of alcohol dehydrogenase for treatment of methanol and ethylene glycol intoxications. Details on study design: 4-Methylpyrazole (4-MP), an inhibitor of alcohol dehydrogenase, may be useful for the treatment of methanol and ethylene glycol intoxications. A placebo-	A slight, transient elevation in one or both serum transaminase values was observed in 6 of the 15 subjects treated with 4-MP. This effect was not dose related nor apparently mediated through a hypersensitivity reaction. Serum triglyceride levels were increased in 30% of 4-MP treated subjects, but also in 25% of the placebo subjects. 4-MP treatment did not produce any other significant changes in objective clinical parameters	2 (reliable with restrictions) supporting study **Test material (Common name): 4-methylpyrazole**	Jacobsen, D. et al. (1990)

Method	Results	Remarks	Reference
controlled, double blind, multiple dose, sequential, ascending-dose study has been performed to determine the tolerance of 4-MP in healthy volunteers. Oral loading doses of 4-MP were followed by supplemental doses every 12 h through 5 days. 4-Methylpyrazole (4-MP), an inhibitor of alcohol dehydrogenase, may be useful for the treatment of methanol and ethylene glycol intoxications. A placebo-controlled, double blind, multiple dose, sequential, ascending-dose study has been performed to determine the tolerance of 4-MP in healthy volunteers. Oral loading doses of 4-MP were followed by supplemental doses every 12 h through 5 days, producing plasma levels in the therapeutic range. Endpoint addressed: basic toxicokinetics	nor in subjective side effects. The results suggest that a mild, transient increase in liver function tests might be observed in some subjects treated with multiple doses of 4-MP. Nevertheless, the slower elimination rate and lesser degree of toxicity of 4-MP would make it preferable to ethanol in therapy of these poisonings.		
Study type: Measurement of pulmonary retention and elimination half life of methanol in five volunteers exposed to methanol vapours for 8 h. Details on study design: Five healthy men, aged 31 to 56 years, served as experimental subjects. The concentration of methanol in air ranged from 103 to 284 mg/m³, total length of exposure was 8 h. Every 2 hours urine samples were taken, lung ventilation was measured in 1 h intervals, the influence of physical load on retention of methanol in the lung was investigated by exercise with weights and by exercise on a bicycle ergometer. Expired air was analyzed by gas chromatography, urine samples were analyzed for density and creatinine concentration, and methanol in urine was determined by gas chromatography, as well. The retention of methanol in the	The mean normal urine level was 0.73 mg/L (range from 0.32 - 2.61 mg/L), data selected from a control group of 31 individuals. Pulmonary retention of methanol in subjects exposed to 103 to 284 mg/m³ methanol was unrelated to duration (except first few min) and level of exposure, the mean retention was 57.7%, ranging from 53.4 to 61.3%. In some persons the retention was constantly low, in others constantly high. During exercise pulmonary ventilation increased but retention remained practically the same in all subjects, indicating that pulmonary retention is independent on lung ventilation. Urine excretion represented nearly 1 % of the retained dose at a normal diuresis. Average urine concentrations reached a peak after 8 h (Fig. 3) and were fairly proportional to the exposure levels (approx. 3.3, 7.0, and 9.5 mg/L). After 18 - 24 h from the start of exposure (about >= 12 h after termination), urine methanol has approached baseline level again. The excretion half-life was about 1.5 to 2 h.	2 (reliable with restrictions) supporting study **Test material (EC name): methanol**	Sedivec, V. et al. (1981)

Method	Results	Remarks	Reference
lungs and the course of its excretion in urine were monitored at single and at daily repeated exposures. From the concentration in inspired air, lung retention, minute lung ventilation and duration of exposure, the methanol dose retained in the organism of the experimental subjects was calculated. The dose correlated well with the methanol concentration (mmol/L or mg/L) in whole-shift urine. Blood levels were not measured. Endpoint addressed: basic toxicokinetics	Methanol concentrations in urine of 4 volunteers exposed to methanol vapors (199 mg/m³ ± 3%) for 8 h in one-week intervals were virtually the same, independent of the regimen of liquid intake (beverages): limited intake 4.37 mg/L on average (4.0 - 5.0 mg/L), higher intake 4.56mg/L on average (4.2 - 5.1 mg/L). In this cross-over drinking experiments it could be shown that the urinary methanol excretion correlated strictly with diuresis, i.e. irrespective of the urine volume produced at the same exposure level, the urine concentrations were identical and were dependent only on the exposure level. This suggests that methanol distributes only passively into the urine in relation to the blood level. This also implies that the total quantity excreted into the urine cannot be the criterion for the exposure level, but only its concentration. The mean equation of regression (Fig. 5) between retained methanol quantitity (body burden) [X in mg] and the whole-shift urine concentration [Y in mg/L] could be formulated as y = 0.7470 + 0.00763x		
Study type: Information on the elimination of methanol after oral doses and the rate of absorption during exposure to methanol vapour. Details on study design: The elimination of methanol after oral doses of 2.5 to 7 .0 mL has been studied in five human subjects. The rates of absorption of methanol by two human subjects during exposure to vapour concentrations of 0.5 - 1.3 mg/L methanol (corresponding to 400 - 1000 ppm) were also examined. Endpoint addressed: basic toxicokinetics	At any time the rate of elimination was found to be proportional to the concentration of methanol in the body. Blood levels of 47 to 76 mg/L were measured 2 to 3 h after oral uptake of 71 - 84 mg methanol/kg bw (6.6 - 7.4 mL per person); methanol disappearance obeyed first-order kinetics with a half-time of about 3 h. Only a very small fraction of ingested methanol (about 2 %) was eliminated via the respiratory and urinary routes. The rates of absorption of methanol by two human subjects during exposure to vapour concentrations of 0.5 - 1.3 mg/L (corresponding to 400 - 1000 ppm) have been investigated. Over short periods the amount of methanol absorbed appears to be approximately proportional to the duration of exposure and to the concentration of vapour in the atmosphere. It is concluded that accumulation in the body would occur at 4 mg/L (corresponding to 3000 ppm) and the maximum safe concentration for occupational exposure is 0.4 mg/L (corresponding to 300 ppm).	2 (reliable with restrictions) supporting study **Test material (EC name): methanol**	Leaf, G. and Zatman, L.J. (1952)
Study type: Information on	This longer-term study demonstrated that	4 (not	Leon, A.S. et al.

Method	Results	Remarks	Reference
blood methanol concentrations after aspartame consumption. Details on study design: This longer-term study determined blood methanol levels in humans after aspartame consumption. Endpoint addressed: basic toxicokinetics	ingesting aspartame equivalent to a methanol dose of 7.5 mg/(kg bw*d) per day resulted in blood methanol levels around 10 mg/L in adults.	assignable) supporting study **Test material (Common name): aspartame**	(1989) National Toxicology Program (2003)
Study type: Determination of relationship between methanol concentration in the blood, urine, and breath of volunteers exposed to methanol vapors for 0.5 to 8 h. Details on study design: Determination of relationship between methanol concentration in the blood, urine, and breath of volunteers exposed to 800 ppm (1.06 mg/l) methanol vapors for 0.5, 1, 2 and 8 h. The 0.5 to 2-h periods of exposure were used to estimate the half-life of methanol in blood, urine and breath. Endpoint addressed: basic toxicokinetics	For methanol, concentrations are not proportional to the exposure duration due to metabolic and other elimination processes that occur concurrently with the exposure. Blood data gave a half-life of 1.44 ± 0.33 h. Comparable but slightly more variable results were obtained using urine data corrected for the voiding time (1.55 ± 0.67 h) and breath data corrected for mucous membrane desorption (1.40 ± 0.38 h). Methanol concentrations in blood lagged some 15-30 min. behind the termination of exposure, and concentrations in urine were further delayed.	2 (reliable with restrictions) supporting study **Test material (EC name): methanol**	Batterman, S.A. et al. (1998)
Study type: A "multicompartment biologically based dynamic" inhalation model based on kinetic methanol inhalation data from rats (Horton et al., 1992), monkeys (Dorman et al., 1994) and humans (Sedivec et al., 1981; Osterloh et al., 1996; Batterman et al., 1998) was developed to describe the time evolution of methanol and its metabolites in the whole body and in accessible biological matrices. Details on study design: Predictions from simulations (PBPK modelling) of continuous inhalation of 200 ppm methanol in humans for 5 days (Bouchard et al. 2001) were based on the following assumptions: - a negligible background burden of methanol,	Prediction: near steady state will be reached in 20 h. After 5 d, methanol in blood and urine is estimated at 5.5 mg/L (171 µmol/L) and 8.1 mg/L (252 µmol/L); formate in blood and urine is 0.16 mg/L (3.5 µmol/L) and 1.5 mg/L (31.7 µmol/L = 0.97 mg/g creatinine or 2390 µmol/mol creatinine). This shows that exposure concentrations of <500 ppm are not sufficient to raise formate levels significantly, while methanol increases. The model, adapted to kinetic data in humans exposed acutely to methanol, predicts that 8-h inhalation exposures ranging from 500 to 2000 ppm, without physical activities, are needed to increase concentrations of blood formate and urinary formic acid above reported background values (4.9-10.3 and 6.3-13 mg/L, resp.). Therefore, according to the authors, blood and urinary methanol levels are the most sensitive biomarkers of absorbed methanol. Pulmonary retention: Using the experimental human data of Osterloh et	2 (reliable with restrictions) supporting study **Test material (EC name): methanol**	Batterman, S.A. et al. (1998) Bouchard, M. et al. (2001) Dorman, D.C. et al. (1994b) Horton, V.L. et al. (1992) Osterloh, J. D. et al. (1996) Sedivec, V. et al. (1981)

Method	Results	Remarks	Reference
- an absorption fraction of 0.577 (Sedivec et al. 1981), - a pulmonary ventilation rate of 10.8 L/min (Sedivec et al. 1981; Batterman et al. 1998), - an apparent distribution volume for methanol of 0.7 L/kg (corresponding to human body fluid), - an apparent distribution volume for formate of 4.6 L/kg (estimations by Bouchard et al. 2001), - a daily urine volume of 1.5 L Endpoint addressed: basic toxicokinetics	al. (1996), Sedivec et al. (1981) and Batterman et al. (1998), the best fit in the model for the average absorption fraction was higher than that given by Sedivec et al. (1981), namely about 80 % and corresponded to the retention of 79 % given by Batterman et al. 1998 (Bouchard et al., 2001).		
Study type: Accumulation of formate in the blood and the relationship between pulmonary intake and blood methanol concentration were investigated in six male human volunteers following a 6-hr exposure to 200 ppm methanol, either at rest or under light physical exercise. Details on study design: Six male human volunteers were exposed to 200 ppm (0.266 mg/L) methanol for 6 hours, either at rest or under light physical exercise. Formate and methanol concetrations were determined in blood samples of the individuals and compared to the values before exposure. Endpoint addressed: basic toxicokinetics	At the end of a 6-hr exposure to 200 ppm at rest, the blood methanol concentration was increased from a mean of 1.8 µg/mL to 7.0 µg/mL (3.8 times). Under light excercise, the total amount of methanol inhaled during the 6-hr exposure period was 1.8 times that inhaled at rest (pulmonary ventilation was increased 1.8 times). However, no statistically significant increase in blood methanol concentration was observed under exercise: 8.1 µg/mL vs. 7.0 µg/mL at rest. The endogenous blood formate (preexposure) concentrations ranged from 5.4 to 10.8 µg/mL. Formate did not accumulate in the blood above its background level following the 6-hr exposure to 200 ppm methanol, regardless whether subjects were exposed at rest or during excercise.	2 (reliable with restrictions) weight of evidence **Test material (EC name): methanol**	Lee, E.W. et al. (1992)
Study type: Study to determine whether concentration of formic acid in blood or urine and the methanol content of aveolar air permit the estimation of methanol exposure. Details on study design: Studies were carried out at three different work places of a printing shop. At each place air samples for methanol determination were taken every 15 min. In 20 workers employed at these places methanol concentration in the alveolar air and concentrations of formic	The concentration of formic acid in blood increased significantly from 3.2 ± 2.4 mg/L (median 3.0 mg/L) before to 7.9 ± 3.2 mg/L (median 7.3 mg/L) after the shift in the exposed workers. In 36 non-exposed persons, the blood formate levels ranged from 0 - 20 mg/L. The corresponding concentration in urine was increased significantly from 13.1 ± 3.9 mg/L (median 12.6 mg/L) to 20.2 ± 7 mg/L (median 19.1 mg/L), respectively. On the contrary, in the control groups there was a small but significant decrease of formic acid concentration in blood from 5.6 ± 4.5 mg/L (median 5.4 mg/L) in the morning to 4.9 ± 4.2 mg/L (median	2 (reliable with restrictions) weight of evidence **Test material (EC name): methanol**	Baumann, K. and Angerer, J. (1979)

Method	Results	Remarks	Reference
acid in blood and urine were determined at the beginning and at the end of the shift. For comparison, formic acid concentrations in blood and in urine were determined at corresponding times of the day in two groups of 36 and 15 subjects who had no contact with methanol. Air was collected using gas sampling tubes. To collect alveolar air expired at the end of expiration, special tubes were used in order to get low resistance. Methanol was analyzed by gas-chromatography. For analysis of formic acid in blood and urine, a specific sensitive technique was developed: formic acid was transformed by concentrated sulfuric acid into water and carbonmonoxide. The latter was reduced to methane directly on a specific part of a gas-chromatographic column connected to a flame ionization-detector (for further detail see Angerer 1976, 1977. For statistical evaluation Student's t-test and t-test for correlated samples were used. Endpoint addressed: basic toxicokinetics	3.9 mg/L) in the afternoon.		
Study type: Information on methanol toxicity in humans (symptoms and signs of methanol poisoning). Details on study design: see "any other information on materials and methods" Endpoint addressed: repeated dose toxicity: inhalation Endpoint addressed: acute toxicity: oral Endpoint addressed: basic toxicokinetics	**The lethal dose of methanol for humans is not known for certain. The minimum lethal dose of methanol in the absence of medical treatment is between 0.3 and 1 g/kg. The minimum dose causing permanent visual defects is unknown.** The symptoms and signs of methanol poisoning, which may not appear until after an asymptomatic period of about 12 to 24 hours, include visual disturbances, nausea, abdominal and muscle pain, dizziness, weakness and disturbances of consciousness ranging from coma to clonic seizures. Visual disturbances generally develop between 12 and 48 h after methanol ingestion and range from mild photophobia and misty or blurred vision to markedly reduced visual acuity and complete blindness. In extreme cases death results. The principal clinical	2 (reliable with restrictions) weight of evidence **Test material (EC name): methanol**	IPCS/WHO (1997)

Method	Results	Remarks	Reference
	feature is severe metabolic acidosis of anion-gap type. The acidosis is largely attributed to the formic acid produced when methanol is metabolized. The normal blood concentration of methanol from endogenous sources is less than 0.5 mg/litre (0.02 mmol/litre), but dietary sources may increase blood methanol levels. Generally, CNS effects appear above blood methanol levels of 200 mg/L (6 mmol/L), and fatalities have occurred in untreated patients with initial methanol levels in the range of 1500-2000 mg/L (47-62 mmol/L). Visual disturbances of several types (blurring, constriction of the visible field, changes in colour perception, and temporary or permanent blindness) have been reported in workers who experienced methanol air levels of about 1.6 mg/L (corresponding to 1200 ppm) or more. A widely used occupational exposure limit for methanol is 0.26 mg/L (corresponding to 200 ppm), which is designed to protect workers from any of the effects of methanol-induced formic acid metabolic acidosis and ocular and nervous system toxicity. No other adverse effects of methanol have been reported in humans except minor skin and eye irritation at exposures well above 0.27 mg/L (corresponding to 200 ppm).		

B.5.1.3. Summary and discussion of toxicokinetics

The data shows that metabolism of methanol occurs in a three-step process initially involving oxidation to formaldehyde by hepatic alcohol dehydrogenase, which is a saturable rate-limiting process. In the second step, formaldehyde is oxidized by aldehyde dehydrogenase to formic acid or formate depending on the pH. In the third step, formic acid is detoxified by a folate-dependent pathway to carbon dioxide. Elimination of methanol from the blood appears to be slow in all species, especially when compared to ethanol. In humans, urinary methanol concentrations have been found to be proportional to the concentration of methanol in blood.

Formate clearance from the blood of exposed primates is at least 50% slower than for rodents.

Methanol is readily absorbed after inhalation, ingestion and dermal contact and distributes rapidly throughout the body according to the distribution of body water. A small amount of methanol is excreted unchanged by the lungs and kidneys.

Metabolism in humans, rodents, and monkeys contributes up to 98 percent of the clearance, with more than 90 percent of the administered dose exhaled as carbon dioxide. Renal and pulmonary excretion contributes only about 2 – 3 percent. The metabolism and toxicokinetics of methanol varies by species and dose. In humans, the half-life time is approximately 2.5 – 3

hours at doses lower than 100 mg/kg bw. At higher doses, the half life can be 24 hours or more (IPCS/WHO, 1977; Kavet and Nauss, 1990).

The general population may be exposed to very low levels of methanol due to emissions in air from its production, end-uses, storage and handling, and the broad range of methanol-containing products.

Occupational exposure may occur during the production of metanol and its storage and handling, as well as in end-use product synthesis. Although the individual responses of humans to methanol may vary considerably, industrial exposures are not considered hazardous if concentrations are maintained within prescribed occupational exposure limits.

Methanol occurs naturally and is present in the diet. It can be absorbed rapidly by the inhalation, oral and dermal routes and distributed in the body, but it is only slowly metabolized to formate (which is believed to be the cause of visual damage) and then excreted. Methanol is rapidly degraded in the environment with no evidence of bioaccumulation.

B 5.2 Acute toxicity

B.5.2.1. Non-human information

B.5.2.1.1. Acute toxicity: oral

The results of studies on acute toxicity after oral administration are summarised in the following table:

Table B.5-3. Studies on acute toxicity after oral administration

Method	Results	Remarks	Reference
rat oral: gavage equivalent or similar to OECD Guideline 401 (Acute Oral Toxicity)	LD_0: >= 2528 mg/kg bw (application as 50% aqueous solution)	2 (reliable with restrictions) supporting study experimental result **Test material (EC name): methanol**	BASF AG (1961)
pig (minipig YU, CR) female oral: gavage Three animals were used per dose group and treated by gavage with the test substance.	LD_{50}: > 5000 mg/kg bw (female)	2 (reliable with restrictions) supporting study experimental result **Test material (EC name): methanol**	Dorman, D.C. et al. (1993)
monkey (Rhesus) oral: gavage Determination of the acute toxicity of the test substance after application of a single dose to monkeys by oral	LD_{50}: 6000 mg/kg bw (4/8 animals survived after bicarbonate supplementation.)	2 (reliable with restrictions) supporting study experimental result	Potts, A.M. et al. (1955) Potts, A.M. (1955)

Method	Results	Remarks	Reference
gavage.		**Test material (EC name): methanol**	
monkey (Rhesus macaca) oral: gavage Determination of the acute toxicity of the test substance in monkeys after application by oral gavage.	LD_{50}: ca. 7000 — 9000 mg/kg bw	2 (reliable with restrictions) supporting study experimental result **Test material (EC name): methanol**	Cooper, J.R. and Felig, P. (1961) Gilger, A.P. et al. (1956) Gilger, A.P. et al. (1959) Potts, A.M. (1955)
rat (Sprague-Dawley) male/female oral: gavage Study performed according to internal company standards (BASF-test) before actual guideline was adopted.	LD_{50}: > 1187 — 2769 mg/kg bw (male/female) (15 to 35% aqueous solution)	2 (reliable with restrictions) weight of evidence experimental result **Test material (EC name): methanol**	BASF AG (1975)

B.5.2.1.2. Acute toxicity: inhalation

The results of studies on acute toxicity after inhalation exposure are summarised in the following table:

Table B.5-4. Studies on acute toxicity after inhalation exposure

Method	Results	Remarks	Reference
rat (Long-Evans) male inhalation Two experiments were conducted to evaluate the acute effects of inhaled methanol on serum hormones associated with reproductive function in male rats.	hormone status (6 h): >= 0.27 — <= 13.3 mg/L air (male) (increased prolactin concentrations)	2 (reliable with restrictions) supporting study experimental result **Test material (EC name): methanol**	Cooper, R.L. et al. (1992)
cat inhalation No information available.	LC_{50} (4.5 h): 85.41 mg/L air	2 (reliable with restrictions) supporting study experimental result **Test material (EC name): methanol**	von Burg, R. (1994)
cat inhalation No information available.	LC_{50} (6 h): 43.68 mg/L air	2 (reliable with restrictions) supporting study experimental result **Test material (EC name): methanol**	von Burg, R. (1994)

Method	Results	Remarks	Reference
monkey (Rhesus) male/female inhalation No information available.	lethal dose (18 h): 13 mg/L air (male/female) lethal dose (41 h): 1.3 mg/L air (male/female) lethal dose (1 h): 52 mg/L air (male/female) (exposure for 1 to 4 h)	2 (reliable with restrictions) supporting study experimental result **Test material (EC name): methanol**	McCord, C.P. (1931)
mouse inhalation No information available.	LC_{50} (134 min): 79.43 mg/L air	2 (reliable with restrictions) supporting study experimental result **Test material (EC name): methanol**	von Burg, R. (1994)
rat (Sprague-Dawley) male/female inhalation: vapour (nose/head only) Study performed according to internal company standards (BASF-test) before actual guideline was adopted.	LC_{50} (4 h): 128.2 mg/L air (male/female) LC_{50} (4 h): 130.7 mg/L air (male) LC_{50} (4 h): > 115.9 mg/L air (female)	2 (reliable with restrictions) weight of evidence experimental result **Test material (EC name): methanol**	BASF AG (1980a)
rat (Sprague-Dawley) male/female inhalation: vapour (nose/head only) Study performed according to internal company standards (BASF-test) before actual guideline was adopted.	LC_{50} (6 h): 87.5 mg/L air (male/female) LC_{50} (6 h): 92.6 mg/L air (male) LC_{50} (6 h): 82.1 mg/L air (female)	2 (reliable with restrictions) weight of evidence experimental result **Test material (EC name): methanol**	BASF AG (1980b)

B.5.2.1.3. Acute toxicity: dermal

The results of studies on acute toxicity after dermal administration are summarised in the following table:

Table B.5-5. Studies on acute toxicity after dermal administration

Method	Results	Remarks	Reference
rabbit No information available.	LD_{50}: 17100 mg/kg bw (corresponding to 20 ml/kg bw according to the authors)	4 (not assignable) supporting study experimental result **Test material (EC name): methanol**	Rowe, V.C and McCollister, S.B. (1981)

B.5.2.1.4. Acute toxicity: other routes

The results of studies on acute toxicity (other routes) are summarised in the following table:

Table B.5-6. Studies on acute toxicity (other routes)

Method	Results	Remarks	Reference
monkey (Macaca fascicularis) male intraperitoneal Determination of the lethal dose after intraperitoneal application of the test substance to monkeys in the context of a metabolism study.	LDLo: 3000 mg/kg bw (male)	2 (reliable with restrictions) supporting study experimental result **Test material (EC name): methanol**	New Energy Development Organization (1987)
mouse (CB6F1) male/female intraperitoneal Determination of LD_{50} for methanol in wildtype, heterozygous and homozygous NEUT2 (FDH-deficient) mice.	LD_{50}: 6080 mg/kg bw (male/female) (wild type) LD_{50}: 6000 mg/kg bw (male/female) (heterozygous NEUT2) LD_{50}: 6030 mg/kg bw (male/female) (homozygous NEUT2)	2 (reliable with restrictions) supporting study experimental result **Test material (EC name): methanol**	Cook, R.J. et al. (2001)
monkey (Macaca mulatta (rhesus macaque) and Macaca nemestrina (pigtail monkey)) male/female intraperitoneal Determination of the lethal dose after intraperitoneal application of the test substance to monkeys in the context of a metabolism study.	LDLo: 4000 mg/kg bw (male/female) (1/4 rhesus macaques, severe metabolic acidosis)	2 (reliable with restrictions) supporting study experimental result **Test material (EC name): methanol**	Clay, K.L. et al. (1975)

B.5.2.2. Human information

The exposure-related observations in humans are summarised in the following table:

Table B.5-7. Exposure-related observations on acute toxicity in humans

Method	Results	Remarks	Reference
Study type: poisoning incident Subjects: - Number of subjects exposed: 24 - Sex: male - Race: Papua New Guinean Endpoint addressed: neurotoxicity Endpoint addressed: acute toxicity: oral	Three groups were identified: Nine patients had no ocular abnormality, 7 had only transient ocular abnormalities, and eight had permanent ocular abnormalites. Transient abnormalities included peripapillary oedema, optic disc hyperemia, diminished pupillary reactions to light, and central scotomata. Permanent ocular abnormalities included optic disc pallor, attenuation of arterioles,	2 (reliable with restrictions) weight of evidence **Test material (EC name): methanol**	Dethlefs, R. and Naraqi, S. (1978)

Method	Results	Remarks	Reference
	sheathing of arterioles, diminished pupillary reaction to light, diminished visual acuity, central scotomata, and other nerve fibre bundle defects. Complete blindness occurred in two patients, while severe visual deficit resulted in four others. The incidence of permanent ocular abnormalities was found to correlate with the incidence of metabolic acidosis ($p<0.01$), and with the stated volume of methanol consumed ($p<0.05$). An inverse correlation was found between stated volume of methanol consumed and onset of blurred vision.		
Study type: Human neurobehavioural effects after acute exposure to methanol vapour. Details on study design: Twenty-six healthy subjects (15 men, 11 women; ages 26-51 years) were exposed to methanol (0.27 mg/L) or water vapour for 4 hours while seated in a chamber. The subjects served as their own controls in a randomized, double-blind study design. The variables assessed were serum and urine methanol and formate levels; visual qualities (color discrimination and contrast sensitivity); and neurophysiological (auditory evoked potentials) and neurobehavioural qualities. Endpoint addressed: acute toxicity: inhalation Endpoint addressed: neurotoxicity	Exposure to methanol increased serum concentrations and urinary excretions of methanol, but did not affect formate levels. Overall visual, neurophysiological, and neurobehavioural test outcomes were not significantly affected, unless certain between-subject variables are considered. Slight effects on P-300 amplitude and Symbol Digit testing were noted.	2 (reliable with restrictions) supporting study **Test material (EC name): methanol**	Chuwers, P. et al. (1995)
Study type: Information on acute toxicity and neurotoxicity by inhaled methanol in humans. Details on study design: Twelve healthy subjects were exposed for 4 h to 0.26 mg/L (corresponding to 200 ppm) and to 0.026 mg/L (corresponding to 20 ppm) (control) in an exposure chamber in a cross-over design. The EEG was recorded before (reference) and at the end of each exposure with, the subject's eyes closed and opened and during a choice reaction test (colour word stress test). Spectral power was calculated by fast Fourier transformation. Subjective symptoms and effects of blinding with 20	During subjects' exposure to 0.26 mg/L, their scores for prenarcotic and irritating symptoms were not different from controls. In the closed-eye condition of subjects, the spectral power of the theta-band and of some electrodes of the delta-band was significantly less at the end of exposure to 0.26 mg/L, than that of controls. In the open-eye condition and during the color word stress test no significant changes were found. The changes in the theta-band suggest a slight excitatory	2 (reliable with restrictions) weight of evidence **Test material (EC name): methanol**	Muttray, A. et al. (2001)

Method	Results	Remarks	Reference
ppm methanol were assessed by questionnaires. The study was a single-blind one. Endpoint addressed: acute toxicity: inhalation Endpoint addressed: neurotoxicity	effect of 0.26 mg/L methanol. The effect was weak, as scores of acute symptoms did not change.		
Study type: Information on methanol toxicity in humans (symptoms and signs of methanol poisoning). Details on study design: see "any other information on materials and methods" Endpoint addressed: repeated dose toxicity: inhalation Endpoint addressed: acute toxicity: oral Endpoint addressed: basic toxicokinetics	The lethal dose of methanol for humans is not known for certain. **The minimum lethal dose of methanol in the absence of medical treatment is between 0.3 and 1 g/kg.** The minimum dose causing permanent visual defects is unknown. The symptoms and signs of methanol poisoning, which may not appear until after an asymptomatic period of about 12 to 24 hours, include visual disturbances, nausea, abdominal and muscle pain, dizziness, weakness and disturbances of consciousness ranging from coma to clonic seizures. Visual disturbances generally develop between 12 and 48 h after methanol ingestion and range from mild photophobia and misty or blurred vision to markedly reduced visual acuity and complete blindness. In extreme cases death results. The principal clinical feature is severe metabolic acidosis of anion-gap type. The acidosis is largely attributed to the formic acid produced when methanol is metabolized. The normal blood concentration of methanol from endogenous sources is less than 0.5 mg/litre (0.02 mmol/litre), but dietary sources may increase blood methanol levels. Generally, CNS effects appear above blood methanol levels of 200 mg/L (6 mmol/L), and fatalities have occurred in untreated patients with initial methanol levels in the range of 1500-2000 mg/L (47-62 mmol/L). Visual disturbances of several types (blurring, constriction of the visible field, changes in colour perception, and temporary or permanent	2 (reliable with restrictions) weight of evidence **Test material (EC name): methanol**	IPCS/WHO (1997)

Method	Results	Remarks	Reference
	blindness) have been reported in workers who experienced methanol air levels of about 1.6 mg/L (corresponding to 1200 ppm) or more. A widely used occupational exposure limit for methanol is 0.26 mg/L (corresponding to 200 ppm), which is designed to protect workers from any of the effects of methanol-induced formic acid metabolic acidosis and ocular and nervous system toxicity. No other adverse effects of methanol have been reported in humans except minor skin and eye irritation at exposures well above 0.27 mg/L (corresponding to 200 ppm).		

