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ACETONITRILE

CAS No: 75-05-8

EINECS No: 200-835-2

Summary Risk Assessment Report

2002 **Special Publication I.01.65**

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SUMMARY RISK ASSESSMENT REPORT

2002

Spain

Rapporteur for the risk assessment of acetonitrile is the Spanish Ministry of Health (DGSP-SGSA) in consultation with the Ministry of Labour (INSHT), Ministry of Environment and Ministry of Agriculture, Fisheries and Food (INIA).

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PREFACE

This report provides a summary, with conclusions, of the risk assessment report of the substance acetonitrile that has been prepared by Spain in the context of Council Regulation (EEC) No. 793/93 on the evaluation and control of existing substances.

For detailed information on the risk assessment principles and procedures followed, the underlying data and the literature references the reader is referred to the original risk assessment report that can be obtained from the European Chemicals Bureau[1]. The present summary report should preferably not be used for citation purposes.

[1] European Chemicals Bureau – Existing Chemicals – http://ecb.jrc.it

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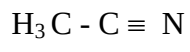
1 GENERAL SUBSTANCE INFORMATION

1.1 IDENTIFICATION OF THE SUBSTANCE

CAS Number:	75-05-8
EINECS Number:	200-835-2
IUPAC Name:	acetonitrile
Synonyms:	cyanomethane, ethanenitrile, ethyl nitrile, methanecarbonitrile methyl cyanide
Structural formula:	



Molecular formula:	$C_2 H_3 N$
Molecular weight:	41.05

1.2 PURITY/IMPURITIES, ADDITIVES

Degree of purity: ≥ 99.5 %

Identity and percentage of impurities:

- Propionitrile (0.02 %)
- Water, distilled, conductivity or of similar purity (0.01%)

1.3 PHYSICO-CHEMICAL PROPERTIES

Physical state (ntp):	Colourless liquid
Melting point:	-45.7°C
Boiling point:	81.6°C at 1,013.25 hPa
Relative density:	0.786 at 20°C
Vapour pressure:	98.64 hPa at 25ºC
Water solubility:	139,000 mg/l in saturated solution
Partition coefficient (log n-octanol/water):	-0.34
Flash point:	5-5.6°C (open cup), 12.8°C (closed cup)
Autoflammability:	524°C
Flammability:	highly flammable, with a lower flammability limit of 4.4% in volume and an upper flammability limit of 16% in volume
Explosive properties:	Forms explosive mixtures with air. The lower explosive limit is 3.05% in volume and the upper explosive limit 17% in volume
Surface tension:	29.04 dynes/cm at 20°C
Dissociation constant:	pKa = 29.1

1.4 CLASSIFICATION AND LABELLING

Classification and labelling according to the 28th ATP of Directive 67/548/EEC[2]:

Classification:	F; R11	Highly flammable.
	Xn; R20/21/22	Harmful by inhalation, in contact with skin and if swallowed.
	Xi; R36	Irritating to eyes.
Labelling:	F; Xn R: 11-20/21/22-36 S: (1/2-)16-36/37	

According to the data mentioned below and to the criteria of Classification and Labelling, acetonitrile has not been classified as dangerous to the environment.

[2] The classification of the substance is established by Commission Directive 2001/59/EC of 6 August 2001 adapting to the technical progress for the 28th time Council Directive 67/548/EEC on the approximation of the laws, regulations and administrative provisions relating to the classification, packaging and labelling of dangerous substances (OJ L 225, 21.8.2001, p.1).

2 GENERAL INFORMATION ON EXPOSURE

Acetonitrile is mainly obtained as a by-product of acrylonitrile synthesis, by a method known as the SOHIO (Standard Oil Company of Ohio) process, which involves a high temperature catalytic reaction between propylene and ammonia and produces crude acrylonitrile containing acetonitrile, hydrogen cyanide and carbon oxides as the main impurities. Acetonitrile is obtained from the reaction product, after cooling, by fractional distillation.

The compound is produced in the EU by two companies in two European countries and one company imports this product from outside.

