

Second opinion on the hazards associated with the substances selected for the REACH SIN* List 1.0



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Abstract

The aim of this study was to evaluate the human and environmental hazards associated with the 267 substances listed on the REACH SIN* (*Substitute It Now!) List 1.0 (SIN*-list). The question to be asked was: is there any chance that one or more of them should be excluded from the list due to lack of hazardous properties?

Each of the substances on the SIN*-list has been evaluated against the European Water Framework Directive list and the World Health Organization's drinking water quality guidelines as well as assessed for their carcinogenic, mutagenic and reprotoxic properties. Finally, the Ranking and Identification of Chemical Hazards (RICH)-tool was applied, which assesses the inherent properties including environmental fate and toxicity in order to identify substances with potential environmental hazards.

Of the 267 substances listed on the SIN*-list 38 are inorganic substances and 229 are either organic or organo-metallic substances. 32 of the organic substances (often mixtures or summary parameters) could not be assessed due to lack of inherent data. 21 could neither be confirmed hazardous nor exempted from side effects. The remaining 177 organic substances were all classified as hazardous. 37 of the 38 inorganic substances have either confirmed or suspected animal or human carcinogenicity. One inorganic substance did not have data for such evaluation.

To conclude, 214 substances have confirmed hazardous properties and 33 could not be properly assessed due to lack of data. The remaining 21 could neither be exempted from having nor confirmed to have hazardous properties. Thus no substance could truly be exempted from being hazardous and the recommendation is to keep the list as it is, but initiate further assessment of the 54 substances lacking solid data to be fully assessed.

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1. Introduction

The REACH SIN*-list (*Substitute It Now!) 1.0 (SIN*-list) comprises 267 substances and was made publicly available on September 17th 2008, (ChemSec, 2008). The SIN*-List has been developed by the International Chemical Secretariat (ChemSec) in collaboration with a Non-Governmental Organization (NGO) Advisory board.

The SIN*-list identifies substances qualifying as Substances of High Concern (SVHC) under REACH (Registration, Evaluation, Authorisation and Restriction of Chemical substances). The list recommends that these substances should be substituted by less harmful chemicals. The aim for compiling the list is that the SIN*-list should be adopted by industry as a guideline for which chemicals to be prioritised for phasing out of use as soon as possible. It is also aiming at causing an acceleration of the implementation of the REACH authorization process.

The SIN*-list 1.0 is ChemSec's first official version and it is planned that more SVHCs will be added it over time. More details are available on the public available SIN*-list homepage (<http://www.sinlist.org/>).

The aim of this study was to evaluate the human and environmental hazards associated with the 267 substances listed on the SIN*-list. The question to be asked was: is there any chance that one or more of them should not be on the list due to lack of hazardous properties?

2. Methodology

The 267 substances on the SIN*-list were evaluated based in their presence on two well-known lists with hazardous and non-wanted substances; EU Water Framework Directive (WFD) and World Health Organization's (WHO) drinking water quality guidelines. The WFD sets out Environmental Quality Standards (EQS) for a range of substances including some metals in their elemental form as well as their derivatives.

In addition human and animal CMR data (carcinogenicity, mutagenic effects and effect on reproduction) were collected and included as criteria for hazardous effects.

Finally, a ranking tool (cf. next paragraph) was applied to evaluate potential hazards for the organic and organo-metallic substances.

2.1. RICH-tool

The tool applied was the 'Ranking and Identification of Chemical Hazards' (RICH) tool. This tool has been developed for ranking and identification of hazardous organic substances in stormwater discharged to surface water (Baun et al., 2006). The tool has also successfully been applied for wastewater and municipal sludge (Eriksson et al., 2008A&B). RICH identify environmentally problematic and hazardous substances based on their inherent physico-chemical and biological properties. The output is 1) a justified list with substances which can be disregarded in hazard/risk assessments 'white' substances; 2) a justified list with priority pollutants which should be included in hazard/risk assessments 'black' substances; and 3) a list of substances which cannot be evaluated due to lack of data 'no data'. Fourthly, substances for which hazards neither can be disregarded nor confirmed are identified as 'grey' substances, but according to the precautionary principle they are handled as they were classified as 'black'.