B.5.2.3. Summary and discussion of acute toxicity

Evaluation of the animal data - oral route, presented in the registration dossier shows that in rats, LD_{50} values after single oral administration range from 1187 to 2769 mg/kg bw, depending on the concentration of the aqueous solution used (BASF 1975, concentrations 15 to 35%, not further specified).

In Rhesus monkeys orally dosed with 6000 mg/kg bw, the retina and the optic papilla showed extended oedema, and the pupils were wide and non-responsive. Six of 8 animals exhibited cystic degeneration of the outer retinal granular layer, and in one animal there was evidence of significant demyelinisation of the optic nerve. Histological lesions were seen in the putamen and nucleus caudatus in 3 of 8 animals. All of these effects were most pronounced after early compensation of acidosis using bicarbonate application, because the monkeys generally did not survive those high doses of methanol but after early treatment with bicarbonate (Potts, 1955; Potts et al., 1955).

There was no evidence of marked acidosis in 12 Rhesus monkeys (28 applications) after sublethal doses up to 6000 mg/kg bw. Specifically, there was no hyperventilation, no increase in urinary excretion of organic acids, or shift in serum bicarbonate. Blindness was seen in only one surviving monkey dosed with 9000 mg/kg bw; the effect was transient four days after exposure. The LD_{50} was between 7000 and 9000 mg/kg bw (Cooper and Felig, 1961).

Evaluation of the animal data-inhalation route, presented in the registration dossier shows that in male and female rats, LC_{50} values of 87.5 mg/L (6 hours) and 128.2 mg/L (4 hours) were determined (BASF, 1980a, b). Clinical signs of toxicity were aqueous secretion of eyes and nose, labored breathing, staggering, apathy, and narcosis.

A similar range of toxicity values is reported for the mouse: LC_{50} (2.25 h) = approx. 79 mg/L (Von Burg, 1994).

In cats, an LC_{50} value of approx. 43.7 mg/L was obtained after a 6 hour exposure (Von Burg, 1994). A shorter duration of 4.5 hours led to a LC_{50} value of 85.4 mg/L (Von Burg, 1994).

Studies in Rhesus monkeys indicate lethal concentrations (percent mortality not reported) of 1.3 mg/L (after 41 hours), 13 mg/L (after18 hours) and 52 mg/L methanol (after1–4 hours). Blindness associated with optic nerve atrophy was reported. Eventual recovery from this lesion was observed (McCord, 1931; only limited documentation).

In rabbits, a dermal LD_{50} of about 17,000 mg/kg bw was found. No further details were reported (Rowe and McCollister, 1981).

According to the Registrant on the basis of human data, oral ingestion dominates as the most frequent route of poisoning, but percutaneous absorption or inhalation of vapours are as effective as the oral route in producing methanol acute toxic syndrome.

A blood level of 500 mg/L methanol in acutely poisoned patients generally is regarded as requiring hemodialysis. This blood concentration can transiently be achieved in an adult person (70 kg) by ingestion of 0.4 mL methanol/kg bw (Kavet and Nauss, 1990). Generally in humans, transient central nervous system (CNS) effects appear at blood methanol levels of 200 mg/L and serious ocular symptoms appear above 500 mg/L ranging from mild photophobia, misty or blurred vison to markedly reduced visual acuity and total blindness (Kavet and Nauss, 1990; Dethlefs and Naraqi, 1978). Acute methanol intoxication evolves in a well-defined pattern. First, a mild depression of the CNS occurs which is followed by an asymptomatic latent period commonly lasting 12 to 14 hours. Clinical symptoms include headache, dizziness, nausea and vomiting, abdominal pain, and labored, periodic breathing and mag progress to coma and death from respiratory failure (Kavet and Nauss, 1990).

The minimal acute methanol dose to humans that can result in death is considered to be 300 to 1000 mg/kg by ingestion. Fatalities have occurred in untreated patients with initial methanol blood levels in the range of 1500 to 2000 mg/L (IPCS/WHO, 1997). In general, coma, seizures and prolonged acidosis were poor prognostic signs (Naraqi et al., 1979). Such high and potentially lethal blood methanol levels are less likely to be achieved from inhalation exposure. Exposure to 0.26 mg/L methanol for 4 hours was without significant physiologic effects in human volunteers (Muttray et al., 2001).

In conclusion, formate is considered to be the ultimate toxicant in acute methanol intoxication in humans. Acidosis and ophthalmologic changes are typical effects in primates. They do not occur in rodents or rabbits, which are able to remove formate more efficiently. In these animals, CNS depression, narcosis and death are the leading sysmptoms of intoxication.

B 5.3 Irritation

B.5.3.1. Skin

Not relevant for this dossier

B.5.3.2. Eye

Not relevant for this dossier

B 5.4 Corrosivity

Not relevant for this dossier

B 5.5 Sensitisation

Not relevant for this dossier

B 5.6 Repeated dosed toxicity

B.5.6.1. Non-human information

B.5.6.1.1. Repeated dose toxicity: oral

The results of studies on repeated dose toxicity after oral administration are summarised in the following table:

Table B.5-11. Studies on repeated dose toxicity after oral administration

Method	Results	Remarks	Reference
monkey male subacute (oral: gavage) 2340 mg/kg bw (actual ingested) Vehicle: water Exposure: 3 days (daily) Daily application of a single dose of methanol to monkeys by gavage over a period of 3 days.	LOAEL: 2340 mg/kg bw/day (actual dose received) (male) (mortality)	2 (reliable with restrictions) supporting study experimental result **Test material (EC name): methanol**	Rao, K.R. et al. (1977)
monkey (Macaca mulatta) male subacute (nasogastric tube) initially 2000 mg/kg, thereafter 500 mg/kg at variable frequencies and time points (exception: one animal 1000 mg/kg at 44 and 72 h and 2000 mg/kg at 144h) (nominal) Vehicle: water Exposure: approx. 1.5 to 6 days (variable) Test model in monkeys for methanol-induced ocular toxicity after short-term exposure to characterize the toxicity syndrome and histological manifestations.	no NOAEL identified:	2 (reliable with restrictions) weight of evidence experimental result **Test material (EC name): methanol**	Martin-Amat, G., Tephly, T.R., McMartin, K.E., Makar, A.B., Hayreh (1977) Martin-Amat, G. et al. (1978) Baumbach, G.L. et al. (1977) Hayreh, M.S. et al. (1977) Martin-Amat, G. et al. (1977) McMartin, K.E. et al. (1975)

5.6.1.2. Repeated dose toxicity: inhalation

The results of studies on repeated dose toxicity after inhalation exposure are summarised in the following table:

Table B.5-12. Studies on repeated dose toxicity after inhalation exposure

Method	Results	Remarks	Reference
rat (Sprague-Dawley) male subacute (inhalation: vapour) 0.265, 2.65, 13.3 mg/L (corresponding to 200, 200, 10000 ppm) (nominal conc.) Vehicle: unchanged (no vehicle) Exposure: 1, 2, 4 or 6 weeks (8 h/d, 5 d/wk) Investigation of sexual hormone status in male mature rats after subacute exposure to methanol vapours.	NOAEC: 2.65 mg/L air (male) LOAEC: 13.3 mg/L air (male) (significant increase in circulating LH after 6 wks of exposure)	2 (reliable with restrictions) supporting study experimental result **Test material (EC name): methanol**	Cameron, A.M. et al. (1984)
rat (Sprague-Dawley) male subacute (inhalation: vapour) 0.26 mg/L (corresponding to 260 mg/m³) (nominal conc.) Vehicle: unchanged (no vehicle) Exposure: 1, 2, 4, and 6 wks (8 h/d, 5 d/wk) Investigation of potential toxic effects of methanol vapours on testicular production of testosterone in normal or folate-reduced rats.	NOAEC: 0.26 mg/L air (male) (testicular production of testosterone)	2 (reliable with restrictions) supporting study experimental result **Test material (EC name): methanol**	Lee, E. et al. (1991)
rat (Sprague-Dawley) male subchronic (inhalation: vapour) 0.066, 0.266, 1.06 mg/L (corresponding to 50, 200, 800 ppm) (nominal conc.) Vehicle: unchanged (no vehicle) Exposure: 13 wk (20 h/d, 7 d/wk) Investigation of potential toxic effects of methanol vapours on the morphology of the testes in normal or folate-reduced rats.	NOAEC: 1.06 mg/L air (male) (testicular histopathology)	2 (reliable with restrictions) supporting study experimental result **Test material (EC name): methanol**	Lee, E. et al. (1991)
rat (Sprague-Dawley) male subacute (inhalation: vapour) 0.265, 2.65, 13.3 mg/L (corresponding to 200, 200, 10000 ppm) (analytical conc.) Vehicle: unchanged (no vehicle)	NOAEL: 13.3 mg/L air (analytical) (male)	2 (reliable with restrictions) supporting study experimental result **Test material (EC name): methanol**	White, L. et al. (1983)

Method	Results	Remarks	Reference
Exposure: 1, 2, 4 or 6 weeks (6 h/d, 5 d/wk) Investigation of biochemical/physiological and cytological parameters of the lung and in lavage-fluid after subacute exposure to methanol vapours.			
monkey (Macaca fascicularis) acute to chronic (inhalation: vapour) (whole body) 1.3; 2.7; 4.0; 5.3; 6.7 mg/L (corresponding to 1000; 2000; 3000; 4000; 5000 ppm) (nominal conc.) Vehicle: unchanged (no vehicle) Exposure: see "any other information on materials and methods" (21 hours/day) The study was designed to investigate the effect of repeated methanol inhalation for various time periods (including recovery phases) in monkeys.	NOAEC: 1.3 mg/L air (nominal) (observed effects were not progressive as evidenced after recovery) LOAEC: 4 mg/L air (nominal) (increase of responsive astroglia seen in the cerebral white substance; degenerative changes in the visual system)	2 (reliable with restrictions) supporting study experimental result **Test material (EC name): methanol**	New Energy Development Organization (1987)
monkey (Macaca fascicularis) male/female subacute (inhalation: vapour) 0.66, 2.65, 6.63 mg/L (corresponding to 500, 2000, 5000 ppm) (analytical conc.) Vehicle: unchanged (no vehicle) Exposure: 4 weeks (6 h/d, 5 d/wk) Investigation of the effects of subacute exposure to methanol vapours in monkeys with histopathological examinations lacking brain and neural tissue.	NOAEC: 6.63 mg/L air (male/female) (clinical signs, histopathology, opthalmoscopy)	4 (not assignable) supporting study experimental result **Test material (EC name): methanol**	Andrews, L.S et al. (1987)
monkey (Macaca fascicularis) subacute (inhalation: vapour) (whole body) 13.26, 9.31, 6.65, 3.99 mg/L (corresponding to 10000, 7000, 5000, 3000 ppm) (nominal conc.) Vehicle: unchanged (no vehicle) Exposure: 3000 ppm: 20 d	LOAEC: 3.99 mg/L air (nominal) (clinical signs; histopathology (liver, CNS))	2 (reliable with restrictions) supporting study experimental result **Test material (EC name): methanol**	New Energy Development Organization (1987)

Method	Results	Remarks	Reference
5000 ppm: 5 d and 14 d, respectively 7000, 10000 ppm: 6 d (21 h/d) Comprehensive study programme on three species including metabolic, pharmacokinetic, short-term, long-term, reproductive and carcinogenicity studies.			
rat (Fischer 344/DuCrj) male/female chronic (inhalation: vapour) (whole body) 0.013; 0.13; 1.3 mg/L (corresponding to 10; 100; 1000 ppm) (nominal conc.) Vehicle: no data Exposure: 12 months (total exposure time: 7318-7341 h: males; 7474 - 7496 h: females) (continuously, average about 20 h/d) equivalent or similar to OECD Guideline 453 (Combined Chronic Toxicity / Carcinogenicity Studies)	NOEC: 0.13 mg/L air (nominal) (male/female) LOAEC: 1.3 mg/L air (nominal) (male/female) (body weight and food consumption; organ/body weight ratio; swelling of the chromophobic cells of the pituitary)	2 (reliable with restrictions) weight of evidence experimental result **Test material (EC name): methanol**	New Energy Development Organization (1987) IPCS/WHO (1997)
rat (Sprague-Dawley) male/female subacute (inhalation: vapour) 0.663, 2.65, 6.63 mg/l (corresponding to 520, 1980, 5010 ppm) (analytical conc.) Vehicle: unchanged (no vehicle) Exposure: 4 weeks (6 h/d, 5 d/wk) equivalent or similar to OECD Guideline 412 (Repeated Dose Inhalation Toxicity: 28/14-Day)	NOAEC: 6.66 mg/L air (male/female)	2 (reliable with restrictions) weight of evidence experimental result **Test material (EC name): methanol**	Andrews, L.S et al. (1987)
monkey (Macaca fascicularis) chronic (inhalation) (whole body) 0.013; 0.13 and 1.3 mg/L (corresponding to 10, 100 and 1000 ppm) (nominal conc.) Vehicle: unchanged (no vehicle) Exposure: a) 7 months b) 1 year + 7 months (19 months) c) 2 years + 5 months (29 months) (21 h/d) Comprehensive study programme on	NOAEC: 0.013 mg/L air (nominal) LOAEC: 0.13 mg/L air (nominal) (slight myocardial effects and slight hyperplasia of the astroglia in the cerebral white substance)	2 (reliable with restrictions) weight of evidence experimental result **Test material (EC name): methanol**	New Energy Development Organization (1987) Vyskocil, A. and Viau, C. (2000)

Method	Results	Remarks	Reference
monkeys including metabolic, pharmacokinetic and short-, long-term studies, reproductive assays and carcinogenicity studies.			
mouse (B6C3F1) male/female chronic (inhalation) (whole body) 0.013; 0.13; 1.3 mg/L (corresponding to 10; 100; 1000 ppm) (nominal conc.) Vehicle: unchanged (no vehicle) Exposure: 12 months (males: 7202-7225 h; females: 7352-7373 h) (continuously, mean daily exposure time: 19.8 hours) equivalent or similar to OECD Guideline 453 (Combined Chronic Toxicity / Carcinogenicity Studies)	NOAEC: 1.3 mg/L air (nominal) (male/female) (histopathological examinations; body weight; food consumption; organ weights) NOEC: 0.13 mg/L air (nominal) (male/female)	2 (reliable with restrictions) weight of evidence experimental result **Test material (EC name): methanol**	New Energy Development Organization (1987) Takeda, K. and Katoh, N. (1988) IPCS/WHO (1997)

5.6.1.3. Repeated dose toxicity: dermal

No relevant information available

5.6.1.4. Repeated dose toxicity: other routes

No relevant information available

5.6.2. Human information

The exposure-related observations in humans are summarised in the following table:

Table B.5-13. Exposure-related observations on repeated dose toxicity in humans

Method	Results	Remarks	Reference
Study type: cohort study (prospective) Details on study design: HYPOTHESIS TESTED (if cohort or case control study): exposure-excretion relationship and possible health effects of exposure to methanol vapour were studied STUDY POPULATION 33 exposed workers during the second half of 2 working weeks COMPARISON POPULATION Urinary methanol concentrations were also determined in 91 nonexposed subjects (Kawai et al., 1991). The geometric mean value for methanol in urine samples from the latter was < 2 mg/L. HEALTH EFFECTS STUDIED	OBSERVATIONS: - blurred vision and headache during or after work - no photophobia - retinal changes - retarded pupil reflex and one mild mydriasis - dimmed vision and nasal irritation were the most frequent symptoms complained during work	2 (reliable with restrictions) weight of evidence **Test material (EC name): methanol**	Kawai, T. et al. (1991) Yasugi, T. et al. (1992)

Method	Results	Remarks	Reference
- photophobia; eye examination (retinal changes; pupil reflex; mydriasis); blurred vision; headache; nasal irritation OTHER DESCRIPTIVE INFORMATION ABOUT STUDY: - methanol levels in urine samples; formate excretion in urine samples Endpoint addressed: repeated dose toxicity: inhalation Endpoint addressed: basic toxicokinetics			
Study type: Information on occupational methanol poisoning. Endpoint addressed: repeated dose toxicity: inhalation	Headache and blurred vision were reportedly frequent symptoms. It is believed, that absorption of 8 grams would seriously affect the eyes and that such a dose could result from inhalation of 1.06 to 1.33 mg/L (corresponding to 800 to 1000 ppm) for 8 hours. Work room concentration of 0.67 to 0.8 mg/L (corresponding to 500 to 600 ppm) were found. It is recommended to keep the levels below 1 ppm.	2 (reliable with restrictions) supporting study **Test material (EC name): methanol**	Mc Nally, W.D. (1937)
Study type: Information on urinary methanol concentrations in humans after repeated methanol inhalation. Details on study design: Five human subjects were exposed to an atmospheric concentration of 0.27 mg/L (corresponding to 200 ppm) of methanol in a test chamber for 7 hours per day for 5 consecutive days. Ambient air in the chamber was monitored continously for methanol, while urine was monitored for methanol and formic acid. Endpoint addressed: repeated dose toxicity: inhalation	Mean urinary methanol concentration were increased from baseline at the end of each exposure session, but returned to baseline in samples collected 16 hours following cessation of exposure. The concentration of formic acid in morning urine specimens did not change significantly over the 7 days of the exposure.	2 (reliable with restrictions) supporting study **Test material (EC name): methanol**	Franzblau, A. et al. (1993)
Study type: Information on methanol toxicity in humans (symptoms and signs of methanol poisoning). Details on study design: see "any other information on materials and methods" Endpoint addressed: repeated dose toxicity: inhalation Endpoint addressed: acute toxicity: oral Endpoint addressed: basic toxicokinetics	The lethal dose of methanol for humans is not known for certain. The minimum lethal dose of methanol in the absence of medical treatment is between 0.3 and 1 g/kg. The minimum dose causing permanent visual defects is unknown. The symptoms and signs of methanol poisoning, which may not appear until after an asymptomatic period of about 12 to 24 hours, include visual disturbances, nausea, abdominal and muscle pain, dizziness,	2 (reliable with restrictions) weight of evidence **Test material (EC name): methanol**	IPCS/WHO (1997)

Method	Results	Remarks	Reference
	weakness and disturbances of consciousness ranging from coma to clonic seizures. Visual disturbances generally develop between 12 and 48 h after methanol ingestion and range from mild photophobia and misty or blurred vision to markedly reduced visual acuity and complete blindness. In extreme cases death results. The principal clinical feature is severe metabolic acidosis of anion-gap type. The acidosis is largely attributed to the formic acid produced when methanol is metabolized. The normal blood concentration of methanol from endogenous sources is less than 0.5 mg/litre (0.02 mmol/litre), but dietary sources may increase blood methanol levels. Generally, CNS effects appear above blood methanol levels of 200 mg/L (6 mmol/L), and fatalities have occurred in untreated patients with initial methanol levels in the range of 1500-2000 mg/L (47-62 mmol/L). Visual disturbances of several types (blurring, constriction of the visible field, changes in colour perception, and temporary or permanent blindness) have been reported in workers who experienced methanol air levels of about 1.6 mg/L (corresponding to 1200 ppm) or more. A widely used occupational exposure limit for methanol is 0.26 mg/L (corresponding to 200 ppm), which is designed to protect workers from any of the effects of methanol-induced formic acid metabolic acidosis and ocular and nervous system toxicity. No other adverse effects of methanol have been reported in humans except minor skin and eye irritation at exposures well above 0.27 mg/L (corresponding to 200 ppm).		

5.6.3. Summary and discussion of repeated dose toxicity

Several data on repeated dose toxicity has been presented by the Registrant. On that basis Registrant defines 8 different levels of NOAEC, but the most critical one is used as a NOAEC

for methanol:

Oral: LOAEL subacute = 2340 mg/kg/bw in monkeys (mortality 7/7 after 3 d exposure)

Inhalation: NOAEC chronic = 0.013 mg/L air in monkeys (7 to 29 months exposure)

In two submitted endpoints (White, L. et al. 1983 oraz Cameron, A. M. et al. 1984) the convertion mg/L into ppm was miscalculated.

Seven male monkeys received daily doses of 2340 mg/kg bw methanol as 30% aqueous solution by oral gavage for three days. Under the test conditions, this dosage was lethal for all seven animals (Rao et al., 1977).

Inhalation:

In a whole body inhalation study in monkeys exposed to 0.013, 0.13, and 1.3 mg/L for 21 hours/day, 7 days/week for 7, 19, and 29 months, several general clinical signs as well as degenerative effects in the brain (at 0.13 and 1.3 mg/L), slight peripheral nerve damage (at 0.13 and 1.3 mg/L), very slight degeneration of the optic nerve (concentrations not noted), increased fat granules and slight fibrosis in the liver (all concentrations) as well as Sudan positive granules in the kidney were observed (at 0.13 and 1.3 mg/L). Also, a slight myocardial disorder (at 0.13 and 1.3 mg/L) and localized effects in the trachea and possible slight fibrosis in the lungs (concentrations not noted) were observed. Although the statistical significance of the effects cannot be verified from the limited study report, the effects observed appear to be associated with methanol (NEDO, 1987).

In a shorttime experiment, monkeys were exposed up to 20 days for 21 hours per day to methanol vapour. Coma and lethality were observed at concentrations > 9.31 mg/(L*d). In the brain, necrosis of the basal ganglia and cerebral edema were observed at 6.65 mg/(L*d) and at 3.99 mg/(L*d), hyperplasia and fibrosis around myelin sheaths of the basal ganglia as well as a slight to moderate increase in astroglia cells were observed. The optic nerve showed atrophy at > 3.99 mg/(L*d), along with reduction in myelin fibers. In the liver, fibrosis was observed at 6.65 mg/(L*d) and mild fatty degeneration was observed at 3.99 mg/(L*d). In the kidney, partly vacuolated hyaline degeneration was observed at 6.65 mg/(L*d) (NEDO, 1987). The liver and kidney effects were recorded at doses already overtly toxic in humans and, hence, are of low relevance.

In rats exposed to methanol up to 6.65 mg/L for 6 hours per day, five days per week for 28 days, no adverse effects were observed except local nasal irritation and increased relative spleen weights, which were observed only at the middle dose. The estimated blood level of methanol was about 250 mg/L under this condition (Andrews et al., 1987).

In a whole body inhalation study in mice exposed for 12 months to concentrations of 0.013, 0.13, and 1.3 mg/L for 20 hours/day, slight changes in clinical signs, body and organ weights, and some changes in histopathology were observed, but these effects were considered to be toxicologically irrelevant (NEDO, 1987). In rats exposed in the same manner, slight changes in body weight and organ weights were observed at the highest dose. The NOEC was 0.13 mg/L, the NOAEC was 1.3 mg/L for rats and mice in these studies (NEDO, 1987). Again, these effects are of low relevance in the light of the onset of human toxicity already at lower doses. The species related differences are very obvious between rodents and primates.

The latter demonstrating a 100-fold greater susceptibility for methanol-related effects due to differences in metabolism of methanol. In rodents methanol is metabolized to carbon dioxide

to a great extent, whereas in primates formate accumulation is responsible for the observed effects.

Human data:

In male and female workers exposed to methanol from 0.3 to 7.8 years, the highly exposed workers (4.7 - 7.3 mg/L) more often complained of blurred vision, headache and nasal irritation during or after work. Nobody stated to suffer from photophobia. The examination of the eye fundus failed to reveal retinal changes. Among three workers exposed to about 1.0 to 1.6 mg/L and one worker exposed to 0.12 to 3.6 mg/L, two showed retarded pupil reflex and one exhibited mild mydriasis (Kawai et al., 1991). Other common complaints were forgetfulness and skin sensitivity (IPCS/WHO, 1997).

A health hazard evaluation was conducted by the National Institute for Occupational Safety and Health (NIOSH) to determine if vapours from duplicating fluid (99% methyl alcohol) used in direct-process spirit duplicating machines were causing adverse health effects among teacher aides (Frederick et al., 1984). The teacher aides reported significantly more blurred vision, headache, dizziness, and nausea than the comparison group. Concentrations of airborne methyl alcohol ranged from 0.48 to 4.0 mg/L. Additional studies also showed that headaches were associated with occupations that involve the operation of duplicating machines (NTP, 2003; IPCS/WHO, 1997).