Acetonitrile is used as a starting material for the synthesis of many chemicals, pharmaceutical compounds and pesticides and in the manufacturing of photographic film. It is also used as a solvent in various extraction processes like butadiene extraction, dissolution of cationic textile dyes, recrystallization of steroids, extraction of fatty acids from animal and vegetable oils and removal of tars, phenols and colouring matter from petroleum hydrocarbons. Acetonitrile is widely used in research and analytical laboratories. It is used as a solvent for genetic engineering research and in the analytical determination of a great number of chemicals by high performance liquid chromatography (HPLC). In addition, it is used as an inert medium in physico-chemical investigations and as a solvent in non-aqueous titrations.

3 ENVIRONMENT

3.1 ENVIRONMENTAL EXPOSURE

Sources of acetonitrile release to the environment can be anthropogenic or natural. Acetonitrile occurs in coal tar in small amounts, has been detected in volcanic gases and quantified in emissions from the combustion of wood and other biomass. Acetonitrile is also released during its manufacture and use, from some industrial operations like shale oil retorting and coal gasification and from combustion processes in gas turbines, ignition engines and automobile exhaust. General characteristics of acetonitrile relevant for exposure assessment are: an estimated atmospheric half-life of about a year, ready biodegradability for local scenarios and inherent biodegradability for regional/continental scenarios, a Henry's Law constant of 2.91 Pa m^3 $mole^{-1}$ and a bioconcentration factor of 0.3 l/kg.

For the environmental exposure assessment of acetonitrile both site-specific and generic emission scenarios are used for calculating the Predicted Environmental Concentrations (PECs) in the different compartments.

3.1.1 PECs at production/processing

Local PECs are summarised in the following table.

Table 3.1 Local PECs for the aquatic, sediment, atmospheric and terrestrial environments

Process	$PEC_{local, water}$ µg/l	$PEC_{local, sed}$ µg/kg	$PEC_{local, air}$ µg/ m^3	$PEC_{local, soil}$ mg/kgwwt
Production of acetonitrile	307	287	59	0.0647
Pharmaceutical industry	16,000	14,900	57.5	2.56
Butadiene	164	153	7.48	0.0281
Other uses	307	287	0.56	0.0491
Lab. Chem.	307	287	1.4	0.0493

3.2 EFFECTS ASSESSMENT

3.2.1 Aquatic compartment

3.2.1.1 Aquatic organisms

The provided information includes a set of data on the acute toxicity of acetonitrile for aquatic organisms. The validable information includes two fish species, several species of aquatic invertebrates from different taxonomic groups including Arthropoda, Platyhelminthes, Mollusca and Annelida, and toxicity threshold based on the first detectable inhibition of cell multiplication for the green alga *Scenedesmus quadricauda* and the blue-green algae *Microcystis aeruginosa*. Additional information, useful as supporting information, regarding the acute toxicity of acetonitrile on four additional fish species is also available.

There are not data on the chronic toxicity of acetonitrile for aquatic organisms. In addition, the information provided for the inhibition of alga growth does not include NOEC calculations or enough data for these estimations. Thus, the effect assessment focuses exclusively on acute toxicity data.

The lowest L(E)C_{50} figure is the 48-h LC_{50} on *Cyprinus carpio*, 730 mg/l. The TTs for algae are in the same range. Therefore, it seems appropriate in this assessment to consider 730 mg/l as the lowest end of the acute toxicity range for aquatic organisms. This range covers three taxonomic groups, fish, invertebrates and algae, and taking into account the lack of chronic figures, the recommendations of the Technical Guidance Document (TGD) suggest the application of the factor 1,000 to the lowest end of the acute toxicity range (730 mg/l), obtaining a PNEC for aquatic organisms of 0.73 mg/l.

$$PNEC_{aquatic\ organisms} = \text{lowest end acute toxicity range}/1{,}000 = 0.73\ mg/l$$

The data set only includes freshwater species. Therefore, in absence of data on saltwater species the above PNEC can be used for both, freshwater and marine environments, while data on marine species are produced.

3.2.1.2 Microorganisms

The toxicity data of acetonitrile on microorganisms includes effects on consortiums of bacteria like aerobic heterotrophs and methanogens, *Nitrosomonas* sp., *Pseudomona putida,* and several protozoa.

The recommendations of the TGD suggest the application of the factor 10 to the EC_{50} and 1 to the NOEC if the test has been performed with nitrifying bacteria and a factor 100 for the EC_{50} obtained using respiration inhibition or similar endpoints.