The tool is based on a decision tree where the substances are tested for different inherent properties in tiers. Firstly, the volatility from aqueous solution and affinity to suspended solids are tested to classify the substances into ‘water phase substances’, ‘solid phase substances’ and ‘evaporating substances’. Secondly, technical problems in stormwater systems are evaluated based on odour, colour, frothing, precipitation or corrosion. Thirdly, resistance to biodegradation (P) and potential for bioaccumulation (B) are tested, which is followed by an evaluation of the acute aquatic toxicity and long-term effects (carcinogenicity, mutagenicity, potential for reproductive damage, and endocrine disruption (CMR/E)) (T). All in accordance with the EU Technical Guidance Document for risk assessment of chemicals (European Commission, 2003). Due to the tiered approach substances first classified as PBT will not be evaluated for CMR/E, thus only those not classified as ‘black’ in the PB or PT filter will be evaluated for their CMR/E properties.

The cut-off values used are based on international agreements (e.g. OSPAR and Stockholm POP-conventions) and a literature study covering cut-off values proposed by groups of experts (e.g. ISO and OECD), stakeholders (e.g. industry and NGOs) and legislation in EU, USA, and Canada. Thus, “high” cut-off values are set as worst-case.

Some adaptations have been made in this study, since the tool was developed for environmental hazard assessment with a stormwater focus:

- Evaporating substances previously not considered relevant for surface water and sediment are of high concerns for consumers, and thus, these have been tested for acute human toxicity (very toxic/toxic by inhalation; very toxic/toxic in contact with skin; very toxic/toxic if swallowed) and long-term effects (CMR/E).
- Technical problems have not been included.
- The CMR/E step has been expanded to include acute human toxicity.
- The tiered approach first identifies PBT substances which is a discrepancy with the SIN*-list where the focus clearly has been on the CMR-criteria.
- Inherent data and fate information were obtained from readily available databases and reference books, see the reference-list, but an excerpt was from the SIN*-list database was also provided by Jerker Ligthart of ChemSec.

3. Results and discussion

The SIN*-list includes in total 267 substances, where 38 are inorganic metal species, 15 organo-metallic substances and 214 are organic substances. Occasionally of these ‘parameters’ comprises of two or more CAS Registry numbers (CAS#s). In order to facilitate data management there was a need to occasionally separate the two or more CAS#s into separate ‘parameters’, hence the evaluated list of organo-metallic substances and organic substances (229) came to consist of 230 ‘parameters’. Here, nonylphenol was included as both the straight chain and a mixture of branched isomers.

3.1. Assessment of organic and organo-metallic substances

Out of 267 substances on the SIN*-list 1.0 230 substances or summary parameters were included in the assessment of organic and organo-metallic substances. Inherent properties and environmental fate data could be obtained from the above mentioned data sources for 198 out of the 230 substances. However, 32 substances could not be assessed due to the lack of data. These were primarily summary parameters and mixtures for which seldom CAS#s exist. In the SIN*-list all of these substances are classified as CMR-substances, something which have not been possible to corroborate in this study, see appendix 1.

The 198 substances were classified as ‘black’, i.e., none of the organic substances or organo-metallic substances on the SIN*-list can be disregarded in hazard/risk assessments, Figure 1.

Of these 198 substances 17 substances were distributing to the air compartment, ‘evaporating substances’ but were caught by the CMR/E-filter, i.e., confirming that at least one human or non-human long-term effects is known. Twenty-one substances were classified as ‘grey’, i.e. hazard cannot be either confirmed or contradicted and hence, according to the precautionary principle these were also included among the black substances, see appendix 2. Of the remaining substances 81 were classified as ‘black’ based on their PBT properties; 88 classified as ‘black’ based on their CMR/E properties and 8 substances as ‘black’ based on their acute human toxicity, Figure 1.

