Douglas Consulting Australia Pty Ltd ACN 88 003 582 385
PO Box 10398, BRISBANE ADELAIDE STREET, QLD 4000

FIREFIGHTER CHEMICAL REVIEW - EXTENSION TO REVIEW ADDITIONAL CHEMICAL SUBSTANCES – ARP1701

A report prepared for the Commonwealth of Australia

(as represented by the Department of Veterans' Affairs, the Repatriation Commission and the Military Rehabilitation and Compensation Commission)

Dr David DOUGLAS MBBS MSc DIH FAFOEM
Dr Ki DOUGLAS MBBS MPH MEL GDipOHS FAFOEM
Consultant Occupational Physicians

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PHONE
+61 428 880 228

EMAIL
daviddouglas6@bigpond.com

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EXECUTIVE SUMMARY

As stated in ARP1701, Australian Defence Force (ADF) firefighters carried out fire training at Point Cook in the 1970s. This required the lighting of large fires which would then be extinguished. The flammable materials used in the fires included a wide range of solid and liquid waste materials, leading to complex mixtures of pyrolysis products to which the ADF firefighters were potentially exposed during their duties.

On receiving the report, ARP1701, firefighter representatives indicated that there was another list of chemicals detected at Point Cook. The additional list, partly redacted, was part of a Defence submission to the Public Works Committee (PWC) Inquiry in 2011 – Attachment 1.

At Attachment 2 is the list of chemicals supplied by the firefighter representatives, but with chemicals previously reviewed in ARP1701 deleted.

At Attachment 3 is the list of additional chemicals identified in the Health Risk Assessment report, but with chemicals previously reviewed in ARP1701, and the chemicals listed in Attachment 2, deleted.

Attachments 2 and 3 also provide toxicological data on all the additional chemicals identified by Department of Defence. Those in Attachment 2 are the chemicals requested by the firefighter representatives, and those in Attachment 3 are the additional chemicals identified from the Health Risk Assessment report. All are possible contaminants at RAAF Williams, Point Cook but there are no quantitative data on the concentrations of the chemicals in either groundwater or soil at Point Cook.

The databases that have been most valuable in sourcing toxicological data on the contaminants listed in Attachments 2 and 3 were the United States Agency for Toxic Substances and Disease Registry (ATSDR) and Occupational Safety and Health Administration (OSHA), and the International Agency for Research on Cancer (IARC).

All the 78 chemicals listed in Attachment 2 have been reviewed by utilizing the reference sources. Most chemicals in Attachment 2 are halogenated hydrocarbons, phenolics, aromatic amines, organo-chlorines, phthalates and nitrosamines.

All the 57 chemicals listed in Attachment 3 have also been reviewed by utilizing the reference sources. Most were organo-phosphates, organo-chlorines, aromatic amines, nitrosamines, halogenated hydrocarbons, dichloropropenes, and other chemicals.

As stated in the previous report ARP1701, the ATSDR has advised that the health assessment of hazardous substances is complicated by the reality that most toxicological testing has been performed on single chemicals; but human exposures are rarely limited to single chemicals. The available data of relevance for this extension of ARP1701 relate to mixtures of chemicals not present in the previous review, namely organo-chlorines, organo-phosphates, aromatic amines, nitrosamines, halogenated hydrocarbons, and phenolics.

The limited data indicate that probable additive or synergistic effects exist between substances within mixtures. The extent of these effects is not currently known or quantifiable, and the toxic effects of the most toxic compound in any mixture are assumed to be the minimum effects of the mixture. A summary of the health effects of mixtures is provided in Table 1.

Based on both the ARP1701 report and this extension review, the occupation of firefighter is listed as a factor in only one SoP – mesothelioma. Smoke from fires is listed as a factor for bronchiectasis and chronic obstructive pulmonary disease, and smoke in an enclosed space is a factor in the SoP for fibrosing interstitial lung disease and malignant neoplasm of the lung. Inhalation of irritants is a factor for asthma, and exposure to irritants is a factor for conjunctivitis and irritant dermatitis.