B 5.7 Mutagenicity

Not relevant for this dossier

B 5.8 Carcinogenicity

Not relevant for this dossier

B 5.9 Toxicity for reproduction

Not relevant for this dossier

B 5.10 Other effects

B.5.10.1. Non-human information

B.5.10.1.1. Neurotoxicity

No relevant information available

B.5.10.1.2. Immunotoxicity

No relevant information available

B.5.10.1.3. Specific investigations: other studies

The results of specific investigations (other studies) are summarised in the following table:

Table B.5-21. Specific investigations: other studies

Method	Results	Remarks	Reference
Type of effects studied: ocular toxicity (in vivo) rat and human (rat: Sprague-Dawley) no administration Vehicle: no administration The study was designed to determine whether components of folate-dependent formate oxidation, (folate and 10-formyltetrahydrofolate dehydrogenase (10-FDH)) exist in retina and whether differences in these components might explain species-determined susceptibility to methanol intoxication. No methanol was administered.	The cell-specific localisation of the enzyme, 10-FDH, was found to be similar in rat and human retina, preferentially located in the Müller-cell type, the principal glia of the retina (by immunohistochemistry). The amount of 10-FDH found in cytosolic as well as in the mitochondrial fraction, was about 3x higher in humans than in rats (Western blot analysis). However, the retinal folate levels were lower in humans (about 14 % of that in rats), compared with the high folate liver pools, the retina contains very much less folate.	2 (reliable with restrictions) supporting study experimental result **Test material (Common name): folate and 10-FDH**	Martinasevic, M.K. et al. (1996) Eells, J.T. et al. (1995)
Type of effects studied: ocular toxicity (in vivo) rat (Long-Evans) male intraperitoneal 4000 mg/kg initial dose (nominal conc.) 1000 or 2000 mg/kg 12 h later (nominal conc.) Vehicle: saline Exposure: an initial dose of 4000 mg/kg followed by a supplemental dose of 1000 or 2000 mg/kg 12 h later The studies were performed to define formate-induced retinal dysfunction and histopathology in a rat modell of methanol intoxication.	Methanol intoxicated rats developed formic acidemia, metabolic acidosis and visual toxicity within 36 hours. Histopathological effect on retinal structure: In the high-dose group (7 - 15 mM blood formate vs. methanol-treated control with 0.5 to 2 mM formate), prominent vacuolation in the photoreceptors near the junction of inner and outer segments, with accumulation of densely stained material in the inner segments near the outer limiting membrane. Mitochondrial swelling and disruption was noted in the retinal pigment epithelium, photoreceptor inner segments and optic nerve (Eells et al., 2000; Seme et al., 2001). Ultrastructural studies by electronmicroscopy revealed that the retinal morphology (as represented by the mitochdrial-rich, inner segment of the photoreceptor) was similar to the control after recovery of 72 h, but subtle photoreceptor changes were still present as a spacing between the cell nuclei of the outer nuclear layer which	2 (reliable with restrictions) supporting study experimental result **Test material (EC name): methanol**	Eells, J.T. et al. (2000) Eells, J.T. et al. (1996) Seme, M.T. (1999) Wallace, K.B. et al. (1997)

Method	Results	Remarks	Reference
	suggests residual histological alterations from formate-induced, previous edema (Seme et al., 2001). In the low-dose group (4 - 6 mM formate in blood), no histopathological changes were apparent at the light-microscopic level (Wallace et al., 1997). However, visual dysfunction was already visible in functional diagnostics, occurring as reductions in the flash evoked cortical potential (FEP) and in electroretinogram (ERG) at formate concentrations lower than those associated with morphological changes and provide functional evidence of direct retinal toxicity in methanol poisoning (Wallace et al, 1997). Rod- and cone-mediated ERG responses were attenuated in a formate- and time-dependent manner (Seme et al., 1999, 2001). Biochemical effects: Retinal ATP, ADP, and GSH were significantly depleted following methonol-treatment under inhibition of formate oxidation after 72 and 144 h with GSH levels about 1/2 of controls, and after recovery still decreased, while energy metabolites showed no difference from the control values (Seme et al., 2001).		
Type of effects studied: behavioural effects (in vivo) rat (Long-Evans) male oral: gavage 1000, 2000, 3000 mg/kg (50-% aqueous solution) (nominal conc.) Vehicle: water Exposure: single dose (only one dose) The study was designed to examine neurobehavioral toxicity in methanol-induced rats.	The rats displayed no signs of overt intoxication such as gait disturbance, but a significant, dose-related reduction in FR20 response was observed at all dose-levels. A NOAEL for behavioural changes cannot be derived.	2 (reliable with restrictions) supporting study experimental result **Test material (EC name): methanol**	National Toxicology Program (2003) Youssef, A.F. et al. (1993)
Type of effects studied: ocular	OPHTHALMOSCOPIC	2 (reliable with	Martin-Amat, G.,

Method	Results	Remarks	Reference
toxicity (in vivo) monkey (Macaca mulatta) male nasogastric tube initially 2000 mg/kg, thereafter 500 mg/kg at variable frequencies and time points (exception: one animal 1000 mg/kg at 44 and 72 h and 2000 mg/kg at 144h) (nominal conc.) Vehicle: water Exposure: approx. 1.5 to 6 days (variable) Test model in monkeys for methanol-induced ocular toxicity after short-term exposure to characterize the toxicity syndrome and histological manifestations.	EXAMINATION The only detectable ocular change was optic disc edema (of the optic papilla). The primary sites of ocular injury were the optic nerve heads and the anterior segment of the optic nerve rather than the retinal ganglion cells themselves. In all eyes with optic disc changes, pupils were dilated and reacted poorly to light. CLINICAL CHEMISTRY Under methanol treatment acc. to this test design, formate levels were between min. 7.2 and max. 14.4 mEq/L in blood and 7.9 to 13.9 mEq/L in cerebrospinal fluid, blood bicarbonate min. 4.0 and max. 10.2 mEq/L, and blood pH min. 7.13 and max. 7.28. Methanol levels ranged from 1540 to 2840 mg/L (Martin-Amat et al., 1977). HISTOPATHOLOGY: NON-NEOPLASTIC All six animals developed fundus changes at the head of the optic nerve (optic disc) within 43 to 171 h after methanol ingestion, expressed as intraaxonal swellings (Hayreh et al, 1977). Electronmicroscopic studies revealed swelling of the nerve fibers with an accumulation/clustering of swollen mitochondria in the optic nerve head being maximally in the lamina cribrosa region. Furthermore, in the retrolaminar and intraorbital optic nerve, swelling of astrocytes was prominent as well as swelling of the cytoplasm of the oligodendroglial cytoplasm in contact with the axons (Baumbach et al., 1977). Alterations were not observed in the retina itself: the ganglion cells of the retina were intact with only minimal swellings of the mitochondria and loss of cristae. But these	restrictions) supporting study experimental result **Test material (EC name): methanol**	Tephly, T.R., McMartin, K.E., Makar, A.B., Hayreh (1977) Martin-Amat, G. et al. (1978) Baumbach, G.L. et al. (1977) Hayreh, M.S. et al. (1977) Martin-Amat, G. et al. (1977) McMartin, K.E. et al. (1975)

Method	Results	Remarks	Reference
	findings were also present in the control tissue (Baumbach et al., 1977).		

B.5.10.2. Human information

No relevant information available

The exposure-related observations on neurotoxicity in humans are summarised in the following table:

Table B.5-22. Exposure-related observations on neurotoxicity

Method	Results	Remarks	Reference
Study type: poisoning incident Subjects: - Number of subjects exposed: 24 - Sex: male - Race: Papua New Guinean Endpoint addressed: neurotoxicity Endpoint addressed: acute toxicity: oral	Three groups were identified: Nine patients had no ocular abnormality, 7 had only transient ocular abnormalities, and eight had permanent ocular abnormalites. Transient abnormalities included peripapillary oedema, optic disc hyperemia, diminished pupillary reactions to light, and central scotomata. Permanent ocular abnormalities included optic disc pallor, attenuation of arterioles, sheathing of arterioles, diminished pupillary reaction to light, diminished visual acuity, central scotomata, and other nerve fibre bundle defects. Complete blindness occurred in two patients, while severe visual deficit resulted in four others. The incidence of permanent ocular abnormalities was found to correlate with the incidence of metabolic acidosis ($p<0.01$), and with the stated volume of methanol consumed ($p<0.05$). An inverse correlation was found between stated volume of methanol consumed and onset of blurred vision.	2 (reliable with restrictions) weight of evidence **Test material (EC name): methanol**	Dethlefs, R. and Naraqi, S. (1978)
Study type: Human neurobehavioural effects after acute exposure to methanol vapour. Details on study design: Twenty-six healthy subjects (15 men, 11 women; ages 26-51 years) were exposed to	Exposure to methanol increased serum concentrations and urinary excretions of methanol, but did not affect formate levels. Overall visual, neurophysiological, and neurobehavioural test outcomes	2 (reliable with restrictions) supporting study **Test material (EC name): methanol**	Chuwers, P. et al. (1995)

Method	Results	Remarks	Reference
methanol (0.27 mg/L) or water vapour for 4 hours while seated in a chamber. The subjects served as their own controls in a randomized, double-blind study design. The variables assessed were serum and urine methanol and formate levels; visual qualities (color discrimination and contrast sensitivity); and neurophysiological (auditory evoked potentials) and neurobehavioural qualities. Endpoint addressed: acute toxicity: inhalation Endpoint addressed: neurotoxicity	were not significantly affected, unless certain between-subject variables are considered. Slight effects on P-300 amplitude and Symbol Digit testing were noted.		
Study type: Information on acute toxicity and neurotoxicity by inhaled methanol in humans. Details on study design: Twelve healthy subjects were exposed for 4 h to 0.26 mg/L (corresponding to 200 ppm) and to 0.026 mg/L (corresponding to 20 ppm) (control) in an exposure chamber in a cross-over design. The EEG was recorded before (reference) and at the end of each exposure with, the subject's eyes closed and opened and during a choice reaction test (colour word stress test). Spectral power was calculated by fast Fourier transformation. Subjective symptoms and effects of blinding with 20 ppm methanol were assessed by questionnaires. The study was a single-blind one. Endpoint addressed: acute toxicity: inhalation Endpoint addressed: neurotoxicity	During subjects' exposure to 0.26 mg/L, their scores for prenarcotic and irritating symptoms were not different from controls. In the closed-eye condition of subjects, the spectral power of the theta-band and of some electrodes of the delta-band was significantly less at the end of exposure to 0.26 mg/L, than that of controls. In the open-eye condition and during the color word stress test no significant changes were found. The changes in the theta-band suggest a slight excitatory effect of 0.26 mg/L methanol. The effect was weak, as scores of acute symptoms did not change.	2 (reliable with restrictions) weight of evidence **Test material (EC name): methanol**	Muttray, A. et al. (2001)

The exposure-related observations in humans (endpoint not specified or other) are summarised in the following table:

Table B.5-23. Exposure-related observations: endpoint not specified or other

Method	Results	Remarks	Reference
Study type: Information on methanol intoxication: pharmacology, clinical and laboratory findings, diagnosis and treatment. Details on study design: no data Endpoint addressed: not applicable	The authors review the pharmacology, clinical and laboratory findings, and pathology and pathophysiology of methanol intoxication. In addition, they discuss the differential diagnosis and treatment of acute intoxication, including the use of 4-methylpyrazole in preventing	2 (reliable with restrictions) supporting study **Test material (EC name): methanol**	Suit, P. and Estes, M.L. (1990)

Method	Results	Remarks	Reference
	the conversion of methanol to formate.		
Study type: Information on formic acid and methanol blood levels in various case studies which ended lethal. Details on study design: Collection of blood concentrations of formic acid and methanol from various case studies. Endpoint addressed: not applicable	During methanol poisoning in man the concentration of formic acid in the blood is quite variable. In 5 lethal cases it ranged from 9 to 68 mg per cent. In three patients who also died it ranged from 5.7 to 19 mg per cent. Furthermore, the methanol concentration in the blood in 23 lethal cases varied between 51 and 274 mg per cent. It becomes obvious that the mere concentrations of these substances are not the only decisive factors in the clinical course of the poisoning.	2 (reliable with restrictions) supporting study **Test material (EC name): methanol**	Roe, O. (1955)
Study type: Review on symptoms, clinical diagnosis, mechanisms and treatment of methanol poisoning in man. Details on study design: Review based on clinical experience with accidental and occupational methanol poisoning. Endpoint addressed: not applicable	Methanol poisoning is an uncommon but an extremely hazardous intoxication. Since methanol is a versatile fuel and is having increasing usage in an energy-conscious society, a high index of suspicion and swift laboratory confirmation is essential in managing this poisoning. Methanol poisoning may occur in sporadic or epidemic circumstances. Chronic exposure may occur in the occupational setting. Man is uniquely susceptible to methanol toxicity, perhaps dependent upon folate metabolism. Classic symptoms of methanol toxicity can only occur in laboratory animals who are rendered folate deficient. Folate may be useful in humans enhancing removal of the toxic products of methanol poisoning. The enzyme responsible for metabolism of methanol is alcohol dehydrogenase. Ethanol has a higher affinity for this enzyme and is preferentially metabolized. Simultaneous ethanol and methanol administration may confuse the onset of the intoxication. Pyrazoles may also be used to inhibit alcohol dehydrogenase thus preventing the intoxication. The most important initial symptom of methanol poisoning is visual disturbance. The symptoms may be delayed up to	2 (reliable with restrictions) supporting study **Test material (EC name): methanol**	Becker, C.E. (1983)

Method	Results	Remarks	Reference
	24 hours after ingestion due to simultaneous alcohol administration and metabolic processes. Laboratory evidence of severe metabolic acidosis with increased anion and osmolar gaps strongly suggest the clinical diagnosis. There may be an important association between mean corpuscular volume which is significantly higher in cases of severe methanol poisoning than in mild cases. Once the diagnosis is suspected, a blood level from methanol should be returned rapidly. Treatment of methanol toxicity after good supportive care is to diminish the metabolic degradation of methanol with simultaneous ethanol and then to perform hemodialysis and alkalinization to counteract metabolic acidosis. Folate should be administered to enhance metabolic breakdown of formate. Alcoholic patients may especially usceptible to methanol poisoning due to relative folate defiency.		
Report	Ingestion of 4-10 ml methanol may cause permanent blindness.		IPCS 2001
Case report, poisoning incident	A glass of 70% methanol, anatomical and functional ocular abnormalities, bilateral irreversible blindness.		Moschos et al. (2013)
Retrospective study, review of 122 patients	pH was the strongest predictor of final VA (visual acuity) and improvement in VA among all markers. The degree of acidosis at presentation appears to determine final VA . The mean (SD) amount consumed was 230 (57) mL (range, 100-700 mL). The proportion of methanol was 6.5% vol/vol in a 40% alcohol concentration. 10 patients died, 4 absconders, 11 asymptomatic, 7 other: 32 patients were left with severe permanent visual damage.		Desai et al. 2013

B.5.10.3. Summary and discussion of other effects

Specific investigations: other studies

In a study by Eells et al. (2000), rats were intraperitoneally dosed to methanol. In all of these animals, the folate dependent formate oxidation was inhibited. After the initial dosage of 4000 mg/kg bw, 12 hours later an injection of 1000 or 2000 mg/kg bw followed. Formic acidemia, metabolic acidosis and visual toxicity occurred (Eells et al., 2000). Histopathology demonstrated vacuolation in the photoreceptors, mitochondrial swelling and mitochondrial disruption in the retinal pigment epithelium, which were dependent on blood formate levels. However, functional changes could already be demonstrated by electroretinogram (ERG) and flash evoked cortical potential (FEP) in animals not showing morphological changes, 72 hours of recovery. These functional tests provide functional evidence of direct retinal toxicity in methanol poisoning at stages not yet pronounced in histopathological changes. The authors stated the hypothetical mechanism that formic acid binds to cytochrome aa3 and inhibits cytochrome oxidase activity with inhibition constant values rangigng between 5 and 30 mM, which is in the range of concentrations found in the retina and vitreous humour of methanol-intoxicated rats. This may explain the effect on mitochondria and resulting visual dysfunction (Eells et al., 2000).

Formate oxidation was found to be about 50% lower in human than in rat retina (Eells et al., 1995). This is in line with the finding that lower folate levels in human retina may limit conversion of formate into CO_2 and result in higher ocular toxicity in humans.

Rodents appear to be a useful model for elucidation of the effects of methanol intoxication in humans, although they are less sensitive than latter. This drawback can be circumvented by inhibition of formate oxidation in rodents.

A subacute oral toxicity study in monkeys indicated that repeated methanol dosing caused ocular lesions after a high initial dose of 2000 mg/kg bw followed by lower doses for up to 6 days, depending on the animal´s acidotic response in blood (Martin-Amat et al., 1977), while acute methanol toxicity did not yield signs of ocular toxicity (McMartin et al., 1975). The only detectable ocular change was optic disc edema (of the optic papilla) which was similar to that seen in raised intracranial pressure in humans, but without this pressure after methanol (Hayreh et al., 1977). The primary sites of ocular injury were the optic nerve heads and the anterior segment of the optic nerve rather than the retinal ganglion cells themselves. It appears that interference with oxidative phosphorylation causes mitochondrial damage, thus disruption of active axoplasmic flow in the retrolaminar optic nerve (Baumbach et al., 1977; Hayreh et al., 1977). Mechanistically, there is a close causal relationship between the prolonged increase in formic acid resulting ffrom methanol and the development of optic edema. Similar effects can be produced by intravenous administration of formate without acidosis (Martin-Amat et al., 1978).

Minimum dose causing permanent visual defects in humans is unknown. **Minimal lethal oral doses of methanol in humans are between 0.3 and 1.0 g/kg bw. However, as little as 15 ml of a 40% solution has resulted in death of one person.** Permanent visual defects are seen below lethal doses. In the retrospective study of 122 patient (Desai et al., 2013) the amount of ingested methanol varied between 6.5 ml and 45.5 ml, this corresponds to 0.07-0.51 g/kg bw for 70 kg person. Ten of those 122 died and one third were left with permanent

visual damage. According to IPCS (2001), acute ingestion of as little as 4 to 10 mL of methanol may cause permanent blindness (for 70 kg person this corresponds to 0.05-0.11 g/kg bw). Individual susceptibility varies widely and this may result from the frequent concurrent ingestion of ethanol and/or differences among individuals and populations in alcohol dehydrogenase (polymorphism).

B 5.11 Derivation of DNEL(s)/DMEL(s)

5.11.1. Overview of typical dose descriptors for all endpoints

Table B.5-24. Available dose-descriptor(s) per endpoint as a result of its hazard assessment

Endpoint	Route	Dose descriptor or qualitative effect characterisation; test type	Reference to selected study (see footnotes for justification)
Irritation / Corrosivity	skin	No adverse effect observed (not irritating)	
Irritation / Corrosivity	eye	No adverse effect observed (not irritating)	
Sensitisation	skin	No adverse effect observed (not sensitising)	
Repeated dose toxicity	oral	Target organs: neurologic: eyes (retina, optic nerve)	
Repeated dose toxicity	inhalation (systemic effects)	Target organs: cardiovascular / hematological: heart; neurologic: brain (multiple sections); digestive: liver	
Mutagenicity	in vitro / in vivo	No adverse effect observed (negative)	see section 5.7.1 / 5.7.2

B.5.11.2. Selection of the DNEL(s) or other hazard conclusion for critical health effects

The risk assessment carried out in this proposal is based on:
- estimation, based on literature methanol lethal dose in humans by oral route, the quantity of a mixture containing various concentrations of methanol, which will cause a fatal effect intake for humans. On the basis of calculated dose, taking into account a safety factor, it is proposed to establish limit for the methanol concentration in the mixtures available to consumers, at which the risk posed by the mixtures covered by this restriction is adequately controlled.

In addition, the risk assessment was also carried out on the basis of calculated in the registration dossier of methanol DNEL value for acute exposure after oral route (DNEL: Systematic effects - Acute).

Table B.5-25. Hazard conclusions for the general population

Route	Type of effect	Hazard conclusion
Inhalation	Systemic effects - Long-term	DNEL (Derived No Effect Level): 50 mg/m³
Inhalation	Systemic effects - Acute	DNEL (Derived No Effect Level): 50 mg/m³

Inhalation	Local effects - Long-term	DNEL (Derived No Effect Level): 50 mg/m³
Inhalation	Local effects - Acute	DNEL (Derived No Effect Level): 50 mg/m³
Dermal	Systemic effects - Long-term	DNEL (Derived No Effect Level): 8 mg/kg bw/day
Dermal	Systemic effects - Acute	DNEL (Derived No Effect Level): 8 mg/kg bw/day
Dermal	Local effects - Long-term	Low hazard (no threshold derived)
Dermal	Local effects - Acute	Low hazard (no threshold derived)
Oral	Systemic effects - Long-term	DNEL (Derived No Effect Level): 8 mg/kg bw/day
Oral	Systemic effects - Acute	DNEL (Derived No Effect Level): 8 mg/kg bw/day
Eyes	Local effects	Medium hazard (no threshold derived)

The Registrant of methanol defines DNELs on OEL value basis according to Appendix R.8-13 (Deriving DNELs when community/national Occupational Exposure Limit (OEL) is available) to Chapter R.8 (Characterization of dose [concentration]-response for human health of Guidance on information requirements and chemical safety assessment (ECHA).

The OEL (Commission Directive 2006/15/EC of 7 February 2006 establishing a second list of indicative occupational exposure limit values in implementation of Council Directive 98/24/EC and amending Directives 91/322/EEC and 2000/39/EC) value is 260 mg/m^3 (200 ppm). The MAK level in Germany is of similar magnitude (270 mg/m^3) and mainly built on the exposure-effect relations and the established innocous concentrations in humans; these are related to the limited capacity in humans to convert formic acid into CO_2. There is not much difference for this metabolic threshold after single or repeated exposure, hence, the OEL which is mainly based on singular experiences in humans is considered to be valid also for chronic exposure. The scientific rationale of the German OEL has been laid down in: Greim et al., loc. cit. Exposure to 260 mg/m3 during a working shift is roughly equivalent to a dose of 2.6 g/person/day (40 mg/kg b. w. and day) which may be considered as a systemic DNEL (40 mg/kg bw/day), too, if the dermal uptake is the same as from inhalation (which is a worst-case consideration neglegting also the high volatility of the material). The systemic inhalation DNEL is considered to be also protective from local irritation.

For the general population, e. g. customer exposure, the workplace DNELs are divided by 5 in order to take into account possible higher sensitivities and possible longer exposure duration.

B.6 Human health hazard assessment of physico-chemical properties

Not relevant for this dossier

B.7 Environmental hazard assessment

Not relevant for this dossier

B.8 PBT and vPvB assessment

Not relevant for this dossier

B.9 Exposure assessment

B.9.1 General discussion on releases and exposure

B.9.1.1 Summary of the existing legal requirements

Methanol is listed by Index number 603-001-00-X in Annex VI, Part 3, Table 3.1 (list of harmonised classification and labelling of hazardous substances) of Regulation (EC) No 1272/2008 (detail information about classification and labelling of methanol are included in chapter B.3.1).

According to Annex II, Part 3 of Regulation (EC) No 1272/2008, containers of whatever capacity of substances or mixtures, having a methanol in a concentration equal to or greater than 3%, which are supplied to the general public, are to be fitted with child-resistant fastenings.

Occupational safety and health - related legislation

The Framework Directive (Directive 89/391 on the introduction of measures to encourage improvements in the safety and health of workers at work) defines the general obligation of the employer in relation to health and safety of workers. On the basis of this Directive, the risk assessment has to be conducted for all activities including use of or exposure to methanol. Appropriate risk management measures would have to be provided, according to the hierarchy of control principles. The risk assessments would have to be documented and periodically reviewed. Workers have to be provided with information and training in relation to use of the substance to and safe work practices. The provisions of the Framework Directive in relation to exposure to chemical substances are reinforced by the Directive 98/24/EC (Chemical Agents Directive - CAD). It 'lays down minimum requirements for the protection of workers from risks to their safety and health arising, or likely to arise, from the effects of chemical agents that are present at the workplace or as a result of any work activity involving chemical agents.' In the directive, 'hazardous chemical agents' are defined as:

"*any chemical agent which meets the criteria for classification as a dangerous substance according to the criteria in Annex VI to Directive 67/548/EEC, whether or not that substance is classified under that Directive, other than those substances which only meet the criteria for classification as dangerous for the environment;*
(ii) any chemical agent which meets the criteria for classification as a dangerous preparation within the meaning of Directive 88/379/EEC, whether or not that preparation is classified under that Directive, other than those preparations which only meet the criteria for classification as dangerous for the environment;
(iii) any chemical agent which, whilst not meeting the criteria for classification as dangerous in accordance with (i) and (ii), may,because of its physico-chemical, chemical or toxicological properties and the way it is used or is present in the workplace, present a risk to the safety and health of workers, including any chemical agent assigned an occupational exposure limit value under Article 3."

Methanol fulfils the classification criteria and therefore any risk to the safety and health arising from its presence must be assessed. The employer must conduct and document an assessment of the risk, in accordance with Article 9 of the Framework Directive. Substitution is the preferred method of controlling the risk. This assessment must be regularly reviewed and updated, particularly if there have been changes to work practices or if the results of health surveillance show it to be necessary.

Directives 91/322/EEC, 2000/39/EC and 2006/15/EC list indicative occupational limit values (OELs). They serve as benchmarks in evaluating workers' exposure to chemical substances. Indicative OEL values are health-based and non-binding. On their basis, the Member States must establish national occupational exposure limit values for the chemical agents listed. They must take into account the Community values, but may determine their national value in accordance with national legislation and practice.

The employer must regularly measure exposure to chemical agents which may present a risk to workers' health and must immediately take steps to remedy the situation if the occupational exposure limit values are exceeded.

Methanol is included in the list of OELs in the Directive 91/322/EEC with the eight hour exposure limit set at 260 mg/m^3 (200 ppm).

B.9.1.2 Summary of the effectiveness of the implemented operational conditions and risk management measures

Currently no general EU-wide restriction of methanol or mixtures containing methanol is in force. Methanol or mixtures containing methanol are not included in Annex XVII (Restrictions on the manufacture, placing on the market and use of certain dangerous substances, mixtures and articles) to REACH Regulation. The classification of methanol is revised by Italian CA in view of a possible classification also as toxic to reproduction Cat. 2 (according to DSD) or 1B (according to CLP Regulation).

It should be highlighted that in some countries like, Scandinavian countries except Finland, Germany, Austria or Lithuania exists a national restriction which prohibits the selling of methanol to the general public. The restriction is part of a national restriction which in general prohibits the selling of mixtures classified as acute toxic and labelled as "toxic" (T and T+) to the general public.

According to the Danish Statutory Order No. 1075 of 24/11/2011 "classification, packaging, labeling, sale and storage of substances and mixtures" (Survey on methanol; Danish Ministry of Environmental):
- it is not allowed to sell products labeled "toxic" to people under the age of 18. With certain exceptions they are not allowed to be sold to the general public either and they are submitted to the rules regarding requisition to use toxic substances. A product must be labeled as "Danger: Causes damage to organs" ("Toxic") if it contains ≥ 10% methanol,
- Very toxic and toxic substances and mixtures are allowed to be sold to hospitals, laboratories, doctors, dentists, etc.

According to the Danish Statutory Order No 857 of 05/09/2009 on "restricting the use of certain dangerous chemical substances and products for specific purposes", methanol is not allowed for use in deicing fluids (washing fluids) – except for water-methanol mix solutions, which are allowed to be used in aircrafts. Methanol is furthermore not allowed for use in engine coolants or in solutions used for preventing the freezing of carburetors – except for water-methanol solutions, which are allowed to be used in aircrafts. The Statutory Order is only valid in Denmark.

B.9.2 Manufacturing

B.9.2.1 Occupational exposure

Not relevant for this proposal.

B.9.2.2 Environmental release

Not relevant for this proposal.

B.9.3 "Consumer use of products containing methanol – use of windshield washer fluids."

B.9.3.1 General information

According to the lead registrant of methanol, the Chemical Safety Report (CSR) and the relevant exposure scenarios are based on the identified uses in accordance with Article 3 (26) of REACH. By definition the identified uses correspond to a particular supply chain. Uses which are not covered by the CSR can be reported by a downstream user in the supply chain in accordance with Article 37 (2) and then become identified uses. The upstream suppliers must then evaluate this use in the context of Article 37. Alternatively, the downstream user can operate directly under Article 37 (4).

In the registration dossier of methanol, the registrant included, inter alia, the following exposure scenario: "Application of cleaning agents and de-icers as liquid non-spray products". For the use of cleaning agents (or de-icers) containing methanol the use of ready-to-use products for which no dilution and mixing steps are necessary was assumed. Furthermore, it is assumed that cleaning agents containing methanol are only sold within cleaners intended for cleaning/de-icing small surfaces (e.g. windshields) and thus small packaging sizes are assumed. According to the Consexpo 4.1 model calculation performed by registrant, the risk characterisation ratios (RCRs) are below 1 indicating no concern for human health while the highest concentration of substance in liquid products is equal to 2.5 % w/w. This value differs from methanol maximum concentration in mixtures, covered with the restriction, proposed in this application, and this is a result of different routes of exposure. The value specified in the registration dossier applies to inhalation exposure route and dermal exposure, while the proposed restriction applies to oral exposure to methanol and mixtures containing methanol (windshield washing fluid, denaturated alcohol containing methanol).