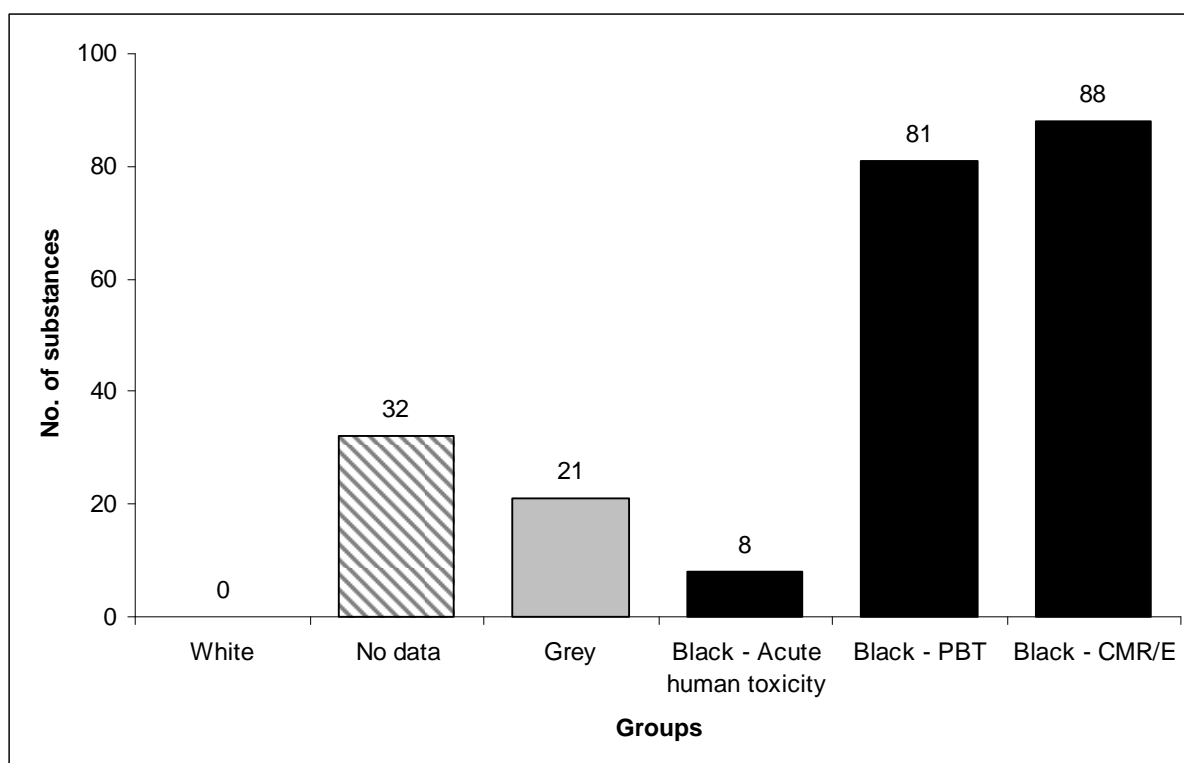


Figure 1 - Outcome from the RICH assessment, number of substances in each classification category.

3.2. Assessment of inorganic metal species

Out of the 267 substances listed on the SIN*-list, 38 are inorganic metal species, only one of them (beryllium) in its metallic form.

The WHO guideline for drinking water quality contain a range of organic substances as well as a range of metals, but none of the inorganic metal species contained on the SIN*-list. Furthermore the US National Library of Medicine’s Hazardous Substance Data Bank has been consulted in order to obtain information about the potential carcinogenic properties of the 38 inorganic metal substances. This kind of information has been considered by authoritative bodies like OSHA, IARC, NTP ACGIH and US EPA.

Figure 2 shows the attention made to these substances. 3 of them are considered on the WFD as the metal and its substances (meaning that 19 substances are included), 6 metals on the WHO guideline for drinking water quality (meaning that 33 substances to some extent are included) and as many as 37 have been considered for their potential carcinogenic properties.

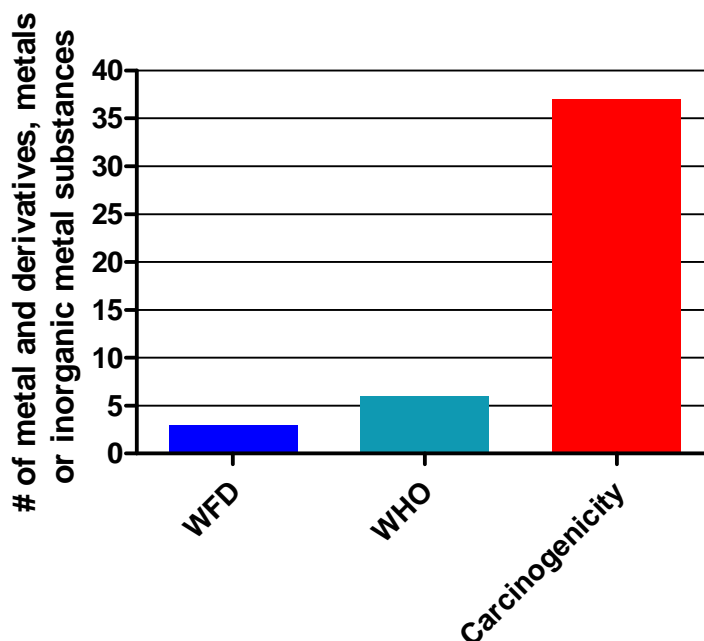


Figure 2 - Consideration from various authorities.