Additionally, many of the contaminants listed in Appendix C of ARP1701, and in Attachments 2 and 3 of this extended review, are causal factors in a wide range of SoPs, but not in exposures experienced by firefighters. These contaminants include arsenic, benzene, carbon disulfide, cobalt, dioxins and furans, manganese, PAHs, vinyl chloride, and VOCs noted in ARP1701, and additional chemicals including aromatic amines, halogenated hydrocarbons, organo-chlorines and organo-phosphates – Table 2.

An additional literature review has been undertaken for this extension study. The publications cited in Section 7 below, together with those cited in ARP1701, support the assumption that the contaminants found at the site of ADF firefighter training at Point Cook could have been present in the smoke to which the firefighters were exposed, and that such smoke exposures were toxic.

Other publications support the SoPs for bronchiectasis, chronic obstructive pulmonary disease, fibrosing interstitial lung disease, and asthma which all list smoke, in various exposures, as a causal factor. There were no publications providing probable causal links between firefighters and other non-cancer long-term health outcomes. The publications also supported the view that, on the balance of probabilities, exposures experienced by firefighters contribute materially to the subsequent development of cancers in general and to some specific malignancies: cancers of the bladder, brain, colon, kidney, lung, prostate, stomach and testes; and leukaemia, multiple myeloma, and non-Hodgkin's lymphoma.

Overall, this Firefighter Chemical Review Extension and ARP1701, together with reviews of the SoPs and the relevant literature, concludes that **"firefighting"**, as in the current SoP for mesothelioma, should be considered as a factor in other SoPs as indicated in Table 3.

1. INTRODUCTION

1.1 Background

Douglas Consulting Australia has been requested to supply additional medical literature research services to the Department of Veterans' Affairs (DVA) in relation to the health effects of chemicals identified as possible contaminants at the former fire training area at Royal Australian Air Force (RAAF) Base Williams, at Point Cook, Australia. This report is in response to the DVA request and should be read as an extension of the previous report: *Firefighter Chemical Review ARP1701, April 2018.*

As stated in ARP1701, Australian Defence Force (ADF) firefighters carried out fire training at Point Cook in the 1970s. This required the lighting of large fires which would then be extinguished. The flammable materials used in the fires included a wide range of solid and liquid waste materials, leading to complex mixtures of pyrolysis products to which the ADF firefighters were potentially exposed during their duties. After some years, the setting of such fires was discontinued; but there is an ongoing concern by ex-serving ADF firefighters regarding the impact on their health of the pyrolysis products, and the materials used to build the fires.

In 2016, the Australian Department of Defence provided a list of chemical contaminants identified by HLA ENSR (HLA – Envirosciences Pty Limited) following an environmental risk assessment of the relevant area[1]. The list contained some 200 contaminants which included chemicals, chemical compounds, and metals. The contaminants had been identified by analysis of five media: soil, groundwater, sediment, soil vapour, and DNAPL (dense non-aqueous phase liquid).

On receiving the report, ARP1701, firefighter representatives indicated that there was another list of chemicals detected at Point Cook. The additional list, partly redacted, was part of a Defence submission to the Public Works Committee (PWC) Inquiry in 2011 – Attachment 1. Subsequently, on 1 November 2018, Defence provided a full report that it had commissioned from HLA-Envirosciences Pty Ltd – *Human Health Risk Assessment Point Cook Foreshore, Former Fire Training Area RAAF Williams, Point Cook, Victoria,02 July 2007,* to DVA. The Health Risk Assessment report identified possible chemical contaminants additional to those provided by the firefighter representatives. Both lists of chemicals have been compared with ARP1701.

At Attachment 2 is the list of chemicals supplied by the firefighter representatives, but with chemicals previously reviewed in ARP1701 deleted.