However, the amount of information available for acetonitrile is clearly higher than that usually available, covering most significant bacterial population and several protozoan species. Nitrifying bacteria seems to be particularly sensitive under laboratory conditions, considering all the available information, the weight of evidence justifies using a factor of 1 on the IC_{50} of 73 mg/l reported for nitrifying bacteria. The value obtained in this way for the most sensitive test on nitrifying bacteria, 73 mg/l, agrees with the application of the factor 100 to the inhibition of oxygen uptake by aerobic heterotrophs, which produces a figure of 75 mg/l, and with the derivation expected from the *Pseudomona* data. Thus a $PNEC_{microorganisms}$ of 73 mg/l is proposed in this assessment.

$$PNEC_{microorganisms} = 73\ mg/l$$

This value is more than 10 times lower than the lowest toxicity threshold reported for protozoa and therefore it is considered appropriate to cover the potential effects on this taxonomic group. Nevertheless, as additional precaution measure, and additional assessment following strictly the TGD recommendations will be included in the risk characterisation.

3.2.1.3 Sediment

The available data set includes a single data on the effect of acetonitrile on the sediment organism *Hyalella azteca*, but for waterborne exposure. The EC_{50} obtained for this organism is similar to that reported for other aquatic invertebrates suggesting that the first assumption of the

partitioning method presented by the TGD can be accepted. In addition, the very low Pow of acetonitrile, indicates that the use of water phase as the single via for uptake is also adequate. Thus, the PNEC may provisionally be calculated using the equilibrium partitioning method with the PNEC for aquatic organisms.

$$PNEC_{sed} = (K_{(sed\text{-}water)} / RHO_{sed}) \cdot PNEC_{aquatic\ organisms} \cdot 1{,}000$$

The value estimated with the EUSES program is:

$PNEC_{sed}$= 0.55 mg/kg.

3.2.2 Atmosphere

There are not data available for this assessment.

3.2.3 Terrestrial compartment

No toxicity data on soil dwelling organisms have been submitted. Thus, the PNEC may provisionally be calculated using the equilibrium partitioning method with the PNEC for aquatic organisms.

$$PNEC_{soil} = (K_{(soil,\ water)} / RHO_{soil}) \cdot PNEC_{aquatic\ organisms} \cdot 1000$$

The value estimated with the EUSES program is:

$PNEC_{sed}$= 0.176 mg/kg.

3.2.4 Secondary poisoning

According to the TGD, the risk characterisation for secondary poisoning is required if three specific criteria are fulfilled.

These criteria can be summarised as:

- Indirect exposure likely,
- Indication of bioaccumulation potential,
- Mammalian toxicity risk.

Acetonitrile is toxic for mammalian species but its low potential for bioaccumulation indicates that secondary poisonings are of low concern.

3.3 RISK CHARACTERISATION

3.3.1 Aquatic compartment

The potential local risks for aquatic (water column) organisms related to the different phases of the life cycle of acetonitrile included in this assessment has been summarised in **Table 3.2.**

Table 3.2 Local risk assessment for the aquatic environment: aquatic organisms

Process	PEC_{local} (µg/l)	PNEC(µg/l)	PEC/PNEC
Production of acetonitrile	307	730	0.42
Pharmaceutical Industry	16,000	730	21.9
Butadiene production	164	730	0.22
Other uses	307	730	0.42
Lab. Chem.	307	730	0.42

In all cases, for both water and sediments, PEC/PNEC ratios are below 1, except for its use as a solvent in the pharmaceutical industry. A similar situation is observed for the local risk characterisation for sediment dwelling organisms (**Table 3.3**), using the PNEC value derived from the toxicity for aquatic organisms according to the equilibrium partitioning method.

Table 3.3 Local risk assessment for the aquatic environment: sediment dwelling organisms

Process	$PEC_{local(sed)}$ (µg/kg)	PNEC (µg/kg)	PEC/PNEC
Production of acetonitrile	287	550	0.52
Pharmaceutical industry	14,900	550	27.1
Butadiene	153	550	0.28
Other uses	287	550	0.52
Lab. Chem.	287	550	0.52

The values for the regional and continental assessment are included in **Table 3.4**.