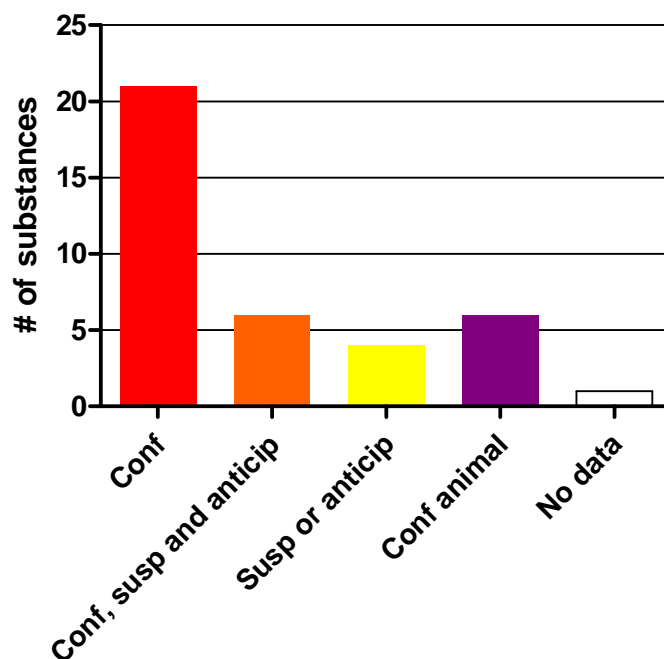
WFD: EU Water Framework Directive; WHO: World Health Organisation; Carcinogenicity: Data obtained through HSDB from OSHA, IARC, NTP ACGIH and US EPA.

The information obtained from the WFD and WHO is EQS and guidelines for drinking water quality, respectively. In other words, concentration limits in surface waters and drinking water, respectively, in order to maintain a healthy environment and safe drinking water. The information obtained from the attention to the potential carcinogenic properties is of another character.

Figure 3 shows the various assessments of the overall potential carcinogenic properties of the inorganic metal substances. It is shown that 37 out of 38 substances have some kind of carcinogenic properties. Of these, 21 have confirmed human carcinogenic properties, 10 have either confirmed, or suspected or anticipated carcinogenic properties, 6 have confirmed animal carcinogenic properties and only 1 substance (lead azide) do not have any data on carcinogenic properties. On the other hand, lead azide is a known explosive (HSDB).

All in all, 37 of the 38 inorganic metal substances should be considered as human or animal carcinogens.

Figure 4 shows the carcinogenic properties of the inorganic metal species based on the metals. Generally, it can be argued that derivatives of aluminium, arsenic, beryllium, cadmium, chromium (only hexavalent) and nickel are confirmed carcinogens. Derivatives of cobalt, lead and antimony are “only” confirmed animal carcinogens or suspected human carcinogens



Carcinogenicity assessment

Figure 3 - Overall potential carcinogenic properties of the inorganic metal substances. Conf: Confirmed human carcinogen; Conf, susp, and anticip: Confirmed human carcinogen, suspected human carcinogen and anticipated carcinogen; Susp or anticip: Either suspected or anticipated carcinogen; Conf animal: Confirmed animal carcinogen; No data: No data found on carcinogenicity.