In the exposure scenario, in registration dossier for methanol, dermal and inhalation route was assessed. Such exposure scenario is not useful for restriction proposal because of the different route of exposure. Consumers' oral exposure only applies to accidental or intentional intake of products containing methanol, and these situations did not have to be included in the exposure scenarios in the registration dossier of methanol.

In the restriction dossier the following scenario is discussed: consumer poisoning caused by swallowing windshield washing fluid containing methanol. In some countries in European Union (Italy, Poland, Finland, Slovakia – detail information in section E) a significant number of poisoning cases by ingestion of mixture containing methanol (for example windshield washer fluids containing high concentration of methanol) or to ingestions of spirits adulterated with methanol was registered.

Windshield washing fluids (also called windshield wiper fluid, wiper fluid, screen wash (in the UK), or washer fluid) is a fluid for motor vehicles that is used in cleaning the windshield

with the windshield wiper while the vehicle is being driven. Windshield washer fluid is sold in many formulations, and some may require dilution before being applied, although most solutions available in most countries come premixed with no diluting required. Winter windshield washing fluids contain alcohol which prevents their freezing in temperatures below zero. Ethanol is the most common alcohol contained in these products, however it may be also methanol or propanol or their mixtures.

B.9.3.2 Exposure estimation

B.9.3.2.1 Workers exposure

Not relevant for this dossier.

B.9.3.2.2 Consumer exposure

Conditions of use**:** ingestion of windshield washing fluid containing methanol.

Exposure: Oral route

Concentration of methanol in windshield washing fluid**:** up to 60 - 70%

Concentration of methanol in liquid products declared by registrant amounts to 2.5% w/w. However, data from Polish product register show concentration of methanol in cleaning products up to 40%. Moreover, Finnish data (FIOH, 2008) demonstrate even 60% solutions present on the market. According to the Finnish data (FIOH, 2008) in 2006, there were approximately 48 windshield washing fluids containing methanol on the market in Finland and 41 of these contained 23-60% methanol. In 2012 there were 44 windscreen washing fluids containing methanol on the Finnish market and 39 of these contained 23 - 70% of methanol showing no change on the market (Finnish Chemical Products Register 2013). In Poland, during the period when methanol was not restricted in products for consumers, there were 47 suppliers of winter windshield washing fluids containing methanol in toxic concentrations, higher than 3%. Together they plased on the market 113 different windshield washing fluids, however in some cases the package of different volume was counted as a different product. The internet search and information from acute poisoning centers show that there were at that time at least three suppliers of denaturated alcohol containing methanol in concentration above 3%.

B 9.3.2.3 Indirect exposure of humans via the environment

Not relevant for this dossier.

B.9.3.2.4 Environmental exposure

Not relevant for this dossier.

B.9.4 Other sources (for example natural sources, unintentional releases)

Not relevant for this dossier.

B.9.5 Overall environmental exposure assessment

Not relevant for this dossier.

B.9.6 Combined human exposure assessment

Not relevant for these dossier.

B.10 Risk characterisation

B.10.1 **"Consumer use of products containing methanol – use of windshield washer fluids."**

B.10.1.1 Human health

B.10.1.1.1 Workers

Not relevant for this dossier.

B.10.1.1.2 Consumers

The aim of the proposed restriction is to eliminate poisonings caused by consumption of windshield washing fluids and denaturated alcohol containing high concentrations of methanol (up to 40-50% based on weight) by individuals chronically abusing alcohol. In case of these individuals those products are used as a surrogate of ethanol, due to financial reasons in particular – the taxation of alcohol in these products is considerably lower than in consumable alcohol and hence they are significantly cheaper than ethanol supplied for consumption. Substitution of ethanol in these products by methanol makes their price even cheaper and more easealy available to those persons.

According to the literature (Tephly T.R., 1991) minimal lethal oral doses of methanol in humans are between 0.3 and 1.0 g/kg bw, however as little as 15 ml of a 40% solution has proven deadly. However they are persons resisting ingestion of very big amounts of methanol. The minimum dose causing permanent visual defects is unknown.

For calculation of doses of windshield washing fluids or denaturated alcohol containg methanol which can result in death to humans, the following assumptions were taken into account:
- lethal oral doses of methanol in humans by oral route: 0.3 g/kg bw (due to the well documented in the literature (Tephly T.R., 1991) lethal oral doses of methanol in humans, these value was firstly taken in calculation of doses of windshield washing fluids containing methanol which can result in death to humans instead of mentioned in section B.10.1.1.2 value of DNEL: oral systemic & local given in the registration dossier of methanol)
- body weight: 70 kg person
- density of methanol at 20°C: 0.792 g/ml

Taking into account these information the lethal oral dose for a 70 kg person was calculated: 26.5 ml. This value was used to calculate the lethal oral dose of windshield washing fluids containing different concentrations of methanol. The calculations are summarized in the table below.

Table B.10-1. The lethal oral dose of windshield washer fluids depends on concentrations of methanol.

Concentration of methanol in windshield washer fluid (% w/w)	The lethal oral dose of windshield washing fluids (ml)
0,5	5303
1	2651
1,5	1767
2	1325
2,5	1060
3	883
4	662

5	530
6	441
7	378
8	331
9	294
10	265
11	241
12	220
13	203
14	189
15	176
16	165
17	155
18	147
19	139
20	132
21	126
22	120
23	115
24	110
25	106
30	88
35	75
40	66
45	58
50	53
55	48
60	44
65	40
70	37

Pursuant to article 69(4) of REACH Regulation, if a Member State considers that the manufacture, placing on the market or use of a substance on its own, in a preparation or in an article poses a risk to human health or the environment that is not adequately controlled and needs to be addressed it may prepare a dossier concerning a restriction which conforms to the requirements of the relevant sections of Annex XV to REACH Regulation.

Consumption of 25 ml of mixture containing 3.0% methanol (e.g. winter windshield washer fluids or denaturated alcohol) in a single dose by an adult person weighing 70 kg, results in the situation where the risk to people is not adequately controlled as the exposure value (0.75 g) is greater than DNEL value (0.56 g) specified in the registration dossier.

DNEL (derived no-effect level) value specified in the registration dossier for methanol – oral route; short-term exposure (acute toxicity) was also used to perform risk characterisation in relation to the considered exposure scenario ‘Consumer use of products containing methanol – use of windshield washer fluids’:

a)

DNEL = 8 mg/kg bw/day

DNEL value for an adult person weighing 70 kg, assuming that the methanol dose is drunk in a single dose

DNEL = 560 mg = 0.56 g

The performed risk characterisation also covered comparison of exposure of the human population which is known to be under the risk (alcoholics for whom windshield washing fluids or denaturated alcohol containing methanol are surrogate of ethanol due to financial reasons in particular) to the appropriate DNEL value.

Estimation of the exposure limit value ($Exposure_{(x\%\ MeOH)\ solution}$) for mixtures containing 'x%' of methanol.
Assumptions:
- lethal dose of methanol: 0.3 g/kg /bw
- weight of adult person: 70 kg
Lethal dose of methanol for adult person weighing 70 kg: 0.3 g/kg /bw x 70 kg = 21.0 g
$Exposure_{(x\%\ MeOH\ solution)}$ = (21g x %)/100

Table B.10-2. Exposure of adult person (70 kg) during drinking windshield washer fluids containing different concentrations of methanol.

Concentration of methanol in windshield washer fluid (% w/w)	$Exposure_{(x\%\ solution\ MeOH)}$	$Exposure_{(x\%\ solution\ MeOH)}$/DNEL
0.5	0.105	**< 1**
1	0.21	**< 1**
1.5	0.315	**< 1**
2	0.42	**< 1**
2.5	0.525	**< 1**
2.6	0.546	**< 1**
2.7	0.567	**> 1**
2.8	0.588	**> 1**
2.9	0.609	**> 1**
3.0	0.63	**> 1**
3.5	0.735	**> 1**
4.0	0.84	**> 1**
5.0	1.05	**> 1**

b)

DNEL = 8 mg/kg bw/day

DNEL value, assuming that the dose of methanol is drunk in a single dose

DNEL = 8 mg/kg bw

The performed risk characterisation covered comparison of exposure of human population known to be at risk (individuals chronically abusing alcohol for whom windshield washing fluids or denaturated alcohol containing methanol are surrogate of ethanol mainly due to financial reasons) to the appropriate DNEL value.

Estimation of the exposure limit value ($Exposure_{(x\%\ MeOH)\ solution}$) for mixtures containing 'x%' of methanol.
Assumptions:
- lethal dose of methanol: 0.3 g/kg bw = 300 mg/kg bw
$Exposure_{(x\%\ MeOH\ solution)}$ = (300 mg x %)/100

Table B.10-3. Exposure to windshield washer fluids containing different concentrations of methanol.

Concentration of methanol in windshield washer fluid (% w/w)	$Exposure_{(x\%\ roztwór\ MeOH)}$	$Exposure_{(x\%\ roztwór\ MeOH)}$/DNEL
0.5	1.5	**< 1**
1	3	**< 1**
1.5	4.5	**< 1**
2	6	**< 1**
2.5	7.5	**< 1**
2.6	7.8	**< 1**
2.7	8,1	**> 1**
2.8	8.4	**> 1**
2.9	8.7	**> 1**
3.0	9	**> 1**
3.5	10.5	**> 1**
4.0	12	**> 1**
5.0	15	**> 1**

The above mentioned calculation apply also to denaturated alcohol containing methanol.

B.10.1.1.3 Indirect exposure of humans via the environment

Not relevant for this dossier.

B.10.1.1.4 Combined exposure

Usually in the products proposed to be restricted there is combined exposure to methanol and ethanol. As it was mentioned earlier ethanol to some extend protects against acute poisoning with methanol. Ethanol is also used as a first measure in curing acute poisonings with methanol.

B.10.1.2 Environment

B.10.1.2.1 Aquatic compartment (including sediment and secondary poisoning)

Not relevant for this dossier.

B.10.1.2.2 Terrestrial compartment (including secondary poisoning)

Not relevant for this dossier.

B.10.1.2.3 Atmospheric compartment

Not relevant for this dossier.

B.10.1.2.4 Microbiological activity in sewage treatment systems

Not relevant for this dossier.

B.11 Summary on hazard and risk

Lethal oral dose of windshield washing fluids containing different concentrations of methanol was calculated (see Table B.10-1). The evaluation, performed by dossier submitter on the basis of lethal oral doses of methanol in humans, indicates a risk for the human health if consumer swallowing windshield washing fluids containing high doses of methanol. If

windshield washing fluids contain about 30% w/w of methanol, the dose which can result in death of person (adult, 70 kilograms) is only 90 ml. These calculation clearly shows that there is a need to introduce restriction which reduce the concentration of methanol in products available for consumers. Based on dossier submitter previous expierience (in Poland till 1 June of 2010 the placing on the market for general public mixtures containing methanol in the concentration higher than 3.0% by weight was banned by Regulation of Ministry of Economy) and based on the specific concentration limit specified for methanol in Table 3.2 in Annex VI to CLP, it is propose to establish maximum concentration of methanol in mixtures available for general public at level of 3.0% w/w. For windshield washing fluids containing methanol in concentration of 3.0 % w/w, lethal oral dose is approximetaly, according to Table B.10-1, 900 ml. There is little likelihood of drinking such high doses of windshield washing fluids or denaturated alcohol.

Moreover, as was mentioned above, specific concentration limits (SCL) for methanol are reported in Annex VI to CLP:

Concentration	Classification
C ≥ 20 %	T; R23/24/25-39/23/24/25
10 % ≤ C < 20 %	T; R20/21/22-39/23/24/25
3 % ≤ C < 10 %	Xn; R20/21/22-68/20/21/22

According to SCL found in Annex VI to CLP, mixtures which contains methanol in concentration lower than 3.0% are not classified for acute toxicity. Introducing such restriction, which determines maximum concentration of methanol in mixtures (windshield washing fluids and denaturated alcohol) available for general public, probably will solve problems with death of several hundred people due to methanol poisoning.

The proposed maximum concentration limit of methanol in mixtures available to consumers (windshiekd washing fluids and denaturated alcohol) - 3% is also confirmed by the performed risk characterisation in which DNEL value presented in the methanol registration dossier has been applied. In accordance with Annex I to REACH Regulation the risk to people may be adequately controlled, if during the stages of existence of substances which are outcomes of the manufacture or identified uses the levels of exposure do not exceed appropriate DNEL values. In accordance with Table B.10-2 and Table B.10-3, with methanol concentration in fluids for windshields reaching approximately 2.7% the calculated exposure value exceeds DNEL value, thus it may be stated that the risk is not adequately controlled. This value is close to the value of 3.0% calculated based on the lethal methanol value to human population per os (0.3 g/kg bw), which is cited in the literature, and on the assumption that there is little likelihood that the windshield fluid is drunk in a single dose of 900 ml. The same calculations apply to denaturated alcohol containing methanol.

In this restriction the concentration limit of methanol in mixtures available to consumers (windshield washing fluids and denaturated alcohol) has been proposed at the level of 3.0%. As stated above, this value was determined on the basis of the calculations based on the lethal methanol value to human population per os (0.3 g/kg bw) which is cited in the literature, and on the assumption that there is little likelihood that the windshield fluid or denaturated alcohol are drunk in a single dose of 900 ml. The proposed concentration value is insignificantly higher than the value calculated based on the DNEL value proposed in the registration dossier (2.7% - Table B.10-2 and Table B.10-3). The decision on proposing the value of 3.0% has been made after comparing DNEL value for methanol after oral acute exposure for a person weighing 70 kg which has been specified in the registration dossier – 0.56 g to the value (minimal – the worst case) of methanol lethal dose for a person weighing 70 kg cited in the literature – 21.0 g (DNEL value specified in the registration dossier is smaller by two orders

of magnitude than the methanol lethal dose for a person weighing 70 kg which is cited in the literature).

C. Available information on alternatives

C.1 Identification of potential alternative substances and techniques

Methanol is contained as a solvent in products such as paints, sealers, and adhesives, which may be available to consumers and used in car care, hobbies, crafts and home maintenance. The following table lists the main uses of methanol and possible use areas.

Table C.1-1. Major uses of methanol products for both consumers and professionals.

USE	CONTEXT
As a component in paints	Professionals/Consumers
Component in paint strippers	Professionals/Consumers
Antifreeze	Professionals
Component in liquid wipers	Professionals/Consumers
Air fresheners	Professionals/Consumers
Component in household detergents	Consumers
In models (fuel for internal combustion engines, paints)	Consumers
In the biofuel production	Professionals/Consumers
Silanic adhesives/sealants	Professionals/Consumers
Liquid fire starters	Consumers
As a component of windscreen fuids	Professionals/Consumers

The substitution of methanol in different formulations (mixtures) is usually obtained with denatured ethanol or isopropanol. It is clear that less toxic than methanol alternatives are available. It is also clear that replacement of methanol in mixtures supplied for general public vovered by this restriction (windshield washing fluids and denaturated alcohol) by ethanol or isopropanol could have the effect of increasing the cost of such mixtures.These issue is discussed in details in Section F “Socio-economic Assessment of Proposed Restriction”.

In this section – Assessment of alternative, the dossier submitter focused on ethanol and isopropanol as a alternative substance.

In Finland, ethanol and isopropanol are used in windscreen washing fluids already in high tonnages.

Table C.1-2 Tonnage placed on the market in Finland in windscreen washing fluids from year 2002 to 2012 (Finnish Chemical Products Register 2013).

	Methanol	Ethanol	Isopropanol
2002	1326	3474	4323
2003	1565	4061	4106
2004	904	5606	3043
2005	1334	4743	1995
2006	1745	5061	2811

2007	1358	5095	2617
2008	1127	5952	1927
2009	1246	6594	2892
2010	1748	6353	1187
2011	2559	7707	1746
2012	935	4382	702

In 2012, according to the Finnish Chemical Products Register, there were windscreen washing fluids on the Finnish market as follows:

- methanol containing: 44 products (39 contained methanol from 23 to 70%)
- ethanol containg: 92 products (83 contained ethanol from 20 to 100 %)
- isopropanol containing: 67 products (35 products contained isopropanol from 20 to 100%).

C.2 Assessment of alternative 1: Ethanol

C.2.1 Availability of alternative 1: Ethanol

Ethanol, as alternative substance, is easily available on the market. According to the information found on ECHA Website more than 400 hundred producers and importers registered ethanol during first and second deadline for registration (http://apps.echa.europa.eu/registered/data/dossiers/DISS-9d8b4df8-d70a-6e6b-e044-00144f67d249/DISS-9d8b4df8-d70a-6e6b-e044-00144f67d249_DISS-9d8b4df8-d70a-6e6b-e044-00144f67d249.html). Based on that information it can be concluded that ethanol is available in the required tonnage in EU to be alternative substance to methanol in mixtures available to consumers cover by proposed restriction.

C.2.2 Human health risks related to alternative 1: Ethanol

Currently, there is no validated risk assessment for ethanol at the European level. Ethanol has been evaluated under the OECD SIDS initial assessments for HPV chemicals programme. Ethanol is readily absorbed by the oral and inhalation routes and subsequently, metabolized and excreted in humans. At exposures relevant to occupational and consumer exposure during manufacture and use of ethanol containing products, the alcohol dehydrogenase metabolic route in the liver dominates and does not become saturated. This mechanism follows first order kinetics. The first step of the metabolic path is the rate-determining step; concentrations of the intermediate metabolite acetaldehyde are very low. Ethanol is not accumulated in the body. Dermal uptake of ethanol is very low. Ethanol has a low order of acute toxicity by all routes of exposure. Ethanol is a moderate eye irritant but is neither a skin irritant nor a sensitizer. For repeat dose effects, the lowest reported NOAEL is approximately 2400 mg/kg bw/day from a dietary study with rats. At higher doses, male rats showed minor changes to organ weights and haematology/biochemistry; female rats showed minor biochemistry changes and increased length of oestrus cycle along with liver nodules; adverse liver effects were observed at concentrations of 3600 mg/kg.bw/day and above.
The balance of evidence is that ethanol is not genotoxic. Negative results from a number of bacterial mutation assays appear to be reliable. Of the mammalian cell mutation assays a weak mutagenic effect in mouse lymphoma cells occurred only at very high ethanol concentrations.

In vivo tests for chromosome aberrations in both rats and Chinese hamsters have given negative results. There is very little evidence to suggest that ethanol is genotoxic in somatic cells and it may have a very limited capacity to induce genetic changes in vivo but under very specific circumstances and at very high doses achievable in humans only by deliberate oral ingestion. Evidence of the carcinogenicity of ethanol is confined to epidemiological studies assessing the impact of alcoholic beverage consumption. These do not indicate any such hazard exists from potential exposure to ethanol in the work place or from the use of ethanol in consumer products. No fertility or developmental effects were seen at inhalation exposures up to 16000 ppm (30,400 mg/m^3). The lowest reported NOAEL for fertility by the oral route was 2000 mg/kg bw in rats, equivalent to a blood alcohol concentration of 1320 mg/l, although this was based on a significant increase in the number of small pups rather than a direct effect on fertility; such direct effects are not seen until much higher doses. Many studies exist examining the developmental end point for ethanol. However, most use very high doses and few are individually robust enough to allow a NOAEL to be established. However, the collective weight of evidence is that the NOAEL for developmental effects in animals is high, typically >=6400mg/kg bw, compared to maternally toxic effects at 3600 mg/kg bw. The potential for reproductive and developmental toxicity exists in humans from deliberate over-consumption of ethanol. Blood ethanol concentrations resulting from ethanol exposure by any other route are unlikely to produce reproductive or developmental effects.

Ethanol is included in Annex VI (a list of substances with harmonized classification and labeling at EU level) to Regulation No 1272/2008. Ethanol is not classified for health hazard. The reduction of the consumer exposure achieved by the adoption of the herewith proposed restriction (using ethanol instead of methanol in some products available for consumers or significantly decreasing the percentage of methanol in some products available for consumer) would significantly minimize both the recurrence of cases of poisoning by ingestion of methanol or methanol containing products.

Replacement of methanol with ethanol in some products available for consumers will not causing other risk that can not be adequately controlled.

C.2.3 Environment risks related to alternative 1: Ethanol

Currently, there is no validated risk assessment for athanol at the European level. As a result, it is not possible to assess the environmental risks related to that alternative. It should be highlighted that ethanol is not classified as hazardous to the environment. According to the information available in the registration dossier ethanol does not fulfil PBT/vPvB criteria of REACH Annex XIII.

Based on these information it can be concluded that using ethanol as alternative to methanol in mixtures available to consumers cover by proposed restriction does not pose any environmental risk.

C.2.4 Technical and economic feasibility of alternative 1: Ethanol

No problem related to technical feasibility is foreseen as the ethanol is already available and authorised in Europe. Ethanol can performe the same function as methanol in windshield washing fluids available for consumers. The application of ethanol instead of methanol in

windshield washing fluids available for consumers will not required changing in process formulation. The application of methanol in winter windshield washing fluids instead of ethanol does not also impact end parameters of the product. Regardless whether methanol or ethanol is applied, the product can be used in the same temperature ranges. In the table below it is presented the content of some winter windshield washer fluids available on Polish market produced by the same manufacturer. The table C.2.4-1 clearly indicate technical feasibility of application of ethanol as an alternative to methanol.

Table C.2.4-1. Composition of some winter windshield washer fluids available on Polish market (source: Safety Data Sheets).

	Ingredients	Concentration %	Crystallization temperature (°C)
Winter windshield washer fluids No 1	Ethanol	< 30	-22
	Methanol	< 2.7	
	Ethylene glycol	< 1	
Winter windshield washer fluids No 2	Ethanol	< 8	-20
	Methanol	< 20	
	Isopropanol	< 5	
Winter windshield washer fluids No 3	Ethanol	15 - 20	-20
	Methanol	3 - 10	
	Ethylene glycol	< 2	

It is also clear that replacement of methanol with ethanol could have the effect of increasing the cost of the mixtures previously formulated with this substance. The increase of cost of such mixtures will depend on the amount of ethanol needed to replace the previous amount of methanol. In some cases it is hard to estimate precise increase of costs of a single pack of windshield washing fluid as safety data sheets very often provide concentration ranges, which are frequently presented in the following form < 30% or 1 – 30%. An analysis of windshield washer fluids available on the Polish market indicates that in the case of a 5 litre pack, replacing methanol with ethanol will result in approx. doubling the product price.

The table below provides an indication of costs in euro/ton for methanol, ethanol and isopropanol.

Table C.2.4-2. The cost of methanol and some alternatives to methanol.

Substance	**Price €/ton**
Methanol	390 (May 2013)
Ethanol	921 (June 2008)
Isopropanol	995 (June 2008)

The cost of alternatives to methanol is about 2.5 times that of methanol. It is also important to underline that methanol is one of the substance of lower cost among organic products.
Cost of mixtures containing methanol and mixtures containing ethanol covered by the restriction will be discussed in details in Section F “Socio-economic Assessment of Proposed Restriction”.

This assessment is not necessary for denaturated alcohol.

C.2.5 Other information on alternative 1: Ethanol

Consumers are widely exposed to ethanol. Products containing ethanol include personal hygiene products, fragrances, cosmetics, adhesives, surface coatings and inks. All routes of exposure (oral, dermal and inhalation) are feasible for these products as a whole but not all routes apply to all products.

Ethanol is unusual in that it also occurs naturally within the body. This natural burden is thought to be due to the metabolism of the intestinal microflora and produces blood alcohol concentration (BAC) levels of typically 0.062 to 0.73 mg/l (Sprung, 1981).

C.3 Assessment of alternative: 2-Propanol

C.3.1 Availability of alternative: 2-Propanol

2-Propanol (Isopropanol, IPA), as alternative substance, is easily available on the market. According to the information found on ECHA Website the tonnage band registered is 100,000 - 1,000,000 tonnes per annum as joint submission. The identified uses include de-icing and anti-icing applications namely anti-freeze and de-icing products for consumers.

Based on that information it can be concluded that 2-propanol is available in the required tonnage in EU to be used as an alternative substance to methanol in windscreen washing fluids.

C.3.2 Human health risks related to alternative 2: 2-Propanol

The harmonised classification of 2-propanol according to the CLP Regulation (1272/2008) is Flam Liq. 2 H225, Eye Irrit. 2 H319, STOT SE 3 H336.

2-Propanol (Isopropanol, IPA) was assessed in the OECD SIDS program and published as a UNEP Publication in 1997 (UNEP 1997). The following information is from the summary of that publication.

Acute Toxicity and Primary Irritancy
Isopropanol has a low order of acute toxicity. It is irritating to the eyes, but not to the skin. Very high vapor concentrations are irritating to the eyes, nose, and throat, and prolonged exposure may produce central nervous system depression and narcosis. Human volunteers reported that exposure to 400 ppm isopropanol vapors for 3 to 5 min. caused mild irritation of the eyes, nose and throat. Although isopropanol produced little irritation when tested on the skin of human volunteers, there have been reports of isolated cases of dermal irritation and/or sensitization. The use of isopropanol as a sponge treatment for the control of fever has resulted in cases of intoxication, probably the result of both dermal absorption and inhalation. There have been a number of cases of poisoning reported due to the intentional ingestion of isopropanol, particularly among alcoholics or suicide victims. These ingestions typically result in a comatose condition. Pulmonary difficulty, nausea, vomiting, and headache accompanied by various degrees of central nervous system depression are typical. In the absence of shock, recovery usually occurred.

Effects Resulting from Repeated Exposure

The systemic (non-cancer) toxicity of repeated exposure to isopropanol has been evaluated in rats and mice by the inhalation and oral routes. The only adverse effects-in addition to clinical signs identified from these studies were to the kidney. Rats exhibited an accumulation in hyaline (protein) droplets in kidney proximal tubule cells (males only, subchronic exposure) and an exacerbation of chronic progressive nephropathy, a spontaneous disease of unknown etiology common in aged rats (males and females, chronic exposure). In the mouse, minimal to mild effects to the kidney including renal tubular proteinosis and tubular dilation were observed following chronic exposure. The incidence of renal tubular proteinosis was generally significantly increased for all male and female treatment groups relative to controls; however, the majority of affected animals showed minimal degrees of tubular proteinosis (i.e., only a few tubules affected), there was no concentration-related gradient in either the frequency of severity of this change, and there was no corresponding evidence of alterations to the glomeruli. Mild to moderate degrees of tubular dilation were observed in a small number of females in the 2500 and 5000 ppm groups (significantly increased only for the 5000 ppm group). This finding, however, was not duplicated in male mice (a significant increase was only seen for the 500 ppm group) nor was it accompanied by evidence of tubular cell degeneration or urinary outflow obstruction.

Effects on Reproductive Capabilities

A recent two-generation reproductive study characterized the reproductive hazard for isopropanol associated with oral gavage exposure. This study found that the only reproductive parameter apparently affected by isopropanol exposure was a statistically significant decrease in male mating index of the F_1 males. It is possible that the change in this reproductive parameter was treatmentrelated and significant, although the mechanism of this effect could not be discerned from the results of the study. However, the lack of a significant effect of the female mating index in either generation, the absence of any adverse effect on litter size, and the lack of histopathological findings of the testes of the high-dose males suggest that the observed reduction in male mating index may not be biologically meaningful. Additional support for this conclusion is provided by the fact that most of the females became pregnant. Furthermore, male and female fertility, and female fecundity indices of rats dosed with isopropanol were not different from those of controls by statistical analysis and were within, or relatively close to, historical control values. No reproductive effects were noted in other studies in which rats were dosed up to 2% in the drinking water. Exposure to 1000 mg/kg/day and to a lesser extent 500 mg/kg/day did result in a reduction in postnatal survival in both F1 and F2 litters. Derivation of an appropriate NOAEL for offspring effects was made difficult because of conflicting interpretations of the reductions in postnatal survival for the 500 mg/kg/day treatment group. The U.S. EPA (1992) and Tyl (1996) concluded the reductions were treatment- and dose-related, a conservative interpretation that supports a NOAEL of 100 mg/kg/day. Alternatively, Bevan *et al.* (1995) and Harris (1995) deemed the observations not to be biologically significant and concluded the NOAEL to be 500 mg/kg/day. In order to clarify this issue a benchmark dose (BMD) assessment was conducted for the study's developmental and reproductive findings (Shipp *et al.,* 1996). For the offspring developmental effects, BMD dosages ($BMDL_5$) of 449 and 418 mg/kg/day were estimated for the F1 and F2 generations, respectively. Based upon the decrease in male mating index observations in the P2 males, a $BMDL_{10}$ of 407 mg/kg/day was estimated for reproductive effects.