At Attachment 3 is the list of additional chemicals identified in the Health Risk Assessment report, but with chemicals previously reviewed in ARP1701, and the chemicals listed in Attachment 2, deleted.

[1] Human Health Risk Assessment Point Cook Foreshore, Former Fire Training Area RAAF Williams, Point Cook, Victoria 02 July 2007. Report by: HLA ENSR.
Prepared for: Property Disposal Task Force Department of Defence BP-2-A017 Canberra ACT 2600

1.2 Scope

The scope of these additional medical literature services to DVA, being an extension of the Firefighter Chemical Review ARP1701, is for Douglas Consulting Australia to: (i) create a toxicological profile of the chemicals identified in Attachments 2 and 3; (ii) cross-reference these chemicals to the Factors under the Repatriation Medical Authority (RMA) Statements of Principles (SoPs); and (iii) carry out a literature review. This extension will help further in the identification of the extent of coverage already established by the RMA, and the need for any additional coverage associated with these chemicals.

1.3 Pyrolysis toxicology

Pyrolysis is defined as the decomposition of materials due to high temperatures, and the process invariably generates toxic gases, vapours and particulates. The toxicity of the products of pyrolysis varies considerably and depends on the chemical nature and concentrations of the substances when released from the materials involved in a fire. These toxic substances may produce acute effects, latent effects, and with repeated exposure, as for firefighters, cumulative and/or long-term effects.

Smoke is a complex mixture of airborne solid and liquid particulates, vapours, and gases which are produced when the materials in the fire undergo vapourisation or thermal decomposition. Therefore, the atmosphere in any fire is extremely complex. Because of the constantly changing conditions during the progress of a fire, the chemical composition, both nature and concentration of materials, varies markedly at different stages of the fire[2].

1.4 Limitations and assumptions.

The Attachments 2 and 3 provide toxicological data on all the additional chemicals identified by Department of Defence. Those in Attachment 2 are the chemicals requested by the firefighter representatives, and those in Attachment 3 are the additional chemicals identified from the Health Risk Assessment report. All are possible contaminants at RAAF Williams, Point Cook but there are no quantitative data on the concentrations of the chemicals in either groundwater or soil at Point Cook.

The concentrations of possible chemical contaminants at Point Cook are not directly relevant to the scope of this review. Any concentrations found in detailed analyses of soil and groundwater cannot be applied to the concentration of contaminants in the smoke to which the ADF firefighters were exposed; but it can be assumed that the chemicals identified from the detailed analyses could have been present at various times, and in variable concentrations, in the smoke generated by the training fires at Point Cook. support the SoPs for bronchiectasis, chronic obstructive pulmonary disease, fibrosing interstitial lung disease, and asthma which all list smoke, in various exposures, as a causal factor. There were no publications providing probable causal links between firefighters and other non-cancer long-term health outcomes.

[2] Norris JC, Ballantyne B. (1993). Combustion toxicology. In General and Applied Toxicology, eds B Ballantyne, T Mars, P Turner, Vol 3, pp 1309-1327. London; MacMillan

2. METHODOLOGY

2.1 Reference sources

During the past thirty years, there has been such an exponential growth in information technology that freely available databases have been established by government agencies in North America and Europe. These include the Agency for Toxic Substances and Disease Registry (ATSDR) and PubChem in the United States, and the Health and Safety Executive in the United Kingdom. Other valuable reference sources include those of the World Health Organisation (WHO) and the International Labor Organisation (ILO).

The databases that have been most valuable in sourcing data on the contaminants listed in Attachments 2 and 3 are summarised in the following paragraphs. The summaries have been based on the material supplied on-line by each database.

2.2 The US Agency for Toxic Substances and Disease Registry (ATSDR)

ATSDR is a Federal public health agency of the U.S. Department of Health and Human Services (DHHS). ATSDR has been established to help protect communities from harmful health effects related to exposure to natural and man-made hazardous substances. It does this by responding to environmental health emergencies; investigating emerging environmental health threats; conducting research on the health impacts of hazardous waste sites; and building capabilities for providing actionable guidance to state and local health partners.