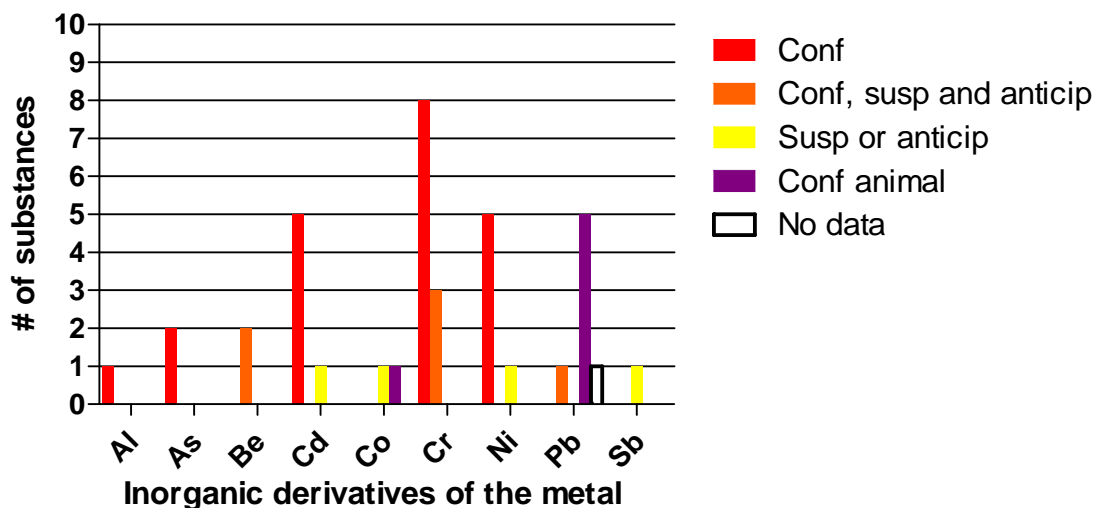


Figure 4 - Carcinogenic potential of the various inorganic derivatives of the metals. Conf: Confirmed human carcinogen; Conf, susp, and anticip: Confirmed human carcinogen, suspected human carcinogen and anticipated carcinogen; Susp or anticip: Either suspected or anticipated carcinogen; Conf animal: Confirmed animal carcinogen; No data: No data found on carcinogenicity.

4. Conclusion

The 267 substances listed on the SIN*-list needed to be counted as 268, as one nonylphenol was considered both as a straight chain and a mixture of branched isomers. 38 are inorganic substances and 230 are either organic or organo-metallic substances.

Applying the RICH-tool 32 of the organic substances (often mixtures or summary parameters) could not be assessed due to lack of data and 21 could neither be confirmed hazardous nor exempted from side effects. A total of 53 organic substances thus need a more thorough investigation to be fully assessed. The remaining 177 organic substances were all classified as hazardous.

37 of the 38 inorganic substances have either confirmed or suspected animal or human carcinogenicity. One inorganic substance did not have data for such evaluation.

To sum up, as many as 214 substances have confirmed hazardous properties and 33 could not be properly assessed due to lack of data. The remaining 21 could neither be exempted from having nor confirmed to have hazardous properties. Thus none of the substances on the SIN*-list can be disregarded in hazard/risk assessments based on the assessment carried out in this study, but the recommendation is to keep the list as it is, however further assessment of the 54 substances having no solid data to be fully assessed need to be initiated.

5. References

- Baun A, Eriksson E, Ledin A & Mikkelsen PS (2006) A methodology for ranking and hazard identification of xenobiotic organic compounds in urban stormwater. *Science of the Total Environment* 370: 29-38.
- ChemSec (2008) REACH SIN* List 1.0. Retrieved from <http://www.sinlist.org/> (2008-11-01)
- Eriksson E, Christensen C, Schmidt JE & Ledin A (2008A) Potential priority pollutants in sewage sludge. *Desalination* 226: 371-388.
- Eriksson E, Hansson K, Hansson B & Ledin A (2008B) Source identification and mitigation options of industrial pollution in municipal sewage sludge. In: 11ICUD, 11th International conference on Urban Drainage, Edinburgh, Scotland, 31st August-5th September 2008 ; CD-ROM-Sheffield, UK : University of Sheffield, 2008
- European Commission (2003) Technical Guidance Document in support of Commission Directive 93/67/EEC on Risk Assessment for new notified substances, Commission Regulation (EC) No 1488/94 on Risk Assessment for existing substances and Directive 98/8/EC of the European Parliament and of the Council concerning the placing of biocidal products on the market. Bruxelles, Belgium.