Effects on Developmental Toxicity

The developmental toxicity of isopropanol has been characterized in rat and rabbit developmental toxicity studies and in a rat developmental neurotoxicity study. The rats were dosed by oral gavage at 400, 800 or 1200 mg/kg from gestational days 6 through 15. The rabbits were dosed by oral gavage at 120, 240 or 480 mg/kg from gestational days 6 through 18. These studies indicate that isopropanol is not a selective developmental hazard. Isopropanol produced developmental toxicity in rats, but not in rabbits. In the rat, the developmental toxicity occurred only at maternally toxic doses and consisted of decreased fetal body weights, but no teratogenicity. These data suggest the developmental NOAEL is 400 mg/kg/day for rats and 480 mg/kg/day for rabbits. Isopropanol has also been tested for developmental toxicity in rats via oral gavage. The rats were dosed at 200, 700 and 1200 mg/kg from gestational days 6 through 21. No exposure-related effects were noted on motor activity, weights of the four regions of the brain, developmental landmarks, or morphological changes to the tissues of the central nervous tissue. These data suggest the developmental neurotoxicity NOAEL for rats is 1200 mg/kg.

Genotoxic Effects

All genotoxicity assays reported for isopropanol have been negative. Characterization of the genotoxicity hazard for isopropanol is provided by both in vitro and in vivo mutation/chromosomal studies. Isopropanol was found to be negative in an in vitro CHO/HGPRT assay, was negative in vitro for aneuploidy in *Neurospora crassa*, and did not increase micronuclei in an in vivo micronuclei assay in mice. Mutagenicity studies also showed that isopropanol was not mutagenic in various Ames assays both in the presence or absence of an S9 metabolic activation system. In vitro sister chromatic exchange (SCE) assays on isopropanol using cultured V79 cells both with and without S9 activation, were also negative. Isopropanol did not induce transformation in Syrian hamster embryos infected with Simian SA7 virus. These studies demonstrate that isopropanol is not a hazard for genotoxic effects.

Carcinogenicity

Two recent chronic exposure, rodent inhalation studies were conduct to evaluate isopropanol for cancer potential. One study was performed exposing Fischer 344 rats to 500, 2500 and 5000 ppm of IPA for 6 hours/day, 5 days/week for 24 months. The only tumor rate increase seen was for interstitial (Leydig) cell tumors in the male rats. Interstitial cell tumors of the testis is typically the most frequently observed spontaneous tumor in aged male Fischer 344 rats (Haseman et al., 1990). Nearly all male Fischer rats will develop these proliferative tumors if they are allowed to complete their lifespan (Boorman et al., 1990). A mouse inhalation study was performed exposing CD-1 mice to 500, 2500 and 5000 ppm of IPA for 6 hours/day, 5 days/week for 18 months. There was no increased frequency of neoplastic lesions in any of the treated groups. These studies demonstrate that isopropanol does not exhibit carcinogenic potential relevant to humans. Furthermore, there was no evidence from this study to indicate the development of carcinomas of the testes in the male rat, nor has isopropanol been found to be genotoxic. Thus, the testicular tumors seen in the isopropanolexposed male rats are considered of no significance in terms of human cancer risk assessment.

C.3.3 Environment risks related to alternative 2: 2-Propanol

2-Propanol (Isopropanol, IPA) was assessed in the OECD SIDS program and published as a UNEP Publication in 1997 (UNEP 1997). The following information is from the summary of that publication.

2-propanol is not classified for environmental hazards either in the harmonised classification in Annex VI, Table 3.1 of the CLP Regulation or in self classifications notified to the European Chemicals Agency.

Environmental Fate
Based on calculated results from a lever 1 fugacity model, isopropanol (IPA) is expected to partition primarily to the aquatic compartment (77.7%) with the remainder to the air (22.3%). IPA has been shown to biodegrade rapidly in aerobic, aqueous biodegradation tests and therefore, would not be expected to persist in aquatic habitats. IPA is also not expected to persist in surface soils due to rapid evaporation to the air. In the air, physical degradation will occur rapidly due to hydroxyl radical (OH) attack. Overall, IPA presents a low potential hazard to aquatic or terrestrial biota. IPA is expected to volatilize slowly from water based on a calculated Henry's Law constant of 7.52×10^{-6} atm•m ^{3} /mole. The calculated half-life for the volatilization from surface water (1 meter depth) is predicted to range from 4 days (from a river) to 31 days (from a lake). Hydrolysis is not considered a significant degradation process for IPA. However, aerobic biodegradation of IPA has been shown to occur rapidly under non-acclimated conditions, based on a result of 49% biodegradation from a 5 day BOD test. Additional biodegradation data developed using standardized test methods show that IPA is readily biodegradable in both freshwater and saltwater media (72 to 78% biodegradation in 20 days). IPA will evaporate quickly from soil due to its high vapor pressure (43 hPa at 20°C), and is not expected to partition to the soil based on a calculated soil adsorption coefficient (log K_{oc}) of 0.03. IPA has the potential to leach through the soil due to it's low soil adsorption. In the air, isopropanol is subject to oxidation predominantly by hydroxy radical attack. The room temperature rate constants determined by several investigators are in good agreement for the reaction of IPA with hydroxy radicals. The atmospheric half-life is expected to be 10 to 25 hours, based on measured degradation rates ranging from 5.1 to 7.1 x 10^{-12} cm^3 /molecule-sec, and an OH concentration of 1.5×10^6 molecule/cm^3 , which is a commonly used default value for calculating atmospheric half-lives. Using OH concentrations representative of polluted (3×10^3) and pristine ($3x\ 10^5$) air, the atmospheric half-life of IPA would range from 9 to 126 hours, respectively. Direct photolysis is not expected to be an important transformation process for the degradation of IPA.

Toxicity to Aquatic Organisms
IPA has been shown to have a low order of acute aquatic toxicity. Results from 24- to 96-hour LC_{50} studies range from 1,400 to more than 10,000 mg/L for freshwater and saltwater fish and invertebrates. In addition, 16-hour to 8-day toxicity threshold levels (equivalent to 3% inhibition in cell growth) ranging from 104 to 4,930 mg/L have been demonstrated for various microorganisms. Chronic aquatic toxicity has also been shown to be of low concern, based on 16- to 21-day NOEC values of 141 to 30 mg/L, respectively, for a freshwater invertebrate. Bioconcentration of IPA in aquatic organisms is not expected to occur based on a measured log octanol/water partition coefficient (log K_{ow}) of 0.05, a calculated bioconcentration factor of 1 for a freshwater fish, and the unlikelihood of constant, long-term exposures.

Toxicity to Plants
Toxicity of IPA to plants is expected to be low, based on a 7-day toxicity threshold value of 1,800 mg/L for a freshwater algae, and an EC_{50} value of 2,100 mg/L from a lettuce seed germination test.

C.3.4 Technical and economic feasibility of alternative 2: 2-Propanol

No problem related to technical feasibility is foreseen as 2-propanol is already available and in use in Europe. 2-propanol can perform the same function as methanol in windscreen washing fluids.

C.3.5 Other information on alternative 2: 2-Propanol

2-Propanol (Isopropanol, IPA) was assessed in the OECD SIDS (Chemicals Sreening Information Dataset) program for high production volume chemicals. According to the conclusion the information obtained from this database allows for the characterization of toxicity hazard of IPA for both human/mammalian and environmental effects. Taken together, these considerations support the conclusion that IPA is a low priority for further work.
Isopropanol (IPA) is a high production volume chemical which has wide use as an industrial solvent and as a component in numerous industrial and consumer products. It has a potential for widespread exposure to both workers and consumers.

Based upon physical and chemical properties, isopropanol is not expected to persist in the environment. Aerobic biodegradation of isopropanol occurs rapidly. IPA is not expected to persist in soil due to low soil adsorption and rapid evaporation to air. In the air, isopropanol is subject to rapid oxidation by hydroxyl radical attack. IPA has a low order of toxicity to aquatic organisms and plants, and bioconcentration in aquatic organisms is not expected to occur.

The mammalian/human toxicological properties of IPA have been well characterized in multiple animal species and humans for a variety of exposure routes, exposure durations and toxicity endpoints. High quality studies have been conducted that evaluate acute toxicity, skin and eye irritation, skin sensitization, subchronic and chronic toxicity, reproductive toxicity, developmental and developmental neurotoxicity, acute and subchronic neurotoxicity, genotoxicity and cancer. In addition, studies are available that characterize the disposition of IPA in mammals.

D. Justification for action on a Union-wide basis

D.1 Considerations related to human health and environmental risks

Currently no general EU-wide restriction of methanol or mixtures containing methanol is in force. Methanol or mixtures containing methanol are not included in Annex XVII (Restrictions on the manufacture, placing on the market and use of certain dangerous substances, mixtures and articles) of REACH Regulation. Methanol or mixtures containing

methanol should be properly labelled (according to Regulation No 1272/2008 or according to Dangerous Preparation Directive - 1999/45/WE). Containers of whatever capacity of substances or mixtures, having a methanol in a concentration equal to or greater than 3.0%, which are supplied to the general public, are to be fitted with child-resistant fastenings.

In Poland till 1 June of 2010 the placing on the market for general public products containing methanol in the concentration higher than 3.0% by weight was banned by Regulation of Minister of Economy. At that date, due to changes in the legislation, this ban ceased to be in force. In December 2011, the increasing number of methanol poisonings was noted by some of the acute poisoning centres, thus verification of this information was commenced in order to determine the extent of this problem. No central poisoning database system is available in Poland, and that is why in 2012, based on the information submitted by some of the acute poisoning centres, it was primarily analysed whether the significant increase in the number of methanol poisonings had really been observed. Several laboratories functioning within the acute poisoning centres were requested to notify the number of positive results of detecting methanol in blood of patients between 2009 and 2011. The data received from 4 laboratories confirmed the increase in the number of positive results confirming presence of methanol in the blood of poisoned patients. In 2009 and 2010, the total number of positive results reached 33 and 21 respectively, while 84 positive results were registered in 2011. These data were confirmed by the Forensic Medicine Centres. The table below presents the results on methanol detection recorded during autopsies performed in order to identify the cause of death of the individuals found dead, who had not undergone hospitalisation.

Table D.1-1. The results on methanol detection recorded during autopsies performed in order to identify the cause of death of the individuals found dead, who had not undergone hospitalisation.

Year	**2009**	**2010**	**2011**	**2012**	Comments
Number of positive results confirming presence of methanol	13	12	79	90	Data received from 11 out of 14 Forensic Medicine Centres

In the years 2011 and 2012, the number of positive results confirming presence of methanol in blood of the selected dead increased by several times. It should be stressed however that the positive result confirming presence of methanol in blood of the dead individuals does not imply that methanol was the exclusive cause of their death in each of these cases.

A detailed analysis of methanol poisonings was performed based on the information submitted by the Head of the Regional Acute Poisoning Centre with the Clinical Toxicology Department of the Occupational Medicine and Environmental Health Institute in Sosnowiec. It covered methanol poisoning cases in the voivodships of Opolskie and Śląskie, and bordering territories of Małopolskie Voivodship, hereinafter referred to as "Silesian Agglomeration". Territory from which the data on the poisonings were collected has the population of approx. 6 million inhabitants (almost one sixth of Poland's population), which enabled to accept the data as a statistical sample, representative for Poland. The table below presents information on the methanol poisonings in this part of Poland in the years 2001 - 2013.

Table D.1-3. Information on the methanol poisonings in "Silesian Agglomeration" in the years 2001 – 2013.

Year	Number of poisonings	Including fatal poisonings
2001	2	Not analysed
2002	9	-
2003	3	-
2004	4	-
2005	3	-
2006	5	-
2007	5	-
2008	6	-
2009	3	-
2010	5	2 (40%)
2011	18	11 (61%)
2012	43	24 (56%)
2013	36	14 (39%)

This analysis primarily indicates a sharp and major increase in the number of poisonings since 2011, i.e. the time when it became commonly known that the ordinance of the Minister of Economy banning methanol in consumer products had ceased to be in force. Between 2001 and 2010, on average 4.5 methanol poisonings were recorded annually, while in 2011 this number reached 18, 43 in 2012 and 36 in 2013. 17 poisonings were recorded in the first two quarters of 2013, and 19 more poisonings in the third and fourth quarter of 2013. A very high rate of fatal poisonings – from over 40% to over 60%, should be emphasised.

The above data on the methanol poisonings recorded in the past three years are consistent with the information of the State Consultant for Clinical Toxicology, who collected information on the poisonings in the individual voivodships in 2012. Such information was submitted by 12 out of 16 voivodships in Poland. 176 poisonings confirmed by positive result indicating presence of methanol in blood were identified in these 12 voivodships. 69 poisonings were recorded between January and August, while 107 poisonings were confirmed in the last four months of 2012. This is consistent with the above-mentioned information of the Head of the Regional Acute Poisoning Centre with the Clinical Toxicology Department of the Occupational Medicine and Environmental Health Institute in Sosnowiec, who in 2012, confirmed 43 poisonings in the agglomeration with approximately 6 million inhabitants.

The poisonings in the "Silesian Agglomeration" mainly took place in winter months. The table below presents the number of poisonings of the individual quarters between 2010 and 2013.

Table D.1-4. The number of poisonings of the individual quarters in "Śląska Agglomeration" between 2010 and 2013.

Quarter	Number of poisonings	Winter/summer	Confirmed poisonings with windscreen washing fluid	Unknown source of methanol	Comments
1st 2010	**3**	**3**	**1 (33%)**	**2**	
2nd 2010	0	0	0	0	

3rd 2010	0		0	0	
4th 2010	**2**	**3**	**1 (50%)**	**1**	
1st 2011	**1**		**1 (100%)**	**0**	
2nd 2011	3	4	0 (0%)	3	
3rd 2011	1		0 (0%)	1	
4th 2011	**13**	**23**	**7 (54%)**	**6**	
1st 2012	**10**		**5 (50%)**	**4**	
2nd 2012	8	16	3 (37%)	5	
3rd 2012	8		0 (0%)	3	5 poisonings with alcohol from the Czech Republic
4th 2012	**17**	**28**	**5 (29%)**	**9**	2 poisonings with alcohol from the Czech Republic
1st 2013	**11**		**2 (18%)**	**5**	2 poisonings with alcohol from the Czech Republic, **1 poisoning with denatured alcohol containing methanol**
2nd 2013	6	6	1 (17%)	3	1 poisoning with alcohol from the Czech Republic, **1 poisoning with denatured alcohol containing methanol**
3rd and 4th 2013	19	19	-	-	
In total	**102**	**102**	**26**	**42**	

Analysis of these data indicates a clear increase in the poisonings in the winter months, when winter windscreen washing fluid containing alcohol, including methanol, is sold.

This analysis also covered sources of the methanol which caused poisonings in the “Silesian Agglomeration” between 2010 and 2013.

Table D.1-5. Sources of methanol poisoning in "Silesian Agglomeration" between 2010 and 2013.

Year	2010	2011	2012	1st and 2nd quarter of 2013	**In total**
Sources of poisoning/number of poisonings	5	18	43	17	**83**
Windscreen washing fluid	2 (40%)	8 (44%)	13 (30%)	3 (18%)	**26 (31%)**
Consumable alcohol containing methanol (vodka from the Czech Republic)	-	-	7	3	**10**
Chemical reagents/technical methanol	-	-	2	1	**3**
Denatured alcohol containing methanol	-	-	-	2	**2**
Unknown source	3	10	21	8	**42**

The following analysis results should be emphasised in particular:

— a large number of poisonings for which the source of methanol could not be established based on the medical history – patient died or could not remember what he/she had drunk, containers of the products he/she had consumed were unavailable, or the source of methanol was not detected due to other reasons,

— 26 poisonings (31% of the total number of poisonings) as a result of confirmed consumption of windscreen washing fluids,

— 10 poisonings caused by alcohol from the Czech Republic – such poisonings had not been recorded previously and they should not re-occur in future years, as they result from contamination of large quantities of consumable alcohol in the Czech Republic with methanol, which was broadly publicised throughout Europe. Such poisonings are not representative for other Polish regions where trips to the Czech Republic to purchase alcohol are not so common as in the analysed region,

— **several poisonings with denatured alcohol** (96% technical ethanol with supplements making it inedible) supplemented with as much as 50% methanol.

The cases for which the source of poisoning was detected (41) included 28 poisonings caused by products containing methanol which were legally placed on the market (winter windscreen washing fluids and a mixture of denatured alcohol with methanol). They represent 68% of the poisonings in which the source of methanol was identified . This percentage will go up to 90%, if we deduct the poisonings caused by consumable alcohol from the Czech Republic, which did not occur before 2012 and it is highly unlikely that they should reoccur, at least in near future. Poisonings with methanol obtained in other ways (chemical reagents, technical methanol) represent only 3 cases (7% of the poisonings with the known source of intoxication). We may assume with high and almost certain probability that the sources of the poisonings for which it was not possible to identify the product causing them were similar. We may assume that also approx. 70% of these cases were caused by products containing methanol legally sold to consumers, and only 10% were caused by the products containing methanol which had been obtained in other way.

The above-mentioned data collected by the National Consultant for Clinical Toxicology in the "Silesian Agglomeration" may be approximated for other Polish regions. We may also assume that the ban on using methanol in such consumer products as the windshield washing fluids and denaturated alcohol should reduce the number of methanol poisonings in Poland by 60 to 90%. Poisonings caused by methanol obtained illegally in Poland and methanol contained in products brought from neighboring countries where the content of methanol in such products is not restricted will remain.

Basing on that data the Minister of Economy restricted by the Regulation the sale for consumers of methanol and mixtures containing methanol in concentration equal or higher than 3%. Some products, namely the fuel for sport motorboats and for models as well as biofuels are exempted from this restriction. As there was a ban on such products in Poland before, the Commission agreed to this restriction. The restriction came into force on January 4, 2014. Fragmentary information from the toxicological centers shows that the number of methanol poisonings is diminishing, however, the full impact of the Regulation will be seen after comparing the poisonings in winters 2012/2013 – 2014/2015.

Bureau for Chemical Substances has also requested other member states to provide information whether they restrict methanol content in consumer products, as well as information on occurrence of methanol poisonings in their respective territories. Content of methanol in products sold to general population (consumers) may not exceed 10% in Denmark, Sweden, Norway and Lithuania. In Germany and Austria, legislation of equivalent effect is applicable – permission to purchase products containing methanol in the concentration of over 10%. Among the states with the climate similar to the climate in Poland or colder, Finland and Estonia have not informed about any restrictions on the content of methanol in consumer products. The Bureau has not received this information from Latvia, the Czech Republic and Slovakia. The states with the climate slightly milder than in Poland, such as the Netherlands, the United Kingdom and Ireland, have not introduced the restriction. There is no data for Belgium. Introducing restrictions for methanol was not necessary in the Southern Europe's states: demand for winter windscreen washing fluid in these states is much smaller, and they are also characterised by wine consumption culture thus consumption of beverages with high alcohol content is significantly lower than in the states located in the north of Europe.

Methanol poisonings with the extent similar to Poland's occur in Finland. The table below presents the number of fatalities caused by methanol poisoning in Finland in the years 1993 – 2011.

Table D.1-6. The number of fatalities caused by methanol poisoning in Finland in the years 1993 – 2012 (Lapatto-Reiniluoto & Ikäheimo 2012, Finnish Poison Information centre).

Year	Number of fatalities	Comments
1993	5	
1994	2	
1995	8	
1996	15	
1997	18	
1998	29	

1999	33	
2000	46	
2001	30	
2002	25	
2003	43	
2004	26	
2005	30	
2006	12	
2007	28	
2008	15	
2009	30	
2010	24	
2011	19	
2012	11	

The number of fatalities caused by methanol poisoning rose significantly after Finland joined the European Union in 1994, and following abolition of the ban on selling products containing methanol to the general population – such ban was previously in force. It is worth emphasising that in the course of the next 6 years after the ban had been abolished, the number of fatal poisonings was growing significantly. Almost all the poisonings were caused by consumption of windscreen washing fluids. It must be also mentioned that the methanol content in denaturated alcohol in Finland is restricted.

Within the past 10 years, 11 – 30 methanol poisonings and 5 fatalities among the poisoned individuals were recorded annually in Lithuania. In 2012, 8 poisonings and 2 fatalities were recorded. The poisonings were caused by windscreen washing fluids and mixtures to remove paint. In Estonia, 6 fatalities caused by consumption of liquids containing methanol were recorded in 2006. In Ireland, in the years 2008 – 2012, 10 – 19 methanol poisonings, where over half of the poisonings affected children, were recorded annually. In Slovenia, one poisoning was recorded in 2011 for a child that had consumed fuel used in car models, and one poisoning in 2012, which was caused by an unidentified mixture of ethanol and methanol. UK and Italian partners of the Bureau for Chemical Substances also reported poisonings caused by windscreen washing fluids or denaturated alcohol with methanol. The reports of the latter case concerned seasonal workers from the Central Europe’s states. Austria, the Netherlands, Cyprus and Malta represented the responding states that had not recorded any methanol poisoning cases. Partners from Bulgaria and Estonia indicated a possibility of stopping the supply on the market of products containing over 5% of methanol pursuant to article 37 (4) of REACH Regulation.

D.2 Considerations related to internal market

Methanol and products containing methanol are traded freely and used in all Member States (in some EU countries methanol and products containing methanol can not be offered to general public). These products are both manufactured and imported in the EU. An EU-wide measure, like a restriction, would remove the potentially distorting effect that a national restriction (or other national measure) may have on the free circulation of goods. The second justification is that regulating through EU wide action ensures that the producers of methanol

or products containing methanol in different Member States are treated in an equitable manner.

D.3 Other considerations

To date, the national legislation prohibiting the sale to general public of mixtures classified or labelled as "Toxic" according to directive 67/548/EEC and directive 1999/45/EC, exists in such countries as Germany, Austria, Lithuania and the Nordic countries (except Finland). This legislation will stay in force till the 1st of June 2015. The legislation restricts the concentration of methanol in products intended for general public to 10% (T, R39/23/24/25). Such restriction, especially as the products proposed to be restricted contain ethanol which protects against the toxic action of methanol, prevents severe poisonings with methanol, and at least prevents fatal poisonings. However this legislation will cease on June 1, 2015, when the CLP Regulation will be used for classification of mixtures. Even if these national legislation is rearranged to fit CLP and the restriction will cover mixtures of category 1 – 3 considering the acute toxicity, mixtures containing methanol will be classified as Acute Tox. 3, H301/311/331 only when the concentration of methanol will be equal or higher than 30%. Mixtures with so high concentration of methanol when drunk, cause severe poisonings with the high rate of fatal cases.

To achieve a similar level of protection of human health each Member State would need to implement national legislation. It appears administratively more efficient to introduce legislation at EU level.

Climate conditions vary among the Member States. The use of anti-freezers is relevant in regions where the annual temperature drops below 0^{o}C. This is especially the case in the eastern/northern European countries. In other countries the winter windshield washing fluids containing alcohol are not necessary and in those countries this product is usually not used as a surrogate of consumable alcohol. There is either no information on methanol poisonins due to drinking such products in those countries.

The situation is different concerning denaturated alcohol. This product is widely used across the EU as a multipurpose cleaning agent and a fuel for touristic appliances. Even if citizens of the countries in which strong alcohols are not preferred do not drink denaturated alcohol, due to the free movement of people in the EU it is a high probability that this product is used as a surrogate of consumable alcohol by people from other countries. At least it was a case in Italy, where denaturated alcohol with methanol was a cause of methanol poisonings.

D.4 Summary

The main reason to act on an EU-wide basis is the protection of human health from the poisoning with some products containing methanol. The introduction of restriction will result in greater protection of health and life firstly of people who use winter windshield washing fluids and denaturated alcohol as a surrogate of consumable alcohol and to some extent of children who may consume those products not properly stored. The fact that people drinking

such products freely travel within the EU stresses the importance of the EU-wide action. Currently some Member States have a national regulation which prohibit placing on the market for consumers mixtures classified or labelled as “Toxic” (mixtures containing more than 10.0% by weight of methanol). However in this context it must be stressed that after 1 June 2015, when provisions of CLP Regulation will become effective for mixtures, countries in which the restriction is binding will have to amend their legislation. These amendments will involve deletion of the reference to classification of products as toxic in accordance with directives, and introduction of the reference to classification due to acute toxicity pursuant to provisions of CLP Regulation. As described in Section A.3.1, these amendments will result in the situation where many mixtures containing methanol, which so far have not been covered by the provisions of this restriction, will become available to consumers. The performed calculations – in which the calculation method provided in the CLP Regulation and used for classification of mixtures in terms of acute toxicity was applied – indicate that this restriction only covers mixtures whose composition includes methanol in the concentration of at least 30%). Thus, to ensure a similar level of protection of human health across the EU and enhance the good functioning of the internal market, the action needs to be taken on a EU-wide basis.

The justification for the possible restriction in the Community is based on the following evidences:

- methanol and methanol-containing products caused poisoning among consumers in some EU Member States, mainly among people drinking winter winshield washing fluids and denaturated alcohol as a surrogate of consumable alcohol;
- methanol and methanol-containing products are widely used in all EU Member States;
- in some Members States (Germany, Austria, Sweden, Denmark, Lithuania) a legislation banning the use of methanol in concentration above 10% in some household products and in several professional uses is already in place. This legislation will cease to be in force on June 1, 2015.
- given the extremely low price of methanol compared to that of possible alternatives (ethanol or isopropyl alcohol) restrictions limited to certain Member States would create a distortion of the market of methanol containing products.

E. Justification why the proposed restriction is the most appropriate Union-wide measure

This section provides justification for the reasoning that the proposed restriction is the most appropriate Community-wide measure. It gives an overview of the effectiveness, practicality and ease of monitoring involved in implementing the proposed restriction. An assessment of other risk management options is also included.

E.1 Identification and description of potential risk management options

E.1.1 Risk to be addressed – the baseline

The proposed restriction is to eliminate poisonings caused by consumption of winter windshield washing fluids and denaturated alccohol containing high concentrations of

methanol (up to 40-50% based on weight) by alcoholics. Using these products as a surrogate of consumable alcohol mainly results from their price, which is several times lower than the price of consumable alcohol, as well as from the fact that in some EU countries their availability is much easier than availability of consumable alcohol. Methanol is added to these products due to its lower price than the price of ethanol. It further lowers the price of these products.
In some countries in European Union (Italy, Poland, Finland, detail information in section D) a significant number of poisoning cases by ingestion of mixture containing methanol (mainly winter windshield washing fluids and denaturated containing high concentration of methanol) were registered.

Without any restriction of concentration of methanol in some mixtures available for consumers, it must be expected that the number of new incidences of poisoning caused by ingestion of winter windshield washing fluids and denaturated alcohol containing high concentration of methanol in some EU Member States will remain at the level seen today. The change in classification of mixtures since June 1, 2015 may exaggerate the problem.