By Congressional mandate, the Agency for Toxic Substances and Disease Registry (ATSDR) produces "toxicological profiles" for hazardous substances found at National Priorities List (NPL) sites. These hazardous substances are ranked based on frequency of occurrence at NPL sites, toxicity, and potential for human exposure. Toxicological profiles are developed from a priority list of 275 substances. ATSDR also prepares toxicological profiles for the Department of Defense (DOD) and the Department of Energy (DOE) on substances related to Federal sites. Toxicological profiles are developed in two stages: the toxicological profiles are first produced as drafts. ATSDR announces in the Federal Register the release of these draft profiles for a 90-day public comment period. After the 90-day comment period, ATSDR considers incorporating all comments into the documents and then finalises the profiles.

The ATSDR toxicological profiles covered most of the substances in Attachments 2 and 3, and have been the major source of data for this review.

2.3 PubChem

PubChem is an open chemistry database at the US National Institutes of Health (NIH). “Open” means that contributors can submit scientific data to PubChem and that others may access it. PubChem collects information on chemical structures, identifiers, chemical and physical properties, biological activities, patents, health, safety, toxicity data, and many others. Since its launch in 2004, PubChem has become a key chemical information resource for scientists, students, and the public. Each month the PubChem website and programmatic services provide data to several million users worldwide. PubChem records are contributed by hundreds of data sources, including: research results from universities, pharmaceutical companies, and others;

government agencies; chemical vendors; journal publishers; and the efforts of curation of chemical biology.

The PubChem database has proved to be an important additional resource to that of ATSDR in this review.

2.4 The International Agency for Research on Cancer (IARC)

IARC is the specialised cancer agency of the World Health Organization. The objective of the IARC is to promote international collaboration in cancer research. The Agency is inter-disciplinary, bringing together skills in epidemiology, laboratory sciences and biostatistics to identify the causes of cancer so that preventive measures may be adopted, and the burden of disease and associated suffering reduced. A significant feature of the IARC is its expertise in coordinating research across countries and organizations; its independent role as an international organization facilitates this activity. Emphasis is placed on elucidating the role of environmental and lifestyle risk factors and studying their interplay with genetic background in population-based studies and appropriate experimental models. This emphasis reflects the understanding that most cancers are, directly or indirectly, linked to environmental factors and thus are preventable. The IARC Monographs Programme is a core element of the Agency's portfolio of activities, with international expert working groups evaluating the evidence of the carcinogenicity of specific exposures. Since commencing its work in 1970, the IARC has published 123 Monographs with the following evaluations:

Group 1	Carcinogenic to humans
Group 2A	Probably carcinogenic to humans
Group 2B	Possibly Carcinogenic to humans
Group 3	Not classifiable as to its carcinogenicity to humans
Group 4	Probably not carcinogenic to humans

The IARC Monographs have been an essential source of data on the carcinogenicity of all substances in this review.

2.5 The US Occupational Safety and Health Administration (OSHA)

OSHA maintains an Occupational Chemical Database as a convenient reference for the occupational safety and health community. It compiles information from several government agencies and organisations, and information available in the database includes: physical properties; exposure guidelines; National Institute for Occupational Safety and Health (NIOSH) pocket guides; and emergency response information. The database originally was developed by OSHA in cooperation with the US Environmental Protection Agency (EPA).

The OSHA Occupational Chemical Database lists over 450 chemicals as carcinogens, and this list has been sourced in the compilation of this review.

2.6 The Australian National Industrial Chemicals Notification and Assessment Scheme (NICNAS)

NICNAS helps protect the Australian people and the environment by assessing the risks of industrial chemicals and providing information to promote their safe use. The focus is on the industrial use of

chemicals and covers a broad range of chemicals used in inks, plastics, adhesives, paints, glues, solvents, cosmetics, soaps and many other products.