Inherent physico-chemical data and data for the fate in the environment were collected from the following sources:

- European Chemicals Bureau (2008). ESIS: European chemical Substances Information System. <http://ecb.jrc.ec.europa.eu/esis/>
- European Chemicals Bureau (2008). IUCLID on-line: International Uniform Chemical Information Database. <http://ecb.jrc.it/esis/index.php?PGM=dat>
- Kemibrug (2009) Database of risk phrases for chemicals used at Danish universities. <http://www.kemibrug.dk/>
- OSPAR Commission (2004). OSPAR Commission for the Protection of the Marine Environment of the North-East Atlantic. <http://www.ospar.org/eng/html/welcome.html>
- Rippen G. (Ed.), *Handbuch Umweltschemikalien*, Ecomed Verlagsgesellschaft, Landberg/Lech, 2008, CD-ROM Germany (in German).
- Syracuse Research Corporation (1999). Interactive PhysProp Database Demo. <http://www.syrres.com/esc/physdemo.htm>
- US Environmental Protection Agency (2007). EPISuite: Estimation Program Interface Suite v3.20. <http://www.epa.gov/opptintr/exposure/pubs/episuite.htm>
- US Environmental Protection Agency (2009). ECOTOX (ECOTOXicology) database 4.0 <http://cfpub.epa.gov/ecotox/>
- US National Library of Medicine (2008). Chemical Carcinogenesis Research Information System (CCRIS) <http://www.toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?CCRIS>
- US National Library of Medicine (2008). Genetic Toxicology Data Bank (GENE-TOX) <http://www.toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?GENETOX>
- US National Library of Medicine (2008). Hazardous Substance Data Bank (HSDB). <http://www.toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB>
- Verscheuren, K. (1996). *Handbook of Environmental Data on Organic Chemicals*, 3. Edition, van Nostrand Reinhold co. Dordrecht, Holland.

Supplementary information for 'substances of equal concern' was received from Jerker Ligthart, ChemSec, whom had collected data from scientific literature for an expert evaluation.

Appendix 1. The 32 organics and organo-metals for which sufficient data could not be obtained.

| Lack both basic physico-chemical properties and CMR data | |
|--|-------------------------|
| Substance name | CAS registration number |
| (6-(4-hydroxy-3-(2-methoxyphenylazo)-2-sulfonato-7-naphthylamino)-1,3,5-triazin-2,4-diyl)bis[(amino-1-methylethyl)ammonium] formate | 108225-03-2 |
| (methylenebis(4,1-phenylenazo(1-(3-(dimethylamino)propyl)-1,2-dihydro-6-hydroxy-4-methyl-2-oxopyridine-5,3-diyl))-1,1'-dipyridinium dichloride dihydrochloride | - |
| [3,3'-dimethyl[1,1'-biphenyl]-4,4'-diyl]diammonium bis(hydrogen sulphate) | 64969-36-4 |
| 1,2-benzenedicarboxylic acid, dipentylester, branched and linear; [1] | 84777-06-0 |
| 1,3,5-tris-[(2S and 2R)-2,3-epoxypropyl]-1,3,5-triazine-2,4,6-(1H,3H,5H)-trione | 59653-74-6 |
| 2-[2-hydroxy-3-(2-chlorophenyl)carbamoyl-1-naphthylazo]-7-[2-hydroxy-3-(3-methylphenyl)carbamoyl-1-naphthylazo]fluoren-9-one | - |
| 3-ethyl-2-methyl-2-(3-methylbutyl)-1,3-oxazolidine | 143860-04-2 |
| 4-amino-3-fluorophenol | 399-95-1 |
| 6-hydroxy-1-(3-isopropoxypropyl)-4-methyl-2-oxo-5-[4-(phenylazo)phenylazo]-1,2-dihydro-3-pyridinecarbonitrile | 85136-74-9 |
| A mixture of: 1,3,5-tris(3-aminomethylphenyl)-1,3,5-(1H,3H,5H)-triazine-2,4,6-trione; a mixture of oligomers of 3,5-bis(3-aminomethylphenyl)-1-poly[3,5-bis(3-aminomethylphenyl)-2,4,6-trioxo-1,3,5-(1H,3H,5H)-triazin-1-yl]-1,3,5-(1H,3H,5H)-triazine-2,4,6-t | - |
| A mixture of: 4-[[bis-(4-fluorophenyl)methylsilyl]methyl]-4H-1,2,4-triazole; 1-[[bis-(4-fluorophenyl)methylsilyl]methyl]-1H-1,2,4-triazole | - |
| A mixture of: disodium 4-(3-ethoxycarbonyl-4-(5-(3-ethoxycarbonyl-5-hydroxy-1-(4-sulfonatophenyl)pyrazol-4-yl)penta-2,4-dienylidene)-4,5-dihydro-5-oxopyrazol-1-yl)benzenesulfonate | - |
| A mixture of: N-[3-hydroxy-2-(2-methylacryloylaminomethoxy)propoxymethyl]-2-methylacrylamide; N-[2,3-bis-(2-methylacryloylaminomethoxy)propoxymethyl]-2-methylacrylamide; methacrylamide; 2-methyl-N-(2-methylacryloylaminomethoxymethyl)-acrylamide | - |
| erionite | 12510-42-8 |
| hydrazine bis(3-carboxy-4-hydroxybenzenesulfonate) | - |
| Hydrazine-tri-nitromethane | - |
| Lead chromate molybdate sulfate red; C.I. Pigment Red 104 | 12656-85-8 |
| lead diazide; lead azide | 13424-46-9 |
| Lead sulfochromate yellow; C.I. Pigment Yellow 34; | 1344-37-2 |
| lead(II) methanesulphonate | 17570-76-2 |
| oxiranemethanol, 4-methylbenzene-sulfonate, (S)- | 70987-78-9 |
| phenylhydrazine hydrochloride | 27140-08-5 |
| phenylhydrazinium sulphate (2:1) | 52033-74-6 |
| R-1-chloro-2,3-epoxypropane | 51594-55-9 |
| R-2,3-epoxy-1-propanol | 57044-25-4 |
| tetracarbonylnickel; nickel tetracarbonyl | 13463-39-3 |
| tetrahydrothiopyran-3-carboxaldehyde | 61571-06-0 |
| toluene-2,4-diammonium sulphate; 4-methyl-m-phenylenediamine sulfate | 65321-67-7 |
| trisodium [4'-(8-acetylamino-3,6-disulfonato-2-naphthylazo)-4''-(6-benzoylamino-3-sulfonato-2-naphthylazo)-biphenyl-1,3',3'',1'''-tetraolato-O,O',O''',O''']copper(II) | 164058-22-4 |
| No CMR data | |
| 1-bromopropane; n-propyl bromide | 106-94-5 |
| 2-bromopropane | 75-26-3 |
| trichloroethylene; trichloroethene | 79-01-6 |