Table 3.4 Risk assessment for the aquatic environment

Surface Water	PEC_{sw} (µg/l)	PNEC(µg/l)	PEC/PNEC
Regional	2.41	730	0.003
Continental	0.45	730	0.0006
Sediment	PEC_{sed}(µg/kg)	PNEC (µg/kg)	PEC/PNEC
Regional	1.77	550	0.003
Continental	0.33	550	0.0006

Regional and continental risks are estimated to be very low.

The exposure assessment uses the default dilution value of 10 and the effect assessment only has information on the toxicity of acetonitrile for freshwater species. In absence of specific

information for the marine environment, this assessment is considered to cover both, freshwater and saltwater ecosystems.

Therefore, it should be considered that for the aquatic compartment, including sediment, the risk characterisation indicates that the present risk of acetonitrile for the aquatic environment is not of concern, except for its use as a solvent in the pharmaceutical industry.

The risk assessment for WWTP is summarized in **Table 3.5**.

Table 3.5 Risk assessment for WWTP microorganisms

Assessment	PEC (mg/l)	PNEC (mg/l)	PEC/PNEC
Effluent Concentration	160	73	2.19
Inflow Concentration Solvent in the pharmaceutical industry	1,300	73	17.8
Effluent Concentration Production and other uses	3.07	73	0.04
Inflow Concentration Production and other uses	30	73	0.41

A potential risk for the use of acetonitrile as solvent in the pharmaceutical industry has been identified. The PEC/PNEC values for all other uses are lower than 1 suggesting a very low risk.

The use of a more conservative approach, following strictly the TGD recommendations (applying and additional factor of 10 for the PNEC derivation), would produce a PNEC value of 7.3 mg/l and a PEC/PNEC ratio of 0.4 (for the effluent concentration as recommended by the TGD), and therefore, the same conclusion of low risk for the production and all uses except as solvent in the pharmaceutical industry, is reached even for this conservative PNEC.

Result

For the aquatic compartment, including water, sediments and biological processes of WWTP:

Conclusion (ii) There is at present no need for further information and/or testing and no need for risk reduction measures beyond those which are being applied already.

This conclusion applies to local risks for production and processing in butadiene production, use as a laboratory chemical, use in the photographic industry and other uses included in the risk assessment except its use in pharmaceutical industries. It also applies to the regional and continental risks related to the acetonitrile life cycle.

Conclusion (iii) There is a need for limiting the risk; risk reduction measures which are already being applied shall be taken into account.

This conclusion applies to the use of acetonitrile as a solvent in the pharmaceutical industry.

3.3.2 Atmosphere

No information has been provided for a proper risk assessment for the atmosphere.

3.3.3 Terrestrial compartment

No information on the toxicity of acetonitrile for terrestrial organisms has been provided, therefore the effect assessment has been estimated using the equilibrium partitioning method. The risk characterisation for the local assessment is included in **Table 3.6**.

Table 3.6 Local Risk assessment for the soil compartment

	PEC (mg/kgwwt) averaged over 30 days	PNEC (mg/kgwwt)	PEC/PNEC
Production	0.0647	0.176	0.36
Pharma. Industry	2.56	0.176	14.5
Butadiene	0.0281	0.176	0.16
Other uses	0.0491	0.176	0.28
Lab. Chem.	0.0493	0.176	0.28

A potential risk has been identified for the use of acetonitrile as solvent in the pharmaceutical industry. All other PEC/PNEC ratios are lower than 1 suggesting a low local risk for soil organisms.

Regional and continental PECs have been calculated according to the TGD giving the following values: $PEC_{agric, soil, regional}$ = 0.124 µg/kgwwt and $PEC_{agric, soil, continental}$ = 0.06 µg / kgwwt. The risk assessment is included in **Table 3.7**.

Table 3.7 Regional and Continental Risk assessment for the soil compartment

	PEC (mg/kgwwt)	PNEC (mg/kgwwt)	PEC/PNEC
Regional	0.00012	0.176	0.00068
Continental	0.00006	0.176	0.00034

These ratios are low enough to consider that the risk for terrestrial organisms at the regional and continental level is of low concern.