2.7 The United States Environmental Protection Agency (US EPA)

US EPA is an agency of the Federal Government of the United States which was created in 1970 for protecting human health and the environment by writing and enforcing regulations based on laws passed by Congress. Its publications cover a wide range of environmental topics including chemicals and toxins. Priority substances are mercury, lead, hazardous/toxic pollutants, PCBs, and pesticides. Hazardous/toxic pollutants, also known as air pollutants or air toxics, are those pollutants that are known or suspected to cause cancer, or other serious health effects such as reproductive effects or birth defects, or adverse environmental effects. The list of 187 air toxics includes PAHs, benzene and benzene derivatives, bromoform, carbon disulphide, carbon tetrachloride, furans, ethylene oxide, trichloroethane, MIBK, ethylene oxide, PCBs, toluene, vinyl chloride, xylenes, and carcinogenic metals. The US EPA refers to the US Agency for Toxic Substances and Disease Registry (ATSDR) for detailed toxicity data.

The US EPA databases have also been utilized in this review, but most have referred to ATSDR as the authoritative source of toxicity data.

2.8 The International Programme on Chemical Safety (IPCS)

IPCS is a programme of the World Health Organisation (WHO) that works to establish the scientific basis for the sound management of chemicals and to strengthen national capabilities and capacities for chemical safety. Its publication in 2016 *Public Health Impact of Chemicals – Knowns and Unknowns* stated that air pollutants from ambient air and household sources are a mixture of many components, including carbon monoxide, sulphur dioxide, nitrogen oxide, and particulate matter. The particulate matter contains substances such as acids, organic chemicals, metals, soil, and dust particles. The largest sources of air pollution are combustion and other processes from energy generation, industry, and transport. The IPCS has estimated that an overall reduction or elimination of exposure to chemicals from air pollution would have a significant impact in reducing morbidity and mortality from a wide range of conditions including: ischaemic heart disease, stroke, cancers, mental and neurological disorders, chronic obstructive pulmonary disease, bronchitis, and asthma.

The IPCS publications support the data from other reference sources that indicate both acute and cumulative effects due to toxic pyrolysis products.

2.9 The UK Health and Safety Executive (HSE)

HSE is an Executive Non-Departmental Public Body of the UK Government, and its core purpose is to reduce work-related injury and ill-health. The HSE is an international centre of expertise for occupational safety and health, and the effective management and control of risks. Control of Substances Hazardous to Health (COSHH) is the law that requires employers to control substances that are hazardous to health (except asbestos and lead which have specific regulations).

The HSE publications focus on implementation, but do not provide the basic toxicological data needed for this review.

3. EVALUATION OF CHEMICALS IN ATTACHMENT 2

3.1 List of chemicals

All the 78 chemicals listed in Attachment 2 have been reviewed by utilizing the reference sources cited above and a summary of the toxicity of each chemical is provided in Attachment 2. Whereas the chemicals reviewed in the previous report (ARP1701) comprised mostly volatile organic compounds (VOCs), dioxins and furans, polycyclic aromatic hydrocarbons (PAH), total petroleum hydrocarbons (TPH), trihalomethanes (THM), and metals, the requested list of chemicals in Attachment 2 includes only eight VOCs, two PAHs, one furan, and one THM. The furan, dibenzofuran, and the THM, chlorodibromomethane, are of low toxicity. Most chemicals in Attachment 2 are halogenated hydrocarbons, phenolics, aromatic amines, organo-chlorines, phthalates and nitrosamines.

3.2 Volatile organic compounds (VOCs)

The **VOCs** of concern in Attachment 2 are:

1,1,1,2-tetrachloroethane
1,2,3-trichlorobenzene
1,2,3-trichloropropane
1,2,4,5-tetrachlorobenzene
2-butanone (MEK)
4-chlorotoluene
Bis(2-chloroethoxy) methane
Bis(2-chloroisopropyl) ether

Adverse health effects reported from these VOCs include: acute and chronic effects on the central nervous system, upper respiratory tract (URT) irritation, eye irritation and skin irritation.