Appendix 2. The 21 substances for which hazards could neither be confirmed hazardous nor exempted.

| Substance name | CAS registration number |
|---|-------------------------|
| 1,2-dibromo-3-chloropropane | 96-12-8 |
| 4-chloroaniline | 106-47-8 |
| 3,3'-dimethoxybenzidine; o-dianisidine | 119-90-4 |
| 2,4,5-trimethylaniline | 137-17-7 |
| 2,4,5-trimethylaniline hydrochloride | 21436-97-5 |
| 1,3,5-tris(oxiranylmethyl)-1,3,5-triazine-2,4,6(1H,3H,5H)-trione; TGIC | 2451-62-9 |
| diaminotoluene, technical product; methyl-phenylenediamine; | 25376-45-8 |
| 6-(2-chloroethyl)-6-(2-methoxyethoxy)-2,5,7,10-tetraoxa-6-silaundecane; etacelasil | 37894-46-5 |
| 2,4-diaminoanisole; 4-methoxy-m-phenylenediamine; [1] 2,4-diaminoanisole sulphate [2] | 39156-41-7 |
| salts of 2-naphthylamine | 553-00-4; 612-52-2 |
| 4,4'-(4-iminocyclohexa-2,5-dienylidene)methylene)dianiline hydrochloride; C.I. Basic Red 9 | 569-61-9 |
| diisopentylphthalate | 605-50-5 |
| 3,4-dinitrotoluene | 610-39-9 |
| 2,4-diaminoanisole; 4-methoxy-m-phenylenediamine; [1] 2,4-diaminoanisole sulphate [2] | 615-05-4 |
| 2,5-dinitrotoluene | 619-15-8 |
| dimethylnitrosoamine; N-nitrosodimethylamine | 62-75-9 |
| cycloheximide | 66-81-9 |
| 1,2-benzenedicarboxylic acid; di-C7-11-branched and linear alkylesters | 68515-42-4 |
| 1,4-dichlorobut-2-ene | 764-41-0 |
| 2-nitrotoluene | 88-72-2 |
| 4-methyl-m-phenylenediamine; 2,4-toluenediamine | 95-80-7 |