Result

For the terrestrial environment:

Conclusion (ii) There is at present no need for further information and/or testing and no need for risk reduction measures beyond those which are being applied already.

This conclusion applies to local risks for production and processing in butadiene production, use as a laboratory chemical, use in the photographic industry and other uses included in the risk assessment except its use in pharmaceutical industries. It also applies to the regional and continental risks related to the acetonitrile life cycle.

Conclusion (iii) There is a need for limiting the risk; risk reduction measures which are already being applied shall be taken into account.

This conclusion applies to the use of acetonitrile as a solvent in the pharmaceutical industry.

3.3.4 Secondary poisoning

The low potential of acetonitrile for bioaccumulation indicates that secondary poisonings are of low concern.

Result

Conclusion (ii) There is at present no need for further information and/or testing and no need for risk reduction measures beyond those which are being applied already.

4 HUMAN HEALTH

4.1 HUMAN HEALTH (TOXICITY)

4.1.1 Exposure Assessment

4.1.1.1 Occupational exposure

Acetonitrile is mainly obtained as a by-product of acrylonitrile manufacture in a closed system, therefore, exposure is only possible during maintenance, repair of equipment, transferring or sampling. The available data indicate that, in the worst case, an inhalation exposure level of 0.1 ppm can be obtained. Dermal exposure is estimated by EASE as 84 mg/day assuming an exposed area of 840 cm^2 (both hands) and incidental contact.

Acetonitrile is mainly used as a solvent or chemical intermediate in chemical industry and pharmaceutical manufacturing processes or in the manufacture of photographic film. All these processes involve closed systems. Exposure is expected in special tasks such as sampling, maintenance or filling activities. The reasonable worst-case exposure level is estimated to be 7.3 ppm based on measured data.

Dermal exposure is estimated using the same approach that in the manufacturing section (84 mg/day assuming an exposed area of 840 cm^2 (both hands) and incidental contact.

There are some companies that purify or distribute acetonitrile. For these companies an intermittent contact level is assumed for filling operations. Dermal exposure is estimated to be 420 mg/ considering that an area of 420 cm^2 can be exposed.

Acetonitrile is mainly used in laboratories as a mobile phase in HPLC. Exposures around 7.3 ppm have been reported. Skin contact is only likely when the mobile phase is prepared before entering the instrument. Dermal exposure is estimated by EASE as 42 mg/day assuming an exposed area of 420 cm^2 and incidental contact.

Table 4.1 Summary of worst-case exposures to workers

Exposure scenario	Activity	Inhalation exposure				Dermal exposure		
		Duration and frequency	Reasonable worst case		Method	Exposure level	Reasonable worst case	Method
			ppm	mg/m³		mg/cm²/day	(mg/day)	
Manufacture	Sampling Filling Cleaning and maintenance	Full shift/daily Up to 25 days/year	0.1	0.17	Measured	0 – 0.1	84	EASE
Use as a solvent or chemical intermediate	Sampling Filling/emptying Cleaning and maintenance	Full shift/daily Up to 25 days/year	7.3	12.3	Measured	0.1 – 1	420	EASE
Use in laboratories (HPLC)	Preparation of the mobile phase	Full shift/daily	7.3	12.3	Measured	0 – 0.1	42	EASE

4.1.1.2 Consumer exposure

Current information indicates that there is no use of acetonitrile in any consumer product. Looking at the accidental intoxication cases to acetonitrile it could be concluded that acetonitrile could be present in nail remover. However, acetonitrile is not in the EC Cosmetics Inventory (96/355/EC) and is not approved for use in cosmetics in Europe. Therefore, it is not of concern for consumers.

4.1.1.3 Humans exposed via the environment

The EUSES model has been used. Model predictions show that the most important human intake routes are via air and drinking water. According to the EUSES estimations, the values for the total human intake of acetonitrile for the local scenario range from 0.00302 mg/kg bw/d to 0.164 mg/kg.bw/d depending on the release/use category. The pharmaceutical industry scenario shows the highest total intake value.