Additionally, 1,2,3-trichloropropane has been classified by the IARC as Group 2A – probably carcinogenic to humans.

3.3 Polycyclic aromatic hydrocarbons (PAHs)

The **PAHs** of concern in Attachment 2 are:

3-methylcholanthrene
7,12-dimethylbenz(a)anthracene

Both these chemicals have been classified by the IARC as Group 1 – carcinogenic to humans.

The toxic effects of PAHs include: dermatitis, photosensitisation, bronchitis and pulmonary oedema, cancer of the skin, cancer of the lung, and leukaemia.

3.4 Organo-chlorines

The **organo-chlorines** of concern in Attachment 2 are:

4,4-DDD	endosulfan sulphate
4,4-DDE	endrin
4,4-DDT	endrin aldehyde
4-chlorophenyl phenyl ether	endrin ketone
a-bhc	heptachlor
b-bhc	heptachlor epoxide
d-bhc	hexachlorobenzene (HCB)
g-bhc	hexachlorobutadiene
aldrin	hexachlorocyclopentadiene (HCCPD)
dieldrin	methoxychlor
cis-1,3-dichloropropene	pentachlorobenzene
endosulfan I	pentachloronitrobenzene
endosulfan II	pentachlorophenol

All organo-chlorine chemicals are toxic to the CNS (central nervous system) by inhalation, ingestion and skin absorption.

Additionally, g-bhc (Lindane) and pentachlorophenol have been classified by the IARC as Group 1 - carcinogenic to humans, as both cause non-Hodgkin's lymphoma; and 4,4-DDT has been classified as Group 2A – probably carcinogenic to humans.

3.5 Aromatic amines

The **aromatic amines** of concern in Attachment 2 are:

1-naphthylamine
2-naphthylamine
3-nitroaniline
4-aminobiphenyl
Aniline
Diphenylamine
Nitrobenzene

All these chemicals are irritants to the skin, eyes and URT (upper respiratory tract); and cause systemic toxicity including methaemoglobinaemia and CNS toxicity by inhalation, ingestion and skin absorption.

Additionally, 2-naphthylamine and 4-aminobiphenyl have been classified by the IARC as Group 1 – carcinogenic to humans, as both cause bladder cancer.

3.6 Phenolics

The **phenolics** of concern in Attachment 2 are:

2,3,4,6-tetrachlorophenol
2,4,5-trichlorophenol

2,4,6-trichlorophenol
2,4-dichlorophenol
2,4-dimethylphenol
2,6-dichlorophenol
2-chlorophenol
2-nitrophenol
4-chloro-3-methylphenol
Phenol

All these phenolic chemicals are irritants to the skin, eyes and URT, and are toxic by inhalation, ingestion and skin absorption causing systemic phenolic poisoning.

3.7 Nitrosamines

The **nitrosamines** of concern in Attachment 2 are:

N-nitrosodi-n-butylamine
N-nitrosodi-n-propylamine
N-nitrosopiperidine

These chemicals are irritants to the skin, eyes and URT.

3.8 Phthalates

The **phthalates** listed in Attachment 2 are:

Bis-(2-ethylhexyl)-phthalate (DEHP)
Butyl benzyl phthalate
Diethyl phthalate
Dimethyl phthalate
di-n-butyl phthalate
di-n-octyl phthalate

Phthalates have been used extensively as plasticisers and are not considered to be toxic to humans.

3.9 Halogenated hydrocarbons (HC)

The **halogenated hydrocarbons** of concern in Attachment 2 are:

1,2-dibromomethane
2-chloronaphthalene
4-bromophenyl phenyl ether
Dibromomethane
Dichlorodifluoromethane
Trichlorofluoromethane

These chemicals are irritant to skin, eyes and URT, and chronic exposure causes chloracne. Few data on inhalation toxicity, but toxic and corrosive by ingestion.