E.1.2 Options for restrictions

Methanol is not yet identified as a SVHC since it doesn't fulfill the criteria of art. 57 of REACH Regulation, unless the classification is revised in view of a possible classification also as toxic for reproduction Cat. 1B (according to CLP Regulation). The process of methanol reclassification is on-going, however taking into account ECHA's preliminary decision drafted after the 30th meeting of the RAC, pursuant to which methanol should either be classified as toxic to reproduction Category 2 or it should not be classified in terms of this type of hazard, it seems that it will not be possible to use methanol classification as a tool to reduce risk. Methanol classification does not allow for:

- entering methanol to candidate list, and then to Annex XIV,
- using restrictions on the prohibition on placing on the market substances/mixtures classified as CMR Category 1A or 1B, which are contained in Annex XVII.

In some countries currently there are regulations which restrict placing on the market for supply to consumers substances/mixtures classified, in accordance with provisions of Directive 67/548/EEC and Directive 1999/45/EC, as very toxic and toxic. This restriction results in the situation where methanol and mixtures containing methanol in concentration equal to, or greater than 10% are not available for consumers. In order to keep this restriction binding, member states in which it is binding, should amend their national legislation by 1 June 2015 to ensure that the restriction contains a reference to classification in accordance with provisions of CLP Regulation. A preliminary analysis of the provisions of CLP Regulation indicates that in the case of mixtures containing methanol, the provisions of the restriction would cover these mixtures that contain methanol in concentrations equal to, or greater than 30%.

A possibility to stop placing on the market of products containing the high concentration of methanol provides also Article 37(4) of the REACH Regulation. According to this provision a downstream user of a substance on its own or in a mixture shall prepare a chemical safety report in accordance with Annex XII for any use outside the conditions described in an exposure scenario or if appropriate a use and exposure category communicated to him in a safety data sheet or for any use his supplier advises against. As a registrant in the registration dossier advised that methanol concentration in mixtures available for consumers should not

exceed 2.5% or 5%, depending on the physical state during the use (as a liquid or as a spray) it gives some possibility for prevention. However, this provisions may be used only if there is a legal possibility in the country to stop further placing of such product on the market and withdrawing the product from the market. It must be mentioned that it can be done by decision addressed to the entity which placed the product on the market. This possibility of preventing methanol poisonings is much less effective than the restriction.

Therefore at present the only way for a risk reduction under REACH is a new restriction.

RMO

Methanol CAS No 67-56-1 EC No 200-659-6	Shall not be placed on the market for supply to the general public: – as a constituent of windshield washing fluids in concentration equal to, or greater than 3.0% by weight, – as an additive to denaturated alcohol (*methylated spirit, denaturated alcohol, brennspiritus*) in concentrations equal to, or greater than 3.0% by weight. Member State may maintain any existing and more stringent restrictions for methanol.

The proposed restriction will ban supplying to the general public of windshield washing fluids and denaturated alcohol containing methanol in concentration equal to, or greater than 3.0% by weight.

Derogation
The proposed restriction does not cover the supplying methanol and mixtures containing methanol to professional users.
The proposed restriction does not cover industrial use of methanol and mixtures containing methanol.
The proposed restriction does not cover the supplying to the general public of windshield washing fluids and denaturated alcohol containing methanol in concentration less than 3.0% by weight.
The proposed restriction does not cover the supplying to the general public other mixtures than are mentioned above containing methanol in concentrations equal or greater than 3.0% by weight.

Timing
Due to a significant number of poisoning cases by ingestion of mixtures, available for general public, containing methanol, the restriction shall apply as soon as possible. It is proposed that the restriction should enter into force three month after publication of the regulation which will add the proposed restriction to Annex XVII to REACH Regulation. The period of three months is proposed due to the fact that the aim of the restriction is to reduce the number of poisonings therefore measures should be implemented as soon as possible. It needs to be stressed that currently the process of introduction of the restriction is transparent, and industry is able to take an active part in the process of introducing the restriction (e.g. through taking part in public consultations which are held via ECHA's website), which contributes to the situation that the proposed changes do not come to the industry as a surprise.

E.1.3 Other Union-wide risk management options than restriction

The aim of this part is to identify appropriate Community legislations (as it was shown in Section D that a Community-wide measure was justified) which are different from the REACH restriction process in order to address the risks identified in Section E.1.1.

No other EU legislation which may have the potential to reduce the identified risks was identified.

Voluntary action by industry is not considered as an effective way of managing the targeted risks in this dossier.

E.2 Assessment of risk management options

E.2.1 Restriction option: RMO

E.2.1.1 Effectiveness

According to REACH Annex XV, “the restriction must be targeted to the effects or exposures that cause the risks identified, capable of reducing these risks to an acceptable level within a reasonable period of time and proportional to the risks”.

E.2.1.1.1 Risk reduction capacity

E.2.1.1.1.1 Changes in human health risks/impacts

The objective of the restriction is to avoid poisoning cases by ingestion of winter windshield washing fluids and denaturated alcohol containing high concentration of methanol by general public, namely by alcoholics. Such mixtures are now available for consumers in a number of countries of the EU. The proposed restriction impacts supplying for the general public:
- windshield washing fluids containing methanol in concentration equal to, or greater than 3.0 % by weight,
- denaturated alcohol containing methanol in concentration equal to, or greater than 3.0% by weight.
The proposed restriction clearly targeted to the identified risks.

The proposed restriction will reduce exposure to mentioned above mixtures containing high concentration of methanol available for general public. This products will not contain more than 3.0% w/w of methanol. It is expected that this limit of 3.0% w/w of methanol in mixtures, mentioned above, available for general public will allow an adequate control of the identified risks which are poisoning cases by ingestion of windshield washing fluids and denaturated alcohol containing high concentration of methanol.

E.2.1.1.1.2 Changes in the environmental risks/impacts

No environmental hazard is related to methanol, thus the restriction proposal is expected to have an impact only on human health.

E.2.1.1.1.3 Other issues

Not relevant for this proposal.

E.2.1.1.2 Costs

The cost of alternatives to methanol is about 2.5 times that of methanol. It is also important to underline that methanol is one of the substance of lowest cost among organic products. Cost of mixtures containing alternatives will increase. Cost of mixtures containing methanol and mixtures containing alternatives covered by the restriction is discussed in details in Section F "Socio-economic Assessment of Proposed Restriction".

E.2.1.1.3 Proportionality

The proposed restriction is targeted to the identified risk (methanol poisoning among consumers in some European countries). The proposed restriction is to eliminate poisonings caused by ingestion of windshield washing fluids and denaturated alcohol containing high concentrations of methanol (up to 40-50% based on weight) by alcoholics. In the case of such persons, these products are consumed as a surrogate of consumable alcohol, namely due to financial reasons – in comparison to taxation of consumable alcohol, tax rate applied for alcohol in these products is several times lower, thus their price is also several times lower than the price of consumable alcohol. Such poisonings are mainly accidental in nature when these persons do not notice that the product they are consuming also contains methanol. This is also facilitated by a lower price of such products as instead of ethanol, they contain methanol, which is cheaper than ethanol.

Additional effort is expected from the actors to implement (for example importers of windshield washing fluids containing high concentration of methanol, downstream users) and from the authorities to enforce the restriction**.** Also, additional costs are expected, because the cost of alternatives (ethanol) are higher than the cost of methanol.

Actors shall comply with the restriction as soon as the amendment of Annex XVII of the REACH regulation enters into force (it is proposed that the restriction should enter into force 3 months after publication of the regulation amending Annex XVII to REACH Regulation).

E.2.1.2 Practicality

E.2.1.2.1 Implementability and manageability

As explained in the previous parts, resignation of adding methanol to those products seems to be economically and technically feasible. Consequently, the actors should be capable in practice to comply with the restriction proposal. The proposed restriction should be regarded as understandable to all affected parties.

The level of administrative burden for the actors concerned is not expected to be high as alternatives exist and are expected to be technically and economically feasible. Given the fact that analytical methods to measure methanol concentration in these mixtures are already available, this restriction is also expected to be manageable for the enforcement authorities.

E.2.1.2.2 Enforceability

For enforcement purposes, it is recommended that the restriction contains a restriction limit so that enforcement authorities can set up an efficient supervision mechanism. The proposed restriction limit is 3.0% w/w of methanol in these mixtures. Analytical methods which can detect the proposed restriction limit of methanol are available. The restriction will be enforceable.

E.2.1.3 Monitorability

According to REACH Annex XV, it must be possible to monitor the results of the implementation of the proposed restriction. ECHA (2007) stipulates that monitoring may cover any means to follow up the effect of the proposed restriction in reducing the exposure.

The evolution of the following indicators may provide an estimation of the effect of the restriction in reducing the exposure:
- (1) number of accidents occurring to consumers as a result of ingestion of methanol,
- (2) percentage of mixtures, available for general public, which have a methanol concentration above 3.0% w/w,
- (3) number of mixtures, available for general public, which have a methanol concentration above 3.0% w/w.

Indicator number 1 can be provided by collecting information about accidents/incidents occurring to consumers as a result of exposure to methanol containing products from poison control centers.

The number of products containing more than 3% of methanol may be assessed now by analyzing the information gathered according to Article 45 of the CLP Regulation. After introducing the restriction in order to provide indicator number 2 and number 3, the concentration of the methanol in mixtures which are placed on the market and which are available for general public has to be monitored. To this end, several methods are available to detect methanol concentration in mixtures. Stakeholders involved in this monitoring activity are authorities responsible for enforcement of the REACH restrictions and laboratories which will be in charge of performing the methanol concentrations analyses. Monitoring should be performed in every Member State. It is highlighted that the indicators number 2 and number 3 will probably be costly as they will require expensive market survey. Indicators will be chosen according to the resources that can be allocated to the monitoring of this measure.

ECHA (2007) advises to specify a frequency of monitoring. However, it is difficult to anticipate such a parameter as all Member States do not have the same resources that can be dedicated to this monitoring activity. It must be also mentioned that the number of poisonings with methanol will affect the frequency of monitoring. It should be also highlighted, that in order to provide indicator number 2 and indicator number 3, the informaction can be collected, by enforcement authorities, from Safety Data Sheets.

E.2.1.4 Overall assessment of restriction option

Key points of the restriction proposal are:

The proposal is targeted to the identified risks: poisoning cases of consumers caused by ingestion of winter windshield fluids and denaturated alcohol containing high concentration of methanol in all Member States.

The proposal is expected to lower the exposure of consumers to methanol and to allow an adequate management of the identified risks.

Given the economical and the technical feasibility of alternatives, the restriction shall be applicable as soon as amendment of Annex XVII of the REACH Regulation enters into force.

Standardised method has been developed to determine methanol concentration.

Results of the implementation of this restriction may be monitored by collecting information about accidents/incidents occurring to consumers as a result of exposure to methanol containing products from poison control centers and by measuring the methanol concentration in mixtures which are available for consumers. Indicators such as "% of mixtures available for consumers which have a methanol concentration above 3.0% w/w" or "number of mixtures available for consumers which have a methanol concentration above 3.0% w/w" or "number of notifications to poison control centers about accidents/incidents occurring to consumers as a result of exposure to methanol containing products" can be used to assess the effects of the restriction proposal.

E.3 Comparison of the risk management options

Not relevant for these dossier. Only one RMO is proposed.

E.5 The proposed restriction(s) and summary of the justifications

Targeted risks in this restriction dossier are poisoning cases occurring among consumers resulting from oral exposure to winter windshield washing fluids and denaturated alcohol containing methanol. The population who faces the risks is constituted by all such potential consumers across the European Union.

No specific risks have been identified concerning the environment compartment.

Formally transposed in Annex XVII, the proposed restriction is the following:

Methanol CAS No 67-56-1 EC No 200-659-6	Shall not be placed on the market for supply to the general public: – as a constituent of windshield washing fluids in concentration equal to, or greater than 3.0% by weight, – as an additive to denaturated alcohol (*methylated spirit, denaturated alcohol, brennspiritus*) in concentrations equal to, or greater than 3.0% by weight. Member State may maintain any existing and more stringent restrictions for methanol.

As explained in Section E.1.3, no other Community-wide risk management option was found to appropriately manage the targeted risks of this restriction dossier.

Key points of the restriction proposal are:

The proposal is targeted to the identified risks poisoning cases occurring among consumers resulting from ingestion, mainly by alcoholics, of winter windshield washing fluids and denaturated alcohol containing methanol in all Member States.

The proposal is expected to lower the exposure of consumer to mixtures containing methanol and to allow an adequate management of the identified risks.

Given the economical and the technical feasibility of alternatives, the restriction shall be applicable as soon as amendment of Annex XVII of the REACH Regulation enters into force.

Standardised method has been developed to determine methanol concentration.

Results of the implementation of this restriction may be monitored by collecting information about accidents/incidents occurring to consumers as a result of exposure to methanol containing products from poison control centers and by measuring the methanol concentration in mixtures which are available for consumers. Indicators such as "% of mixtures available for consumers which have a methanol concentration above 3.0% w/w" or "number of mixtures available for consumers which have a methanol concentration above 3.0% w/w" or "number of notifications to poison control centers about accidents/incidents occurring to consumers as a result of exposure to methanol containing products" can be used to assess the effects of the restriction proposal.

F. Socio-economic Assessment of Proposed Restriction

In this section, the human health and economic impacts of the proposed restriction are assessed. Proposed restriction covers the supplying to the general public some mixtures containing methanol in concentration equal, or greater than 3.0% by weight.

Manufacture and professional use of methanol in industrial processes is very common and extensive. On the European market consumption of methanol exceeds 8 mln t (2007), of which 25% is produced in UE (http://export.by/en/?act=s_docs&mode=view&id=2399&type=&mode2=archive&doc=64).
The main consumer of methanol in Western Europe is production of formaldehyde (nearly 47%), for methyl-tert-butyl ether MTBE (12%), and 7% for acetic acid production.
The consumer use of methanol is low in comparison to industrial one, mostly in antifreezes, as a component in household detergents and as a solvent. Nowadays there are available also mixtures with a high methanol concentration in the consumer market (for example windshield washer fluids).

F.1 Human health and environmental impacts

F.1.1 Human health impacts

Methanol is present in various consumer and professional products such as paints, varnishes, windshield washer fluids, antifreezes, adhesives, de-icers and cleaning agents. According to information found in section B, methanol has harmonized classification and it is classified in hazard classes for human health. It has been set an occupational exposure limit value (260

mg/m^3) for occupational exposure (Directive 2006/15/EC).

Exposure to methanol is mainly expected via inhalation, ingestion but can also occur by dermal contact with the substance. Methanol is readily absorbed via all exposure routes, after inhalation, ingestion, dermal contact and distributes rapidly throughout the body. The most relevant risks associated with exposure to methanol are the consequence of its misuse, in particular the direct ingestion. Exposure to methanol present in consumers products may however also cause severe poisoning. The worst effect of methanol poisoning is irreversible disturbance of vision (blindness) and death.

The risk reduction capacity of the proposed restriction would be achieved by the ban - the supplying of windshield washing fluids and denaturated alcohol with methanol concentration equal to or above 3% w/w to consumers. The restriction would significantly minimize poisoning causes by ingestion of methanol contained in these products.

A significant number of poisoning cases was registered in several EU countries occurring due to misuse as surrogate alcohol of methanol containing mixtures or to ingestion of spirits adulterated with methanol.

It is expected that adoption of proposed restriction will limit access to methanol by consumers, what allow significantly minimize poisoning cases, therefore allow avoiding the health effects of poisoning (disability, death causes).

F.1.2 Environmental impacts

Methanol, ethanol and isopropanol are not classified for environmental hazard. Both substances, methanol and ethanol are volatile, have similar freezing and boiling point and easy evaporated. In the restriction scenario, in view of the fact that the alternative, which is ethanol has similar physical properties to methanol, it is assumed that the alternative would be added at the same concentrations as methanol to the mixtures. Considering the above environmental compartments are likely not to be affected in the restriction scenario.

F.2 Economic impacts

The proposed restriction scenario will reduce production and import of methanol to very small extent. Simultaneously it can be expected to slightly increase production and import of alternatives (mainly ethanol).

The identified stakeholders that may be affected by any economic impacts are:

- producers of methanol,
- importers of methanol and methanol mixtures,
- some downstream users (producers of winter windshield washing fluids with methanol and those downstream users which placed on the market denaturated alcohol with methanol),
- distributors, wholesalers and retailers,
- consumers.

In methanol mixtures intended for general public, methanol plays a role of a solvent, a defrosting factor or a component in detergents mainly. Resignation of adding methanol into

windshield washing fluids or denaturated alcohol is technically feasible and easy to implement. It will not cause changes in the characteristics of these products, as the properties of ethanol and methanol are very similar. It is assumed that ethanol is the main alternative substance for replacement of methanol in restricted mixtures intended for general public.

Methanol is partly produced in EU and partly imported from outside UE. In UE market methanol is applied mainly for industrial production of other chemicals in almost 70% (e.g. formaldehyde, methyl-tert-butyl ether, acetic acid) and as an additive for fuels. It can be assumed that proposed restriction affects very slight part of the whole methanol market only. Restrictions on the sale of methanol in high concentration in products intended to be provided to general public have already been introduced in some EU countries. Bearing in mind that the volume of methanol added to windshield washing fluids and to denaturated alcohol is very low in comparison to the total use (for example in the industrial production), we do not believe that the introduction of restrictions would lead to major changes in the methanol market.

Ethanol, the widespread alternative substance, is produced currently in the EU for industrial and not industrial applications. Ethanol indicates technical feasibility with similar physical properties to methanol, however it is not classified for health hazard. It is estimated, that ethanol could be the main alternative for methanol. We could expect a slight drop in tonnage from the manufacturers and importers of methanol and at the same time a slight increase in tonnage for manufacturers and importers of ethanol in the restriction scenario. Small changes on the methanol/ethanol producers and importers supply chains are expected - a slight decline in demand for methanol which would cause a slight increase in demand for ethanol in the EU market.

Taking into account physical properties of ethanol it can be assumed that methanol can be easily replaced with ethanol in these mixtures. Production volume of ethanol mixtures in comparison with methanol mixtures should not change. It can be assumed that quality and the lifetime of alternative mixtures could not be different in restriction scenario. Manufacturers of mixtures could replace restricted methanol with alternatives, e.g. ethanol without problems.

In the Finnish survey it was found that methanol is a better solvent and a cost-efficient anti-freezing component than the substitutes (ethanol or propanol). In order to achieve technical applicability as anti-freezer in -20 ^{o}C temperature, the proportion of alternatives needed in the product was stated to be higher, contributing to a 20 - 50% increase in price.

It is expected that production technology of alternative mixtures would be similar. It is estimated that investment costs and operating costs (capital, instrumentation, equipment, labour and energy costs) would not change, but costs of the raw material, e.g. ethanol in the restriction scenario. Increasing costs of alternative mixtures base solely on the increase in price of a substitute (ethanol). The main cost of alternative mixtures is expected to be higher than methanol mixtures. A price of ethanol is from 2 to 3-fold greater than the market price of methanol. Depending on the content of ethanol in mixtures the price of final products increases respectively. The increased cost of alternative will be included in the price of the final product and will be passed on the consumers. It can be expected that, depending on the concentration of ethanol in the final product, its price will rise accordingly, comparing with the price of the winter windshield washing fluid containing methanol. Despite the higher cost of ethanol mixtures it can be expected that demand for the alternative mixtures would be identical as for mixtures with methanol.

In case ethanol is purchased from other sources than methanol or from other suppliers (manufacturer / importer / distributor), producers of mixtures would have to find new suppliers of alternative component with appropriate quality. However, it must be remembered that that both mixtures to be restricted contain ethanol. If it is assumed that producers of methanol mixtures for general public will still be able to deliver alternative mixtures, their sales volume will not be reduced in spite of increasing price. It seems also that these changes will not result in any employment changes for mixture producers.

Methanol poisoning costs to society could be very high. Direct financial effects of methanol poisoning are the costs of medical and non-medical care which are difficult to monetization.
The cost of the methanol poisoning should be considered as direct medical costs of treatment of acute poisoning (diagnostic tests, medical care, hospitalization, medicines, side-effects), direct non-medical costs (non-medical care, transport), indirect costs (absence from work, loss of potential earnings and productivity, premature death). The costs to be taken into account have yet to include the intangible costs such as suffering, pain, reduction of activity or reduction of quality of life. The direct non-medical costs should also include long-term costs of caring for an irreversible visually impaired person due the methanol poisoning which could be generated thorough long time, depending on case-by-case.

Benefit for society generated by the introduction of the restriction is avoidiance of all costs generated by ingestion of containing methanol, poisonous products to be restricted .

Some cost estimation of methanol poisoning were performed by Finish CA. There were 431 fatal methanol poisonings in Finland during 1995-2011, in average 25.35 deaths per year. Over the period 1986 to 1994 (before Finland joined the EU and had to free the placing on the market of methanol containing windscreen washing fluids) there were only 22 incidents, in average 2.44 deaths per year. This implies that a restriction comparable to the one in force in Finland earlier would help avoid 22.91 deaths per year (Lampinen et al. 2013).

A typical victim of methanol poisoning in Finland is a 50-year old man with a drinking problem. Male life time expectancy at birth in Finland was 78 years in 2011 (WHO 2013). It is recognized that people with a drinking problem might be concentrated at the lower end of the lifetime distribution but because a distinct estimate for this subgroup is not available, the mean value will be used. Therefore, it is assumed that 28 life years will be lost per death.[1] Thereby, the number of lost life years due to one year deaths in Finland is 641.48.[2] Assigning a life year the value of 70172 €[3] (55800 € of year 2003 in the 2013 price level) following the ECHA Guidance on Socio-Economic Analysis - Restrictions would then yield a monetary estimate of €45 Million[4].

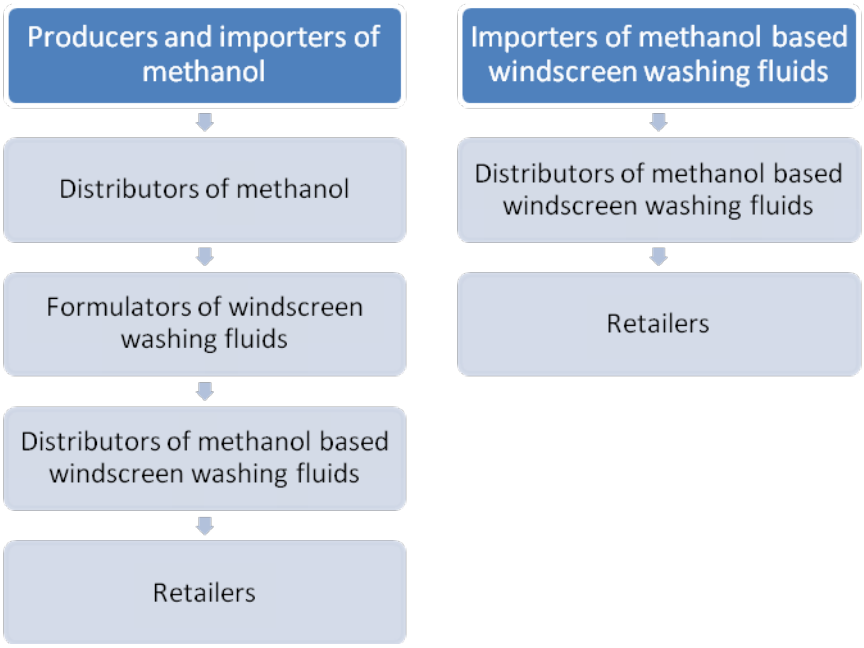
The proposed restriction is not expected to have an impact on the free movement of goods, capital and workers. Furthermore there in no single member state, region or sector that will be affected in particular by the proposed restriction. The restriction of methanol mixtures would neither bring any overall impacts on economic growth nor the employment. The proposed restriction is not expected to bring any major additional administrative burden in terms of cost

[1] The uncertainty analysis performed uses 10 years for a lower side estimate.
[2] 28*22.91=641.48.
[3] 55800 €*120.21/95.59 =70172 €
[4] 641.48*70172 € = 45013935 €

for inspection and enforcement. The imposition of the restriction will not entail any additional tax burden for methanol/alternatives and mixtures manufacturers.

The supply chains affected by the proposed restriction appear to be quite straightforward. A simplified chain of the recognized actors are presented in Figure F.2-1.

Figure F.2-1. A simple representation of the actors in the supply chains relevant for the restriction proposal.



The proposed restriction is not supposed to have a notable effect on producers and importers of methanol. The amount of methanol used yearly in the formulation of windscreen washing fluids is low compared to the total amount of methanol placed on the market. For example, in Finland during 2004-2011, the total amount of methanol placed on the market varied between 52 285 T and 577 963 T (mean 410 447 T, median 524 119 T), whereas the amount of methanol placed on the market in windscreen washing fluids varied between 904 T and 2559 T (mean 1502 T, median 1346 T) during the same time period. The amount of methanol now supplied to the windscreen washing fluid sector is well within annual fluctuation of manufacture and import tonnages. The manufacturers/ importers of methanol will not be able to supply their product to windscreen washing fluid formulators in the volumes they previously have, but no problems in finding other industrial or professional uses for such small volumes or methanol are foreseen.

It must be also stressed that the restriction will affect only a part of actors in the supply chain, namely those actors which placed on the market winter windshield washing fluids and denaturated alcohol with the content of methanol higher than 3%. The information gathered on the basis of Article 45 of the CLP Regulation, shows that in Poland, during the period when methanol was not restricted in products for consumers, there were 47 suppliers of winter windshield washing fluids containing methanol in toxic concentrations, higher than 3%. Together they plased on the market 113 different windshield washing fluids, however in some

cases the package of different volume was counted as a different product. The number of producers or importers of such products was rasing in the period 2011 - 2013. In 2011 there were 9 producers or importers placing on the market for the first time windshield washing fluids with the content of methanol higher than 3%, while in 2012 the number of new such enterprises raised to 17 and in 2013 to 21. The real number of suppliers or products could be higher as some suppliers might not submit such information to the Bureau for Chemical Substances, which is responsible for gathering the information. It must be stressed that during this period a number of suppliers of winter winshield washing fluids did not add methanol to their products in concentration higher than 3%. Sometimes their products contained methanol in concentrations 2 – 3%. The exact number of these products without methanol in concentrations higher than 3% is not known.

In case of denaturated alcohol no one of the suppliers of this product with methanol concentration higher than 3% submitted the required information to the Bureau for Chemical Substances. The internet search and the information from acute poisoning centers showed that there were at least 3 such suppliers, sometimes placing on the market the product with slightly changed name, e.i. the name DENATURO instead of Polish name “Denaturat”.

As to distributors of methanol, for big and non-specialized actors the above applies. For actors specialized in supplying methanol to windscreen washing fluid formulators, it is assumed that they will either replace methanol in their portfolio by technical ethanol/isopropanol or move to customers in other types of business. The latter is considered possible because the market is diverse and only a very minor part of methanol is used in the formulation of windscreen washing fluids. Most distributors are expected to have multiple clients operating in different sectors.

The formulators of windscreen washing fluids are expected to respond to the introduction of the proposed restriction in three alternative ways: by substituting methanol by ethanol and/or isopropanol, by closing down their windscreen washing fluid business or by specializing on professional users. An estimate of the division of actors between the options is represented in Table F.2-1. It is based on the responses to the Finnish survey.

Importers, distributors and retailers of methanol based windscreen washing fluids will have the same options of action than the formulators will. As the demand of windscreen washing fluids continues even after the methanol restriction, the importers, distributors and retailers will shift to operate on alternative products. Professional users of methanol-based windscreen washing fluids and their retailers are not expected to be affected.

It is possible that some actors would relocate outside the EU. However they would not be able to legally market their products for the general public inside the Union any more.

Table F.2-1. Assumed behavioural response of the actors placing methanol based windscreen washing fluids on the market to be available to the general public.