4.1.2 Effects assessment

Toxicity and toxicodynamic data show that acetonitrile is well absorbed from the lungs, gastrointestinal tract and through the skin. Free and conjugated hydrogen cyanide was detected in all the studied organs. Acetonitrile is metabolised to cyanide via cytochrome P450. Several studies have indicated that cyanide formed *in vivo* is subsequently conjugated with thiosulphate to form thiocyanate, which is eliminated in urine. The cyanide is responsible for the acetonitrile toxicity.

The acute toxicity studies were performed with GLP information. Mouse and Guinea pig seem to be the most sensitive species. In a well-conducted study in mice, the oral LD_{50} of acetonitrile was 617 mg/kg. In humans, a LD_0 570 mg/kg was estimated in a case of acute acetonitrile intoxication. These data show the substance as harmful after oral administration. A LD_{50} >2,000 mg/Kg was obtained in a well-conducted acute dermal toxicity study in rabbits. This data do not support classification of acetonitrile via dermal. However, classification as harmful in

contact with skin is proposed based on human data, which reported symptoms and levels of cyanide in blood as result of paediatric accidental exposure to a cosmetic containing acetonitrile. All studies in animals, including a well-conducted study in mice, gave LC_{50} > 2mg/l. Two deaths after exposure to acetonitrile in the workplace have been reported. Although the level of the exposures were unknown, it was probably very high due to the elevated cyanide concentrations found in the tissues in post-mortem examination of these cases. Therefore, classification as harmful by the inhalation route is appropriated.

Acetonitrile is an eye irritant, but not a skin or respiratory irritant. Classification as sensitising agent is not indicated.

There is no information available on the effects of repeated exposure to acetonitrile in humans. In animals, mice are one of the most sensitive species to inhaled acetonitrile. A subcronic 13-week study carried out by NTP showed a NOAEL of 100 ppm based on forestomach lesions observed and on an increase of liver weight. In a 2-year study carried out later by NTP it was observed that the lesions that appeared in the forestomach in the 13-week study were not related with exposure to the substance. There was no correspondence either with other effects as organ weight. Both studies lacked of chemical biochemistry and haematology. Therefore, a NOAEL from this study cannot be established. Preliminary data from two unrelated not fully reported studies showed a NOAEL of 100 ppm in mice based on haematological data.

In rats a NOAEL of 200 ppm was established based on a two-year study, since the haematological effects were seen at 400 ppm. This NOAEL in rats is in accordance with the NOAEL of 100 ppm obtained in two not fully reported studies in mice, providing mice are a more sensitive specie than rats.

Taken into account all considerations, a NOAEL of 100 ppm in mice is considered as meaningful and is used for risk characterisation.

Acetonitrile is not considered to be mutagenic.

Two inhalation assays carried out with rats and mice indicated that acetonitrile was not carcinogenic. There was an increase in liver adenomas and carcinomas separately and jointly in male rats at the highest test level (400 ppm). However, this was not significant when compared with the dedicated controls or historical control ranges. There were no exposure-related liver lesions in female rats. There were no chemical-related increases in malignant or benign neoplasm in male or female B6C3F1 mice exposed to 50, 100 or 200 ppm. The increase in the incidence of squamous hyperplasia of the forestomach found in male and female mice were related with the prolonged acetonitrile exposure, but the magnitude of the neoplastic findings are insufficient to attribute them to the chemical with any confidence.

In relation to fertility, there is no information available in humans and there are no animal studies specifically investigating such effects. However, no changes in (absolute or relative) weight of the right caudal or right testis and no effect on sperm motility in rats or mice exposed for 13 weeks with 100, 200 and 400 ppm of acetonitrile were observed. Several developmental studies are available in animals, two of them well conducted. A NOAEL for maternal toxicity of 1,200 ppm, and a NOAEL for developmental toxicity of 1,200 and 1,500 ppm were established from two inhalation developmental toxicity studies carried out on rats. In rabbits, a NOAEL of 15 mg/kg bw/d and a NOAEL of 30mg/kg bw/d were established for maternal and developmental toxicity, respectively. In most of the available assays teratogenicity was associated with maternal toxicity. In conclusion, acetonitrile is not a reproductive toxicant.

4.1.3 Risk characterisation

4.1.3.1 Workers

Relevant routes for workers exposure to acetonitrile are inhalation and dermal routes. Most relevant effects produced by acetonitrile are eye irritation and those arising from repeated-exposure.