Additionally, 1,2-dibromomethane has been classified by the IARC as Group 2A - probably carcinogenic to humans.

3.10 Dinitrotoluenes

The **dinitrotoluenes** of concern in Attachment 2 are:

2,4-dinitrotoluene

2,6-dinitrotoluene

Dinitrotoluenes are toxic by inhalation causing lung damage in humans and experimental animals.

3.11 Cresols

The **cresols** of concern in Attachment 2 are:

2-methyl phenol

3-methyl phenol

4-methyl phenol

Cresols are irritant and corrosive to skin, eyes and URT.

3.12 Other chemicals

The other chemicals listed in Attachment 2 are:

4-(dimethylamino) azobenzene – toxic by inhalation, ingestion and skin absorption causing liver and kidney damage.

Acetophenone – no known toxicity to humans.

Vinyl acetate – irritant to skin, eyes, URT and CNS.

4 EVALUATION OF CHEMICALS IN ATTACHMENT 3

4.1 List of chemicals

All the 57 chemicals listed in Attachment 3 have also been reviewed by utilizing the reference sources cited above and a summary of the toxicity of each chemical is provided in Attachment 3. Whereas the chemicals reviewed in the previous report (ARP1701) comprised mostly volatile organic compounds (VOCs), dioxins and furans, polycyclic aromatic hydrocarbons (PAH), total petroleum hydrocarbons (TPH), trihalomethanes (THM), and metals, the list of chemicals in Attachment 3 includes only eight VOCs. The other 49 chemicals are organo-phosphates, organo-chlorines, aromatic amines, nitrosamines, halogenated hydrocarbons, dichloropropenes, and other chemicals.

4.2 Volatile organic compounds (VOCs)

The **VOCs** of concern in Attachment 3 are:

2-hexanone (MBK)
2-pentanone
Azobenzene
Benzyl alcohol
Isophorone
Pentachloroethane
p-isopropyl toluene
Tert-butylbenzene
Tributylmethylether (TBME)

Adverse health effects reported from these VOCs include: acute and chronic effects on the central nervous system; upper respiratory tract (URT) irritation; eye irritation and skin irritation.

4.3 Organo-chlorines

The **organo-chlorines** of concern in Attachment 3 are:

Cis-chlordane
Dichlorvos
Hexachloropropene

All organo-chlorine chemicals are toxic to the CNS (central nervous system) by inhalation, ingestion and skin absorption.

4.4 Organo-phosphates (O-P)

The **organo-phosphates** of concern in Attachment 3 are:

Azinophos methyl
Chlorpyrifos
Coumaphos
Demeton-O
Malathion
Methyl parathion
Parathion
Mevinphos

Demeton-S
Diazinon
Dimethoate
Disulfoton
EPN
Ethoprop
Fenitrothion
Fensulfothion
Fenthion
Naled
Phorate
Profenofos
Prothiofos
Ronnel
Stirophos
Sulfotepp
Trichloronate

All these organo-phosphates are toxic by inhalation, ingestion and skin absorption due to cholinesterase inhibition.

Additionally, diazinon and malathion have been classified by the IARC as Group 2A – probably carcinogenic to humans.

4.5 Aromatic amines

The **aromatic amines** of concern in Attachment 3 are:

1,4-dinitrobenzene
2-nitroaniline
4-chloroaniline
4-nitroaniline
5-nitro-o-toluidine
Carbazole
0-toluidine

All these chemicals are irritants to the skin, eyes and URT (upper respiratory tract); and cause systemic toxicity including methaemoglobinaemia and CNS toxicity by inhalation, ingestion and skin absorption.

Additionally, o-toluidine has been classified by the IARC as Group 1 – carcinogenic to humans, causing cancer of the bladder.