Behavioral response	Share of actors, %
Substituting methanol by ethanol, isopropanol or mixture of the two	70
Substituting methanol by another solvent	0
Closing down windscreen washing fluid business	20
Specializing on professional users	10

The estimates presented in Table F.2-1 are highly uncertain. They have been estimated based on response received from Finnish actors following consultation, where the response rate relating to the respective question was far too low to allow an accurate estimation.

Consumers are assumed to choose the product they use based on price, availability and technical properties (freezing point and washing capacity) and to some extent on other issues such as the smell. The content of the product as such is assumed not to have an effect. In the Finnish survey it was found that methanol is a better solvent and a cost-efficient anti-freezing component than the substitutes. In order to achieve technical applicability as anti-freezer in -20°C temperature, the need of alternative components was stated to be higher, contributing to a 20 - 50% increase in price.

F.3 Social impacts

As mentioned above (see section F.2) ethanol is a main alternative substance for restricted methanol in mixtures subsequently supplied to consumers. We estimate that methanol occurs in restricted concentrations represents a very small percentage in relation to the general use of methanol in EU therefore changes in demand of methanol/ethanol will be minor.

It is assumed that the majority of manufacturers of methanol mixtures could quite easily replace methanol with ethanol in the mixtures using the same concentrations. It is assessed that the replacement will have no impact on the manufacturers and employment, because this difference in the price of raw materials will be likely included in the price of the final product. The higher price of alternative mixtures will lead to increase of consumer expenditures.

Introduction of restrictions would eliminate methanol poisonings due to ingestion of containing methanol winter windshield washing fluids and denaturated alcohol, which seems to be the major cause of serious methanol poisonings. It will not eliminate or diminish ingestion of these products. Significant diminishing of methanol poisonings should result in decrease in the cost of social medical care during acute intoxication and long-term effects of poisoning which is inter alia the blindness.

F.4 Wider economic impacts

Resignation of adding methanol to windshield washing fluids and to denaturated alcohol is technically rather easy, quite feasible and does not induce the deterioration of quality or stability of these mixtures. The market price of methanol is lower than the price of its alternatives (such as ethanol). Ethanol is readily available and widely used on EU market, but its price is 2-3-fold higher. It is estimated that increased rate of raw material (ethanol) for the production of alternative mixtures as compared to the methanol will affect an slight increase of the final product's price. The restriction would be in force in EU and would affect all Member States, but it is no foreseen changes of competition within the EU.

Outside of the UE it would likely be no changes to competitiveness, since the restriction will not apply to the manufacture and the export of methanol mixtures outside the EU. Member States will still be allowed to produce and sell their methanol mixtures outside the EU or for professional use.

No wider economic impacts such as overall impacts on the economic growth or development, changes to competition within the EU or direct impacts on the macro-economic stabilisation

have been identified if the proposed restriction were to be implemented.

Impacts on innovation are not expected. Alternatives are available and already widely in use. The manufacturing technology is quite straightforward and major improvements are not expected.

F.5 Distributional impacts

In general methanol production will not be restricted. The restriction covers only a small part of the EU methanol market. Concerning the large production of methanol, restriction would not cause big changes for methanol producers and importers.

The introduction of the restriction will benefit consumers as they will not be directly exposed to methanol, which has as toxic effects on human health. General public will not have access to methanol or mixtures of 3% and greater the concentrations of methanol, which can save medical expenses in case of poisoning accident.

Methanol is a component of among others de-icing fluids and windscreen washers, therefore methanol mixtures are available for all car owners, who use these liquids widely at less than zero temperatures. These mixtures are mostly used in those EU regions, where winter temperatures falls below zero. As prices of alternative mixtures significantly increase after the introduction of restriction, higher costs will affect car owners especially in the regions where the winter temperature stay long below zero. Most likely to benefit from the restriction proposal are people and their families in term of reduced potential methanol exposure that may result in avoiding losing of health or life.

Many of the actors placing windscreen washing fluids on the market are SMEs. Among the actors that responded to the consultation of Finnish CA, actors putting windscreen washing fluids on the market, all 11 out of 11 actors dealing with methanol containing products reported the company they present to be a SME based on a simple head count. Four of them are micro enterprises (1-9 employees), two of them are small (10-49 employees) and five of them are medium sized enterprises (50-249 employees). Similarly, in Poland most of the big players (big petrol companies) did not supply on the market windshield washing fluids containing methanol.

It is foreseen that a ban of methanol would bring severe difficulties for those SMEs whose product portfolio leans on methanol based windscreen washing fluids strongly or exclusively. Moving to products not containing methanol would be challenging because the profit margin would be narrower. The product price would probably need to be increased leading to loss of market share. Some companies might end up out of business.

The questionnaire was sent directly by e-mail to actors notified to the Finnish Chemical Products Register and placing windscreen washing fluids on the market in Finland. Notifying to the register is compulsory in Finland. According to the survey, most of the enterprises have several products in their portfolio and windscreen washing fluids containing methanol only constitute a very minor share of their turnover (range 0.002%…70%, mean 12%, median 2 %). Consequently, a few enterprises having a major share of their turnover based on methanol might face severe problems due to the introduction of the proposed restriction.

F.6 Main assumptions used and decisions made during analysis

Restricted scenario would let avoiding delivering to general public of windshield washing fluids and denaturated alcohol containing methanol in concentration above 3%. It is assumed that the restriction would affect enterprises producing those products on the European Union market only. The restriction does not cover enterprises producing methanol mixtures for outside the EU and their market situation would not change, exporters would not have to change composition of their products. Methanol in mixtures is feasible and technical possible to replace. Quality and stability of the most products with alternatives substances would be comparable or higher. The supply chain of restricted methanol mixtures would have to change. Mixtures manufacturers sometimes will have to find out new suppliers of alternative substances. Alternative mixtures manufacturers would have to find a source of relevant alternatives with proper indicator of quality/price.
It may be noted that in some cases, the changes will apply to the production changes in the period before and during winter (for winter washer fluids or de-icing). By introducing a general ban despite the change of the final product, the restriction would not affect the competitiveness of enterprises, as would be related to whole EU chemical market.

F.7 Uncertainties

There is the lack of information on issues critical for a quantitative cost-benefit analysis, such as:

- the exact number of windshield washing fluids and denaturated alcohol with methanol concentration higher than 3% supplied to general public,
- costs of alternatives other than ethanol,
- the real number across the EU of people using those products as a surrogate of consumable alcohol,
- costs of medical care and treatment of poisoned people,
- cost of relevant non-medical care of blind people,
- the loss of potential productivity,
- costs of premature death.

The above information has been found not to be readily available. A detailed quantitative cost-benefit analysis has therefore not been performed.

For windscreen washing fluids a partial quantification and monetization of costs and benefits has been undertaken by Finish CA. It has to be noted that due to unavailability of relevant information, the numbers depict the situation in Finland only and their validity to represent the situation at EU level is unclear.

Other sources of uncertainty to be noted with regard to the analysis on windscreen washing fluids include:

- the prices of both ethanol and isopropanol have been set at exactly 2.5 times the cost of methanol (direction of a possible mistake unknown),
- it is assumed that to achieve similar performance, the amount of ethanol needed to replace 1 tonne of methanol is 1.3 tonnes, and the amount of isopropanol needed to replace 1 tonne of methanol is 1.5 tonnes (direction of a possible mistake unknown; suspected overestimation),
- it is assumed that the consumption of methanol, ethanol and isopropanol in windscreen washing fluids stayed the same during 2004-2011 and will stay the

same in the future in the absence of a restriction (an arithmetic mean of consumptions each year has been used) (direction of a possible mistake unknown),
- methanol tonnages underlying the cost estimate include tonnages directed to professional use which is actually out of scope of the proposed restriction (source of overestimation of costs),
- WTP and VSL estimates derived for an average person have been applied to the members of a specific group under risk,
- it is assumed that the victims of lethal methanol poisoning are 50-year old men who would otherwise live 28 more years (suspected overestimation).

Three scenarios have been generated to allow an estimation of the significance of the parameters used and the values assigned for those. The total (partial) estimates for costs and benefits and calculation thereof are presented in Table F.7-1 for substitution costs and in Table F.7-2 for benefits (WTP approach).

On the cost side, lower and higher estimates for the quantity of methanol to be substituted are represented by the lowest and highest amounts appearing during 2004-2011. There is a slight increase in the consumption trend. The slope is so small that it was considered unimportant to be taken into account in the calculation of the central estimate. However the slightly increasing trend gives confidence in that the lower estimate is low enough. An absolute maximum for methanol consumption would be the scenario where in the absence of a restriction, all ethanol and isopropanol now used in windscreen washing fluids would in the future be substituted by methanol. However this happening is not considered plausible because an increasing trend can be seen in the consumption of ethanol in windscreen washing fluids as well. The highest yearly consumption is quite high above the trend curve and was considered a suitable value for the calculation of a higher estimate.

For the price of methanol, variation of +-30% has been accounted for. Regarding the price of substitutes, the lower estimate uses a price twice that of methanol and the higher estimate a price three times that of methanol.

Table F.7-1. Estimates of substitution costs under three different scenarios in Finland.

	lower estimate	central estimate	higher estimate
Quantity of methanol to be substituted /T	900	1502	2600
Quantity of ethanol to be used /T	843,57	1407,8246	2436,98
Quantity of isopropanol to be used /T	376,65	628,587	1088,1
Total quantity of substitutes /T	1220,22	2036,4116	3525,08
Price of methanol /€/T	273	390	507
Total cost of methanol to be substituted /€	245700	585780	1318200
Price of substitutes /€/T	546	975	1521
Price of substitutes used/€	666240,12	1985501,31	5361646,68
Additional cost /€	420540	1399721	4043447

On the benefits side, in the generation of a lower estimate when applying the willingness to pay approach, 10 is used for the number of life years lost per death. There is no separate high value used in the generation of the higher estimate. For WTP for an additional life year, 157446 €[5] is used as a high reference value.

Table F.7-2. Estimates of benefits under different parameter values using the WTP approach in Finland.

	lower estimate	central estimate	higher estimate
Nr of deaths per year	22.91	22.91	22.91
Nr of years lost per death	10	28	28
Nr of years lost per year	229.1	641.48	641.48
WTP for an additional life year /€	70172	70172	157446
Total /€	**16076405,2**	**45013934,56**	**100998460,1**

In some Member States there are already comparable restrictions in force, and it is assumed that the costs and benefits experienced in those countries would be lower than the estimates presented here depending on the formulation of the present restriction.

F.8 Summary of the socio-economic impacts

To sum up, the proposed restriction for methanol is considered to effectively reduce the identified risk associated with ingestion of methanol contained in windshield washing fluids and denaturated alcohol supplied for general public whilst keeping the societal cost at a lower level than the societal benefits. Furthermore, alternatives to methanol in mixtures are available on the market.

Introducing of restriction is the right way to reduce poisoning cases. The increased costs are expected to be passed down the supply chain to consumers. It is not in the public health (for both consumers and workers) and socio-economic interest of the EU to allow such mixtures to be placed on the market.

Information from acute poisoning centers in Poland shows that introduction at the beginning of 2014 of the ban on sale to consumers of methanol mixtures at concentration equal to or greater than 3.0% w/w decreased considerably the number of poisoning cases with methanol solutions. And likewise a rapid increase of poisoning incidents was noticed after the expiry of the previous ban regulation. A full impact of the ban on the number of methanol intoxication

[5] 125200 € *120.21/95.59=157446 €

will be known in secod quarter of 2015 when it will be possible to compare methanol poisonings in winter 2013/2014 with those of the winter 2014/2015. Based on this information, the benefits of the proposed restriction are clearly much higher than the costs.

A complete analysis of benefits and costs was not feasible to carry out due to lack of data mostly related to the economic impacts.

G. Stakeholder consultation

A questionnaire has been sent to the REACH Competent Authority of all Member States in order to gather information on the number of registered cases of accidents/incidents occurring among consumers as a result of exposure to methanol containing products in other MS countries. The questionnaire is provided below. The answers were received and are summarised in Annex to these dossier - Table 1.

Table G-1: Questionnaire on Methanol. Screening of information for a possible Restriction proposal on the Use of Methanol in products intended for consumer use.

Q1 Can you indicate what specific types of methanol containing products are available on your market for use by consumers?	
Q2 Do you hold any information on accidents/incidents occurring among consumers as a result of exposure to methanol containing products in your country? If you believe that information on consumers accidents could be available in the poison control centres in your country, please provide the contact details of the relevant organisations.	
Q3 Is there currently any national legislation banning or otherwise controlling the marketing and use of Methanol? If yes, please provide below the relevant information (including the legal reference). This information may also include other non-regulatory action such as voluntary agreements, etc.	
Q4 A range of possible risk management options for controlling the risks from exposure to methanol	

<table>
<tr><td>during consumers use is provided below. Kindly indicate whether you would, in principle, support each of the possible options and whether you envisage problems arising from the implementation of any of these options.</td><td></td></tr>
<tr><td>Option No 3: A differentiated limitation for product/use categories. In case you think this is an appropriate option please indicate such products/use categories.</td><td>
<table>
<tr><th>Possible Risk Management Option</th><th>Would you support this? (Y/N)</th><th>Envisaged problems/ comments</th></tr>
<tr><td>Option No 1

Methanol shall not be supply to the general public,
- as a substance,
- or in mixtures.</td><td></td><td></td></tr>
<tr><td>Option No 2

Methanol shall not be supply to the general public:
- as a substance,
- or in mixtures, in concentrations equal to, or greater than ... % by weight.</td><td></td><td></td></tr>
<tr><td>Option No 3

Methanol shall not be supply to the general public,
- as a substance,
- or in mixtures, in concentrations equal to, or greater than ... % by weight.

However, the ban not apply to the following substances or mixtures, supply to the general public, containing methanol in concentrations equal to, or greater than ...% by weight:</td><td></td><td></td></tr>
</table>
</td></tr>
<tr><td>Using the space provided below, you may add any suggestions you have</td><td></td></tr>
</table>

on any other risk management options you would like us to consider; these could be variations or combinations of the options already mentioned or something completely different.	
Q5 Has any organisation in your country undertaken research on (or taken steps towards controlling): • the use of methanol containing products by consumers; • the exposure to methanol of consumers (incl. hobbyists) derived from the use of methanol containing products; If yes, please provide below details and appropriate Internet links, contact names or attach copies of relevant reports to your response.	

The problem of methanol poisoning was also discussed during Risk Management Expert Meeting (Copenhagen; RiME 2/2013). One of the topic during Session 3: RMO was dedicated to methanol: "Methanol in windscreen fluids – possible restriction?". The representative of Polish CA and Finish CA informed about the problem of methanol poisoning in Poland and in Finland. The presentations from RiME concerning methanol are detached below. Participants were requested to give views on whether they feel restriction under REACH should be used to regulate for misuse of windscreen fluids containing methanol, due to the apparent risk to human health. It was put forward that the apparent high number of deaths associated with methanol poisoning can be taken as proof of risk. During the discussion which occurred after the presentation of Polish and Finish CA the following issues were highlighted:

- some countries (Finland, Poland) has experienced problems with people dying from ingestion of mixtures containing high concentration of methanol,
- in some countries (for example Denmark) such problem does not exist,
- in some countries (like Denmark) exist legislation which ban to sell consumers product classified as toxic (in case of mixtures containing methanol, they are classified as toxic, if methanol concentration in mixture is equal or higher than 10%),
- some countries raise the question if we can regulate "misuse" by restriction proposal,
- some countries has mentioned that Italy has proposed a new classification of methanol. The new classification defines methanol as toxic to reproduction. If new classification will be approved by RAC, in the opinion of many countries, the problem of mixtures available for consumers containing high percentage of methanol will be solved. According to Annex XVII of REACH Regulation substances and mixtures classified as toxic to reproduction category 1A and 1B shall not be supply to the general public. If the new classification of methanol will be approved, mixtures containing equal or higher than 0,3% methanol will be classified as toxic to reproduction category 1 and will not be allowed to be supply for general public.


Bureau for Chemical Substances
www.chemikalia.gov.pl
Outbreak of methanol poisonings in Poland in 2011 – 2012
RiME meeting
Copenhagen, June 3, 2013
© Bureau for Chemical Substances


Bureau for Chemical Substances
www.chemikalia.gov.pl
Regulations till June 1, 2010
• Since 1967 – under the Act on poisonous substances (repealed) – practical ban for consumers – authorisation of the Minister of Health necessary for purchase (industry, universities and some other entities exempted)
• Since 2004 till June 1 2010 – under the Act on chemical substances and preparations – ban on methanol >3% for consumers (with exemptions - some fuels)
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Outbreak of poisonings

- Winter season 2010/2011 – the lack of the ban on methanol not yet noticed by producers of windshield fluids
- Late November and December 2011 – alarmistic data from Poison Centers on the wave of methanol poisonings, probably due to consumption of windshields fluids containing methanol (the source of methanol usually difficult to establish)

Gathering the data

- The system of toxicovigilance not yet established in Poland – we do not have full data on poisonings
- The data were voluntarily provided by Acute Poison Centres, Departments (Institutes) of Forensic Medicine, laboratories in clinical toxicology centres (departments), National Health Fund
- Basing on the gathered data we can estimate that the number of fatal poisonings **raised in 2011 and 2012 to approximately 120 yearly from around 20 in 2010**


Bureau for Chemical Substances
Sources of methanol for consumers
www.chemikalia.gov.pl
• Difficult to establish
• Windshield fluids manufactured in Poland
• Windshield fluids from outside the EU
• Other products (containing methanol) for consumers – technical ethanol for various purposes (fuel for touristic cooking appliances and all purpose cleaning agent)
• Methanol stolen from elsewhere
• Alcohols containing methanol
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Regulations and poisonings in other countries
www.chemikalia.gov.pl
• In Scandinavian countries (apart of Finland), Austria, Germany, Lithuania – bans or practical ban for consumers due to prooving qualifications necessary for buying toxic and very toxic chemicals (>10% of methanol)
• Apart of Poland poisonings recorded in Finland, Italy (among immigrants from Central Europe), probably other countries
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Bureau for Chemical Substances
What should be done?
www.chemikalia.gov.pl
• It seems that poisonings occur in countries with the habit of drinking heavy spirits
• Poisonings should not be expected in counties with the wine culture
• Poland and Finland are finishing preparation of Annex XV for restrictions of methanol
• However, do we need the EU wide measure for methanol?
• Thank you for your attention
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Finnish Safety and Chemicals Agency (Tukes)
Hinni Papponen | 3-4.6.2013
Methanol
tukes

Methanol CAS 67-56-1

Harmonised classification

Flam. Liq. 2	H225	*
Acute Tox. 3 *	H301	STOT SE 1; H370: C ≥ 10% STOT SE 2; H371: 3% ≤ C < 10%
Acute Tox. 3 *	H311	
Acute Tox. 3 *	H331	
STOT SE 1	H370 **	

Ongoing processes

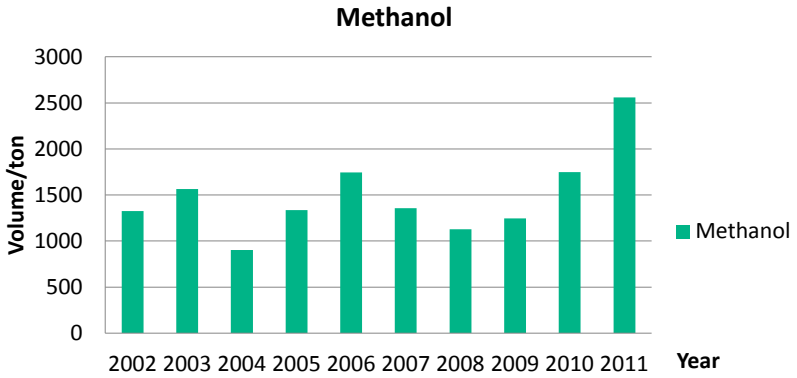
- Dossier evaluation
  - terminated in March, ECHA
- Substance evaluation
  - Evaluated 2012, Poland
- Proposal for harmonised classification
  - Reproductive toxicity, Italy

The Finnish Government Decree on Retail Sales of Chemicals

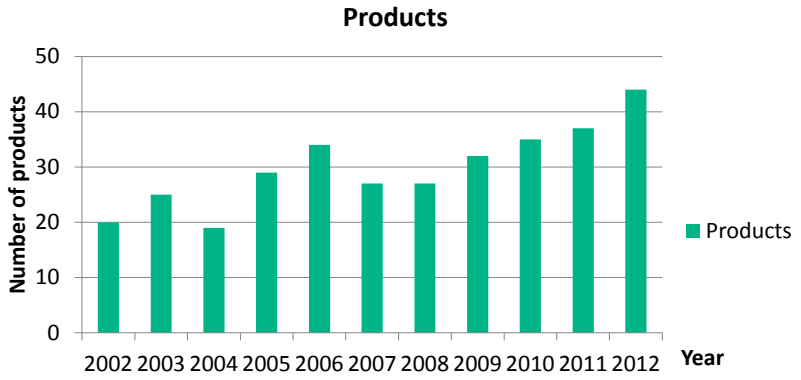
includes e.g.

- In retail outlets or their storage facilities, toxic chemicals shall be stored in locked-up premises
- Toxic chemicals shall only be supplied to persons over the age of 18
- No chemical whatsoever shall be supplied, if there is reason to suspect the chemical is likely to be used for the purpose of intoxication or for any other misuse that may cause serious health risks

Volume of methanol in windscreen fluids



Number of methanol containing windscreen fluids on the market



- 326 deaths since 2000
- A typical victim is 50-year old man with a drinking problem
- Number of methanol containing windscreen fluid products seems to be increasing
- Volume of methanol used in windscreen fluids seems to be increasing
- Classification and labelling of mixtures according the CLP-regulation will affect products containing methanol – more products without skull and crossbones (GHS06)

How to deal with the situation?

- Does the definition of use also include misuse?
- How to deal with the risks arising from an intentional misuse of a toxic chemical?
  - EU wide restriction?
    - If so, how to demonstrate that there is a risk?

tukes Finnish Safety and Chemicals Agency
3-4.6.2013 | RiME 2/2013, Hinni Papponen 9

H. Other information

The information from the joint REACH registration dossier was considered during preparation of the Annex XV restriction proposal for methanol.

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Annexes

As was mentioned in section G (Stakeholder consultation), a questionnaire has been sent to the REACH Competent Authority of all Member States, in order to gather information on the

number of registered cases of accidents/incidents occurring among consumers as a result of exposure to methanol containing products in other MS countries. The received answers are summarised in table below.

Annex 1. Ouestionnaire on methanol – received answers from MS Competent Authorities.

Questionnaire on Methanol
Screening of information for a possible Restriction proposal on the Use of Methanol in products intended for consumer use

Q1 **Can you indicate what specific types of methanol containing products are available on your market for use by consumers?**	**Finland** Altogether there are 132 products for consumer use on the market: - 52 detergents or cleaning agents (of which 38 windscreen fluids) - 10 paints, lacquers and/or varnishes - 9 solvents - 8 "other chemicals" (of which 1 windscreen fluid) - 7 fuels - 7 listed without a specific product description (incl. fillers - 7 corrosion inhibitors - 5 biocides - 5 colorants - 4 construction/building materials - 4 adhesives, glues and binding materials - 3 fragrances - 3 fillers - 3 lubricants and additives - 2 surface treatment agents - 1 disinfectant/general purpose biocide - 1 heat-transfer agent - 1 anti-freeze agent **Norway** Vehicle fuels, other fuels, fillers, undersealing agents, paints and varnishes, paint and varnish removers and cleaning agents. **Estonia** Yes, we have available on our market car glass cleaner liquid -20 °C used in car spray systems and liquids for fire ignition with methanol for consumer use. **Cyprus** Semi solidified methanol gel in cans Methanol in gel fuels Methanol as additive in ethanol Biodiesel **Netherlands** Methanol is produced within the Netherlands in quantities by various companies with most of these having a production of >1000 tonnes/year Methanol is applied as a.o.: - antifreeze - lock-defroster

	- solvent (in e.g. paint) Furthermore, in the Netherlands, methanol is added in a concentration of 3% to methylated spirits (i.e. 85% ethanol), in order to make this unsuitable for human consumption and to prevent abuse of these products containing a very high % ethanol. **Lithuania** Ink, lacquer, glue, windshield washer fluid, cleaner, disinfectant, thinner, corrosion inhibitor, wax, hardener, undercoat. **Malta** Windscreen washing liquid Race car fuel **Germany** Potentially incomplete list - Marker pens (lining felt) - Joint sealing mass Plane modeling fuel **Ireland** Methanol containing products available to consumers in Ireland include – surgical spirits; vehicle screenwash; vehicle antifreeze; de-icer; paint thinner; paint remover; stain and odour removers. **United Kingdom** The UK holds no central product registry. As indicated below, de-icers and screen washes are the most common consumer products involved in reported incidents. **Bulgaria** The identified methanol containing products available on the Bulgarian market are the following: • windshield washer fluids • solvents • methylated spirit • Antifreeze • Some types of glue • Alcoholic beverages of poor quality (illegally produced) • Fuels **Slovenia** solvents, diluters, inks, glues, antifreeze
Q2 **Do you hold any information on accidents/incidents occurring among consumers as a result of**	**Finland** Finland has compiled statistics on methanol-related deaths and deaths have been verified by forensic analyses. Methanol-related deaths are reported in several Finnish peer reviewed articles (available mostly in Finnish) with some minor inconsistencies in the reported numbers. However, the overall number of deaths by poisoning has decreased in recent years, but the number of methanol-related deaths has remained on the higher level reached after FI entry into EU. This indicates that the relative proportion of methanol-related deaths has increased in the recent past. In Finland methanol-related deaths are

exposure to methanol containing products in your country? **If you believe that information on consumers accidents could be available in the poison control centres in your country, please provide the contact details of the relevant organisations.**	known to be caused by the misuse of windscreen fluids. Other causes for methanol poisonings are extremely rare. Year — Methanol-related deaths 1993 5 1994 2 1995 8 1996 15 1997 18 1998 29 1999 33 2000 46 2001 30 2002 25 2003 43 2004 26 2005 30 2006 12 2007 28 2008 15 2009 30 2010 24 2011 17 preliminary The Finnish Poison Information Center +358 (0)9 4711 (switchboard) **Estonia** Estonian Poisoning information Center info@16662.ee In 2006 we had criminal case with 6 deaths (people ingested methanol containing fire ignition liquid). **Cyprus** This question was directed to the Emergencies Department of the General Hospital. They informed us that no poisoning due to methanol has taken place the last 3 years. **Austria** no case of poisoning since 2007 **Netherlands** The information as requested might be available at the Dutch National Poisoning Information Centre (NVIC). However, this concerns probably accidental exposure. e-mail: NVIC@umcutrecht.nl postal address:

	NVIC University Medical Centre Utrecht P.O. Box 85500 3508 GA Utrecht The Netherlands **Lithuania** According to the data provided from The National Health Insurance Fund under the Ministry of Health there were 11 – 30 in-patients treated and 0-5 deaths registered per year with the diagnosis T51.1 (poisoning with methanol) during past 10 years. In the year 2012 there were 8 in-patients and 2 deaths registered with the diagnosis T51.1. 1 call during 2012 was received in the Poison Control and Information Bureau regarding suspected poisoning with methanol. **Malta** According to the local Department of Health Information & Research in the last five years there were no poisonings related to methanol containing products. **Germany** A number of notificatons by physicians (according to german law: ChemG §16e Abs.2) about poisonings with methanol is known. The respective consumer products were: fuel for model aircraft, windshield/glass cleaner, denaturated alcohol. It is not known whether poison control centers in Germany have such information. **Ireland** The following data was obtained from the Irish National Poisons Information Centre – 2008 – 15 incidents recorded, 9 of which involved children 2009 – 16 incidents recorded, 8 of which involved children 2010 – 19 incidents recorded, 9 of which involved children 2011 – 13 incidents recorded, 10 of which involved children 2012 – 10 incidents recorded, 8 of which involved children Almost all incidents involving children were as a result of ingestion. Adult incidents involve ingestion/skin/eye contact or inhalation. **United Kingdom** NPIS (National Poisons Information Service) has information on enquiries relating to reported exposure to products that may contain methanol in the UK. However, these data are not comprehensive as (a) the circumstances of exposure may not be well described (accidental or otherwise) and the exact products involved or their constituents may not be known. Amongst consumer products, de-icers and screen washes containing methanol appear to be most commonly involved. **Bulgaria** The intoxication cases in Bulgaria are mainly by accident – consumer or professional use. The last case happened in February 2013. Six young people (16-20 years old) were hospitalized due to acute intoxication after windshield washer fluid consumption. According to the data from the National Poison center for western Bulgaria there are 15-30 cases per year with mortality and disability caused mainly by abuse with methylated spirit. For the last 5 years (in southern Bulgaria) there have been 13 cases of methanol

	intoxication (7 with lethal outcome). *Contact details of Bulgarian National Poison center*: **National Toxicology Center**, Hospital for Active Medical Treatment and Emergency Medicine "N.I.Pirogov" contact person: Ms MARGARITA GESHEVA – head of the Poison center Emergency number/ fax: +359 2 9154 409 E-mail: **poison_centre@mail.orbitel.bg** http://www.pirogov.bg **Slovenia** There are occasional cases of methanol poisoning, in year 2012 there was a case when child drank fuel for model aircraft, in year 2011 older man (alcoholic) drank mixture of methanole and ethanole - the product was not identified. In Slovenia self-sown grape "šmarnica" is sometimes used for self production and self consumption of wine consisting high level of methanol, which is believed to be the reason of different health problems in case of regular consumption of such wine. There is no such wine on the market, due to the prohibition of planting such grapes and selling this type of wine.
Q3 **Is there currently any national legislation banning or otherwise controlling the marketing and use of Methanol?** **If yes, please provide below the relevant information (including the legal reference). This information may also include other non-regulatory action such as voluntary agreements, etc.**	**Finland** At the moment there is no specific legislation banning the marketing and use of methanol. The retail of methanol is regulated as follows: The provisions concerning retail of chemicals are in Finland laid down in the Finnish Chemicals Act (744/1989) and the Decree of the Finnish Government on retail of chemicals (573/2011). The provisions are as follows: Substances and mixtures classified as toxic (T) or extremely toxic (T+) or as Acute Toxic category 1-3 according to the CLP Regulation: . may only be sold to persons 18 years of age or older, except for fuels, which may be sold to customers regardless of age. However, methanol containing fuels may be sold to persons younger than 18 years if they have a written permission from their statutory guardian. . when sold from a pharmacy, the receiver must on a separate form give the information mentioned beneath. The receiver shall confirm his identity and date and sign the form. The pharmacy shall keep the form for a period of five years. o personal details and address o name and amount of the chemical bought o intended use of the chemical . shall be kept locked up in the retail shop or in its storage. This obligation doesn't concern other fuels than those containing methanol. Chemicals may not be sold, if there is reason to assume that they are going to be used for intoxication or otherwise used in a way which could cause harm to health. Dangerous chemicals may only be sold unpacked to be used as motor fuel or lubricant, directly to a driving engine/operating equipment or to a container of at least 200 liters. The distribution device/container shall be labeled according to the CLP Regulation or DPD 1999/45/EEC. **Norway** According to the Norwegian Regulations relating to restrictions on the manufacture, import, export, sale and use of chemicals and other products hazardous to health and the

	environment (Product Regulations) (FOR 2004-06-01 nr 922), section 5-1, the import for private use of chemicals labelled with the risk phrase and the hazard description «meget giftig» ("very toxic") or «giftig» ("toxic") in accordance with the Regulations on the classification, labelling, etc., of dangerous chemicals is prohibited. This applies to the placing on the market of mixtures containing more than 10% methanol for supply to the general public. Furthermore, any person (except pharmacies) who wishes to sell such chemicals for private use must obtain a permit from the Norwegian Environment Agency. These kinds of chemicals can only be sold for private use to persons over the age of 18 who, by means of a requisition from the police, can document the need for such substances or preparations. For more information, cfr. http://www.klif.no/artikkel____38645.aspx#5_1 Special rules apply for fuels for model vehicles, cfr. the same regulations. The Norwegian General civil penal code (Act of 22 May 1902 No. 10), Section 153 is also relevant for the case of controlling the marketing and use of methanol. This law was applied in a High Court Sentence following incidents with bootleg (=smuggler spirits) sale in Norway in the period 2002-2004. The General civil penal code states that "*any person who adds poison or other such substances to any product for general use or sale so that the product cannot be used for the purpose intended without causing a person's death or injuring his health (…) shall be liable to imprisonment for a term not exceeding 21 years.*" **Estonia** No **Cyprus** No **Netherlands** The Health Council of the Netherlands concluded in 2006 that Methanol should be considered as reprotoxic to humans (comparable with Repro 1B according to the CLP-regulation) (http://www.gezondheidsraad.nl/sites/default/files/06@04OSH.PDF). This classification was taken over in the list of CMR-substances of the Ministry of Social Affairs and Employment in the Netherlands resulting in additional obligations for employers. **Lithuania** The Law on Control of Poisonous Substances: http://www3.lrs.lt/pls/inter3/dokpaieska.showdoc_l?p_id=145531 (Lithuanian language) or http://www3.lrs.lt/pls/inter3/dokpaieska.showdoc_l?p_id=151702 (Russian language) and by-law acts. Permissions (for legal or natural persons who fulfil some defined requirements) for trade, distribution, purchase and use of methanol as a substance or in mixtures classified as toxic. **Malta** No **Germany** **Directives on Safety in School (BGR/GUV-SR 2003)** Activity ban for pupils till grade 4 (form) inclusive. Substance list to GUV-SR 2004 (as of 11.2010) Special substitute check required (substances with CMR, T+, E, and C with R35). Substance list to GUV-SR 2004 (as of 11.2010) **Consumer Goods Ordinance; status - February 2011**

	Attachment 1 to § 3, Point 5 General entry: "Substances and preparations, classified as dangerous according to the German Ordinance on Hazardous Substances (GefStoffV, now adapted to CLP-regulation) shall not be used for the production or treatment of joke articles." **German Consumer Goods Ordinance (Bedarfsgegenständeverordnung) (as of 7 February 2011)** Methanol is listed in Annex 3 on substances and products for the manufacture of food contact materials, Section 1 (Monomers and other starting substances), Part A (List of monomers and other starting substances, which are allowed for the manufacture of plastic food contact materials. **Ireland** EC Regulation 1272/2008 and the Dangerous Preparations Directive (1999/45/EC) require products sold to the general public containing greater than or equal to 3% methanol, to have child resistant fastenings. Not aware of any other however we have referred the matter to Government for confirmation. If there are any other legislative instruments addressing methanol, we will communicate this in due course. **United Kingdom** None we are aware of. **Bulgaria** The following limit values for methanol are introduced in some products, as well as at workplace: 1. According to **Regulation concerning the requirements for the quality of liquid fuels, the terms, order and manner of their control**, the limit values for methanol are: • In motor benzine: 3 % (V/V) • In biodiesel: 0,20 % (m/m) 2. According to **Regulation for protection of workers from the risks connected with the chemical agents at workplace**, the OEL for methanol in the air of the working environment is: 260 mg/m^3 (skin absorption) for 8 hours exposure. **Slovenia** There is no national legislation concerning methanol in the area of chemicals. Still, planting of "šmarnica grapes" and selling of wine from such grapes is prohibited.
Q4 **A range of possible risk management options for controlling the risks from exposure to methanol during consumers use is provided below. Kindly indicate whether you would, in**	

<table>
<tr><td>principle, support each of the possible options and whether you envisage problems arising from the implementation of any of these options.</td><td></td></tr>
<tr><td>Option No 3: A differentiated limitation for product/use categories.
In case you think this is an appropriate option please indicate such products/use categories.</td><td>
<table>
<tr><th>Possible Risk Management Option</th><th>Would you support this? (Y/N)</th><th>Envisaged problems/ comments</th></tr>
<tr><td>Option No 1
Methanol shall not be supply to the general public,
- as a substance,
- or in mixtures.</td><td></td><td></td></tr>
<tr><td>Option No 2
Methanol shall not be supply to the general public:
- as a substance,
- or in mixtures, in concentrations equal to, or greater than ... % by weight.</td><td></td><td></td></tr>
<tr><td>Option No 3

Methanol shall not be supply to the general public,
- as a substance,
- or in mixtures, in concentrations equal to, or greater than ... % by weight.

However, the ban not apply to the following substances or mixtures, supply to the general public, containing methanol in concentrations equal to, or greater than ...% by weight:</td><td></td><td></td></tr>
</table>
</td></tr>
<tr><td>Using the space provided below, you may add any suggestions you have on any other risk management options you would like us to consider; these could be</td><td></td></tr>
</table>

variations or combinations of the options already mentioned or something completely different.

Finland

Possible Risk Management Option	Would you support this? (Y/N)	Envisaged problems/ comments
Option No 1 **Methanol shall not be supply to the general public,** **- as a substance,** **- or in mixtures.**	N	A general ban is not deemed to be necessary (nor possible) as not all products (especially non-liquid ones) containing methanol pose a risk for consumers.
Option No 2 **Methanol shall not be supply to the general public:** **- as a substance,** **- or in mixtures, in concentrations equal to, or greater than ... % by weight.**	N	
Option No 3 **Methanol shall not be supply to the general public,** **- as a substance,** **- or in mixtures, in concentrations equal to, or greater than ... % by weight.** **However, the ban not apply to the following substances or mixtures, supply to the general public, containing methanol in concentrations equal to, or greater than ...% by weight:**	N	

Finland is in favor of a restriction proposal only limited to the use of methanol in windscreen fluids as follows:

> *Windscreen fluids containing methanol in a concentration equal to or greater than 0.1 %(* by weight shall not be placed on the market for supply to the general public after xx.xx.xxxx*

However, this could be extended to cover also such uses in consumer products that are relevant for health concern, if there is information on other uses causing risk.

* The aim is to ban the placing on the market. A ban is deemed needed because there are harmful effects on optic nerve even at lower concentrations than those leading to classification and because the amounts drunk by misusers are often several liters. A low concentration limit is still needed because small amounts of methanol can exist as impurity in ethanol products.

Norway

Possible Risk Management Option	Would you support this? (Y/N)	Envisaged problems/ comments
Option No 1 **Methanol shall not be supply to the general public,** **- as a substance,** **- or in mixtures.**		There are restrictions in Norway on the placing on the market of mixtures containing more than 10% methanol on the marked for supply to the general public, cfr. Product regulations § 5.1. Special rules apply for fuels for model vehicles, cfr. the same regulations.
Option No 2 **Methanol shall not be supply to the general public:** **- as a substance,** **- or in mixtures, in concentrations equal to, or greater than ... % by weight.**		
Option No 3 **Methanol shall not be supply to the general public,** **- as a substance,** **- or in mixtures, in concentrations equal to, or greater than ... % by weight.** **However, the ban not apply to the following substances or mixtures, supply to the general public, containing methanol in concentrations equal to, or greater than ...% by weight:**		

Estonia

Possible Risk Management Option	Would you support this? (Y/N)	Envisaged problems/ comments
Option No 1 **Methanol shall not be supply to the general public,** **- as a substance,** **- or in mixtures.**	No	
Option No 2 **Methanol shall not be supply to the general public:** **- as a substance,** **- or in mixtures, in concentrations equal to, or greater than ... % by weight.**	No	
Option No 3 **Methanol shall not be supply to**	Yes	Up to 5% - please look to the ES of the attached SDS.

the general public, **- as a substance,** **- or in mixtures, in concentrations equal to, or greater than ... % by weight.** **However, the ban not apply to the following substances or mixtures, supply to the general public, containing methanol in concentrations equal to, or greater than ...% by weight:**		

Cyprus

Possible Risk Management Option	**Would you support this? (Y/N)**	**Envisaged problems/ comments**
Option No 1 **Methanol shall not be supply to the general public,** **- as a substance,** **- or in mixtures.**	Y	
Option No 2 **Methanol shall not be supplied to the general public:** **- as a substance,** **- or in mixtures, in concentrations equal to, or greater than ... % by weight.**		Difficult to control.
Option No 3 **Methanol shall not be supply to the general public,** **- as a substance,** **- or in mixtures, in concentrations equal to, or greater than ... % by weight.** **However, the ban not apply to the following substances or mixtures, supply to the general public, containing methanol in concentrations equal to, or greater than ...% by weight:**		Difficult to control.

Austria

Possible Risk Management Option	**Would you support this? (Y/N)**	**Envisaged problems/ comments**

Option No 1 **Methanol shall not be supply to the general public,** **- as a substance,** **- or in mixtures.**	Y	
Option No 2 **Methanol shall not be supply to the general public:** **- as a substance,** **- or in mixtures, in concentrations equal to, or greater than ... % by weight.**	N	
Option No 3 **Methanol shall not be supply to the general public,** **- as a substance,** **- or in mixtures, in concentrations equal to, or greater than ... % by weight.** **However, the ban not apply to the following substances or mixtures, supply to the general public, containing methanol in concentrations equal to, or greater than ...% by weight:**	N	

Netherlands

Possible Risk Management Option	Would you support this? (Y/N)	Envisaged problems/ comments
Option No 1 **Methanol shall not be supply to the general public,** **- as a substance,** **- or in mixtures.**	no	In the Netherlands, methanol is added in a concentration of 3% to methylated spirits (i.e. 85% ethanol), in order to make this unsuitable for human consumption and to prevent abuse of these products containing a very high % ethanol. If this risk management option would be selected, adding of methanol to these products would no longer be allowed. This might increase the abuse of these products containing a very high % ethanol. An alternative should then be searched for.
Option No 2 **Methanol shall not be supply to the general public:** **- as a substance,**	no	In the Netherlands, methanol is added in a concentration of 3% to methylated spirits (i.e. 85% ethanol), in order to make this unsuitable for

- or in mixtures, in concentrations equal to, or greater than ... % by weight.		human consumption and to prevent abuse of these products containing a very high % ethanol. If this risk management option would be selected, adding of methanol to these products would no longer be allowed. This might lead to an increase of the abuse of these products containing a very high % ethanol. An alternative should then be searched for.
Option No 3 **Methanol shall not be supply to the general public,** **- as a substance,** **- or in mixtures, in concentrations equal to, or greater than ... % by weight.** **However, the ban not apply to the following substances or mixtures, supply to the general public, containing methanol in concentrations equal to, or greater than ...% by weight:**	no	In the Netherlands, methanol is added in a concentration of 3% to methylated spirits (i.e. 85% ethanol), in order to make this unsuitable for human consumption and to prevent abuse of these products containing a very high % ethanol. If this risk management option would be selected, adding of methanol to these products would no longer be allowed. This might lead to an increase of the abuse of these products containing a very high % ethanol. An alternative should then be searched for.

Lithuania

Possible Risk Management Option	Would you support this? (Y/N)	Envisaged problems/ comments
Option No 1 **Methanol shall not be supply to the general public,** **- as a substance,** **- or in mixtures.**	Y	Methanol is a highly toxic substance, which could be quite easily replaced with other less toxic substances alone or in the mixtures.
Option No 2 **Methanol shall not be supply to the general public:** **- as a substance,** **- or in mixtures, in concentrations equal to, or greater than ... % by weight.**	Y	As general requirement, it is rational that methanol shall not be supply to general public as a substance or in mixtures, when concentrations are equal to, or greater than 10 %, because the specific concentration limits are established for this substance and classification then is "toxic", unless some products with any other lower concentrations are actual for consumers.
Option No 3 **Methanol shall not be supply to the general public,** **- as a substance,**		

	- or in mixtures, in concentrations equal to, or greater than ... % by weight. **However, the ban not apply to the following substances or mixtures, supply to the general public, containing methanol in concentrations equal to, or greater than ...% by weight:**		

Malta

Possible Risk Management Option	**Would you support this? (Y/N)**	**Envisaged problems/ comments**
Option No 1 **Methanol shall not be supply to the general public,** **- as a substance,** **- or in mixtures.**	Y	N
Option No 2 **Methanol shall not be supply to the general public:** **- as a substance,** **- or in mixtures, in concentrations equal to, or greater than ... % by weight.**	Y	N
Option No 3 **Methanol shall not be supply to the general public,** **- as a substance,** **- or in mixtures, in concentrations equal to, or greater than ... % by weight.** **However, the ban not apply to the following substances or mixtures, supply to the general public, containing methanol in concentrations equal to, or greater than ...% by weight:**	N	We envisage problems related to enforcement of this option.

Ireland

In the absence of wider statistical data on incidents involving methanol, and public consultation views on any proposed restriction, it is difficult to advocate any particular restriction wording at this time. From the information obtained, there is an issue with ingestion/skin and eye contact and inhalation of consumer products containing methanol. It is difficult for IE to consider risk management options without information on how exposure occurs, risks and the populations at risk. Perhaps one risk management measure

that could be considered is the quantity and type of packaging sold to the general public e.g. child resistant fastenings. We are aware that products sold to the general public containing more than 3% methanol must have child resistant packaging under the CLP Regulation (EC 1272/2008) and the Dangerous Preparations Directive (1999/45/EC)

United Kingdom

We would need to see more information on uses and the risks identified (ie the annex XV dossier) to be able to form a judgment on the best option.

Bulgaria

Possible Risk Management Option	Would you support this? (Y/N)	Envisaged problems/ comments
Option No 1 **Methanol shall not be supply to the general public,** **- as a substance,** **- or in mixtures.**	N	
Option No 2 **Methanol shall not be supply to the general public:** **- as a substance,** **- or in mixtures, in concentrations equal to, or greater than 5 % by weight.**	Y	According to the opinion of the Poison center, the concentration in all methanol containing products, supplied to the general public, shall not exceed 5 % (based on an old state standard applicable in the past, concerning methylated spirit), since in case of abuse with/misuse methanol containing products, at this limit value the risk for lethal outcome is minimized.
Option No 3 **Methanol shall not be supplied to the general public,** **- as a substance,** **- or in mixtures, in concentrations equal to, or greater than 3 % by weight.** **However, the ban not apply to the following mixtures, supplied to the general public, containing methanol in concentrations equal to, or greater than 3 % by weight:** **…**	Y	This option is also acceptable; however reliable information in terms of the safe threshold and the exemption in other products does not exist.

Ministry of Health and the National Poison Center suggest the following additional measures for the risk management purposes:

- Warning notice on the label of the methanol containing mixtures: "**Contains METHANOL! RISK at inhalation and absorption (intake)**".
- **Marking for high toxicity**.

The use of **additives with bitter and unpleasant taste** in the methanol containing mixtures in order to prevent the risk of absorption (intake).

Slovenia

Possible Risk Management Option	Would you support this? (Y/N)	Envisaged problems/ comments
Option No 1 **Methanol shall not be supply to the general public,** **- as a substance,** **- or in mixtures.**	N	
Option No 2 **Methanol shall not be supply to the general public:** **- as a substance,** **- or in mixtures, in concentrations equal to, or greater than ... % by weight.**	N	
Option No 3 **Methanol shall not be supply to the general public,** **- as a substance,** **- or in mixtures, in concentrations equal to, or greater than ... % by weight.** **However, the ban not apply to the following substances or mixtures, supply to the general public, containing methanol in concentrations equal to, or greater than ...% by weight:**	N	

Q5
Has any organisation in your country undertaken research on (or taken steps towards controlling):

- **the use of methanol containing products by consumers;**
- **the exposure to methanol of consumers (incl.**

Finland

Anette Malinen. Survey of the Use of Alcohol Surrogates in Finland Year 2002. Helsinki 2003. 79p. (Reports of the Ministry of Social Affairs and Health, ISSN 1236-2115; 2003:3) ISBN 952-00-1313-X (in Finnish, only summary in English). http://www.stm.fi/c/document_library/get_file?folderId=28707&name=DLFE-3496.pdf&title=Kartoitus_alkoholikorvikkeiden_kaytosta_Suomessa_vuonna_2002__tiivistelma_fi.pdf

Development of Initial REACH Exposure Scenarios for Methanol. Finnish Institute of Occupational Health. Helsinki 2008. Translation 2009.
http://www.ttl.fi/en/publications/Electronic_publications/Documents/Methanol.pdf

The Finnish Ministry of Social Affairs and Health has requested the Finnish Safety and Chemicals Agency to prepare an Annex XV restriction dossier on the use of methanol in windscreen fluids as specified above.

Estonia

After the incident in 2006 with 6 deaths Health Board inspectors investigated all liquids for

hobbyists) derived from the use of methanol containing products; **If yes, please provide below details and appropriate Internet links, contact names or attach copies of relevant reports to your response.**	fire ignition available on the Estonian market. **Netherland** No **Malta** No **Ireland** Our organization has not undertaken any research and we are not aware of any other research. **United Kingdom** None we are aware of. **Bulgaria** N/A **Slovenia** N

Annex 2.

A rough translation into English of the questionnaire used in the consultation of Finnish actors placing windscreen washing fluids on the market.

Questionnaire

1. Basic information

***1.1. Name of the enterprise:**

***1.2. Address:**

***1.3. Telephone:**

***1.4. Name, address and details of the contact person:**

All the following questions are voluntary and You can provide an answer with the appropriate detail. However, the more information is received, the better the impact of the restriction to enterpreneurs can be acknowledged.

1.5. Size of the enterprise (please select one)

- Micro: 1 - 9 employees
- Small: 10 - 49 employees
- Medium: 50 - 249 employees
- Large: 250 employees or more

1.6. Please indicate the share of methanol containing windscreen washer fluids of your whole business (estimated % of sales)

1.7. Which alternative substitutes for methanol do You know for windscreen washer fluids?

1.8. Are You an importer of methanol? (please select one or several)

- No
- Yes, from other EU-countries
- Yes, from outside EU, from:

1.9. Are you an importer of methanol containing windscreen washer fluids? (please select one or several)

- No
- Yes, from other EU countries
- Yes, from outside EU, from:

1.10. Are You an exporter of methanol containing windscreen washer fluids? (please select one or several)

- No
- Yes, to other EU countries
- Yes, to outside EU, to:

1.11. Are you a formulator or distributor of windscreen washer fluids? (please select one)

- No
- Yes

1.11. What is the range of methanol concentration in Your windscreen washer fluids? (please select one or several)

- < 0.1 %
- 0.1 % ≤ C < 3 %
- 3 % ≤ C < 10 %
- 10 % ≤ C < 34 %
- ≥ 34 %

Percentage figures are O % by weight O % by volume.

2. Health and environmental incidents

2.1. Are you aware of any methanol related health or environmental incidents occurred at Your enterprise, customers or supply chain? (please select one)

☐ We are not monitoring them

☐ We are monitoring them, but have not experienced any

☐ Yes

If yes, please describe the details of the incident (e.g. the volume of methanol, time and type of the incident, consequences and the value of the harm caused)

If yes, please describe the action taken after the incident and related costs

2.2 Do You have any other comments on the health and environmental incidents related to use of methanol?

3. Economic impact

3.1. Please declare composition of Your current products (please use the same examples in the whole questionnaire)

The percentages are expressed as O % by weight O % by volume.

Product applicable for use at -20 °C, components and their concentrations

The sales price of the product, €/L

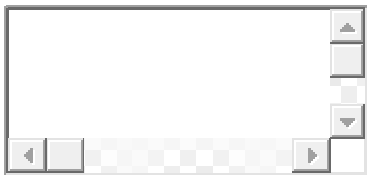
Optional product 1*, *components and their concentrations

Anti-freezing temperature :

°C

The sales price of the product, €/L

Optional product 2*, *components and their concentrations



Anti-freezing temperature : °C

The sales price of the product, €/L

Further information and comments:

3.2 Foreseen impact of the methanol restriction on the composition of Your products

If the content of methanol in wind screeen washing fluids will be restricted to 3 %, what kind of product is applicable for use at -20 °C (unless similar than above); components and their concentrations?

The sales price of the product:

€/L

If the content of methanol in wind screeen washing fluids will be restricted to 0.1 %, what kind of product(s) is (are) applicable for use at -20 °C (unless similar than above)?

The sales price of the product:

€/L

Further information and comments:

3.3 Other foreseen impact of the restriction

3.3.1. Would the restriction in Your opinion affect the purchasing price of methanol substitutes? If yes, please estimate how much.

3.3.2. Impact on investment costs

If You consider that product changes due to restriction would need investments (e.g. an equipment), please describe and assess the costs here (the price and assumed utilization time of the equipment)

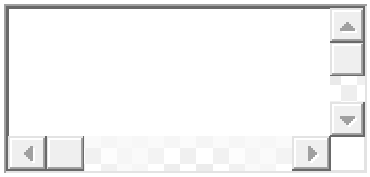
Restricting methanol concentration to 3 %:

Restricting methanol concentration to 0.1 %:

Further information and comments:

3.3.3. What kind of additional costs could be expected, if the methanol content in windscreen washer fluids would be restricted to 3 %:or 0.1 %? (E.g. possible changes in production process, energy consumption or labour costs.) Please describe where the costs would come from and estimate their increase (e.g. €/year, preferably also €/L finished product if possible). The justifications are important.

3.3.4. Would the substitution of methanol with other solvents affect the consumption of windscreen fluids in Your opinion? If yes, how and to what extent?



3.3.5. Other possible consequences (e.g. business changes)

Which are the foreseen additional actions and their costs (€/year and preferably also €/L if possible) if the methanol content would be restricted to 3 %?

Which are the foreseen additional actions and their costs (€/year and preferably also €/L if possible) if the methanol content would be restricted to 0.1 %?

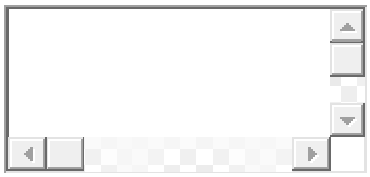
3.3.6. Will it be possible in Your opinion to shift the full costs of the restriction to the price of the final product?

Restricting methanol concentration to 3 %:
O No
O Yes

Restricting methanol concentration to 0.1 %:
O No

O Yes

Further information/comments:

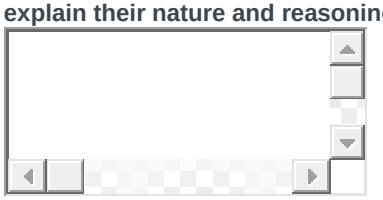


3.3.7. If the use of methanol in windscreen washing fluids will be restricted, what kind of time span will be needed to implement necessary changes? (please select one)
O 0 - 1 years
O 2 - 3 years
O 4 - 5 years
O More than 5 years

Your comments (e.g. regarding the impact of the transitional period on costs):

3.3.8. Any other comments on economic impact in Finland, EU or global level?

3.3.9. Do You have voluntary change plans for substituting methanol in windscreen washer fluids? Please explain their nature and reasoning. Do they have cost implications?



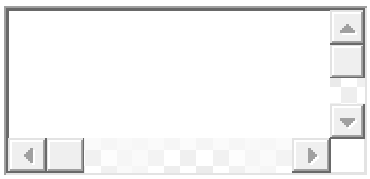
[4. Social impact

4.1. How many persons does methanol business employ in Your enterprise?

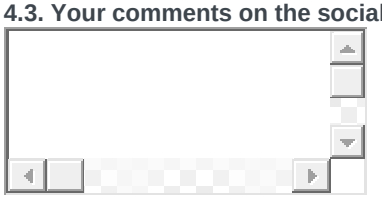
4.2. Which employment effects would the restriction options cause to Your enterprise?

Restricting methanol concentration to 3 %:

Restricting methanol concentration to 0.1 %:



4.3. Your comments on the social impact of restriction options in Finland:



4.4 Your comments on the social impact of restriction options within the EU or wider:

5. Any other comments on the topic

THANK YOU FOR YOUR ANSWER!