Despite the fact that acetonitrile is an eye irritant, contact to the eyes should be rather uncommon regarding the industrial processes. Therefore, **conclusion (ii)** is reached for all scenarios.

Conclusion (ii) There is at present no need for further information and/or testing and for risk reduction measures beyond those, which are being applied already

Regarding repeated dose toxicity, the Margin of Safety (MOS) between the inhalative NOAEL of 100 ppm in mice and the inhalation exposure levels is considered sufficient for all scenarios. The MOS between the extrapolated dermal NOAEL of 54 mg/kg/day and dermal exposure levels is considered sufficient in all but one case regarding companies that purify or distribute acetonitrile for which **conclusion (iii)** is reached. Therefore, in this case, there is also concern regarding combined exposure.

Conclusion (iii) There is a need for limiting the risk; risk reduction measures which are already being applied shall be taken into account.

4.1.3.2 Consumers

Since acetonitrile is not present in the consumer products, **conclusion (ii)** is applied

4.1.3.3 Humans exposed via the environment

According to the EUSES estimations, the values for the total human intake of acetonitrile for the local scenario range from 0.00302 mg/kg bw/d to 0.164 mg/kg bw/d depending on the release/use category.

Using a NOAEL of 39 mg/kg/day, derived from the inhalation NOAEL, the calculated MOS are ranging from 238 to 12,900.

These MOS are considered acceptable, indicating no concern for human safety after indirect exposure.

The lowest MOS of 238 will be increased when additional measures will be applied, taking into account that conclusion (iii) has been reached for environment when acetonitrile is use as a solvent in pharmaceutical industry, **conclusion (ii)** is applied.

4.2 HUMAN HEALTH (PHYSICO-CHEMICAL PROPERTIES)

Regarding its physico-chemical properties, flammability is a property of concern for acetonitrile since it is a volatile liquid, which is highly flammable. In the industry setting, the flammability risk is not of concern provided adequate safety measures are taken.

Information is provided on the label and in the safety data sheet.

Concerning use by consumers, acetonitrile is not present in the consumer products.

Conclusion (ii) There is at present no need for further information and/or testing and no need for risk reduction measures beyond those that are being applied already.

5 RESULTS

5.1 ENVIRONMENT

Conclusion (ii) There is at present no need for further information and/or testing and no need for risk reduction measures beyond those which are being applied already.

Conclusion (ii) applies to atmosphere.

Conclusion (iii) There is a need for limiting the risks; risk reduction measures which are already being applied shall be taken into account.

Conclusion (iii) applies to the aquatic, terrestrial ecosystems and microorganisms in the sewage treatment plant as a consequence of exposure rising from the use in the pharmaceutical industry.

5.2 HUMAN HEALTH

5.2.1 Human health (toxicity)

Workers

Conclusion (ii) There is at present no need for further information and/or testing and no need for risk reduction measures beyond those which are being applied already.

Conclusion (ii) applies to acute toxicity, irritation/corrosivity, sensitisation, mutagenicity, carcinogenicity and reproductive toxicity for all occupational scenarios.

Conclusion (iii) There is a need for limiting the risks; risk reduction measures which are already being applied shall be taken into account.

Conclusion (iii) applies to general systemic toxicity as a consequence of dermal exposure arising from use as a solvent and as an intermediate.

Consumers

Conclusion (ii) There is at present no need for further information and/or testing and no need for risk reduction measures beyond those which are being applied already.

Humans exposed via the environment

Conclusion (ii) There is at present no need for further information and/or testing and no need for risk reduction measures beyond those which are being applied already.

This conclusion applies to workers for end uses scenarios .

5.2.2 Human health (risks from physico-chemical properties)

Conclusion (ii) There is at present no need for further information and/or testing and no need for risk reduction measures beyond those which are being applied already.

5.2.3 Unintentional sources

The risk assessment has identified other sources of exposure of the substance to humans and to the environment, in particular, the substance is produced during biomass burning and is present in automobile exhaust, which do not result from the life-cycle of the substance produced in or imported into the European Community. The assessment of the risks arising from these exposures are not part of the this risk assessment. The comprehensive Risk Assessment Reports as forwarded to the Commission by the Member State Rapporteur however provides information about these risks.