4.6 Nitrosamines

The **nitrosamines** of concern in Attachment 3 are:

N-nitrosodiethylamine
N-nitrosomorpholine
N-nitrosopyrrolidine

These chemicals are irritants to the skin, eyes and URT.

Additionally, N-nitrosodiethylamine has been classified by the IARC as Group 2A – probably carcinogenic to humans.

4.7 Halogenated hydrocarbons

The **halogenated hydrocarbons** of concern in Attachment 3 are:

1,2-dibromo-3-chloropropane

4-bromofluorobenzene

These chemicals are irritant to skin, eyes and URT, and chronic exposure causes chloracne. Few data on inhalation toxicity, but toxic and corrosive by ingestion.

4.8 Dichloropropenes

The **dichloropropenes** of concern in Attachment 3 are:

1,1-dichloropropene

Cis-1,3-dichloropropene

Trans-1,3-dichloropropene

These chemicals are skin irritants and sensitisers.

4.9 Other chemicals

The **other chemicals** of concern in Attachment 3 are:

Ethyl methanesulfonate – a laboratory chemical with carcinogenic action in experimental animals. Irritant to skin, eyes, URT and CNS in humans.

Safrole and isosafrole – naturally occurring chemicals of low toxicity.

Methyl methane sulfonate – a laboratory and pharmaceutical chemical classified by the IARC as Group 2A – probably carcinogenic to humans.

Phenacetin – a toxic pharmaceutical chemical causing methaemoglobinaemia and nephropathy by ingestion. Classified by the IARC as Group 1 – carcinogenic to humans, causing cancer of the renal pelvis and ureter.

5. HEALTH EFFECTS OF MIXTURES

5.1 Overview

As stated in the previous report ARP1701, the ATSDR has advised that the health assessment of hazardous substances is complicated by the reality that most toxicological testing has been performed on single chemicals; but human exposures are rarely limited to single chemicals. Exposures resulting from smoke inhalation, and from hazardous waste sites generally, involve more than one hazardous substance. At issue is whether a mixture of contaminants may be more hazardous due to additivity, interactions, or both. The available data of relevance for this extension of ARP1701 relate to mixtures of chemicals not present in the previous review, namely organo-chlorines, organo-phosphates, aromatic amines, nitrosamines, halogenated hydrocarbons, and phenolics.

5.2 Organo-chlorines

Organochlorine pesticides are chlorinated hydrocarbons used extensively from the 1940s through the 1960s in agriculture and mosquito control. Representative compounds in this group include DDT, methoxychlor, dieldrin, chlordane, and lindane. As neurotoxicants, many organochlorine pesticides were banned in the United States, although a few are still registered for use in the US.

Organochlorine pesticides accumulate in the environment. They are very persistent and move long distances in surface runoff or groundwater. Prior to the mid-1970s, organochlorines resulted in widespread reproductive failure among birds because birds laid eggs with thin shells that cracked before hatching.

Exposure to organochlorine pesticides over a short period may produce convulsions, headache, dizziness, nausea, vomiting, tremors, confusion, muscle weakness, slurred speech, salivation and sweating.

Long-term exposure to organochlorine pesticides may damage the liver, kidney, central nervous system, thyroid and bladder in humans. Many of these pesticides have been linked to elevated rates of liver or kidney cancer in animals.

Lindane and pentachlorophenol have been classified by the IARC as Group 1 – carcinogenic to humans causing non-Hodgkin lymphoma.

There is some evidence indicating that organochlorine pesticides, including DDT, may also cause cancer in humans.

5.3 Organo-phosphates

Organophosphates are a group of human-made chemicals that poison insects and mammals. Organophosphates are the most widely used insecticides today. They are used in agriculture, the home, gardens, and veterinary practice.

Organophosphate insecticides (such as diazinon) are one type of pesticide that works by damaging an enzyme in the body called acetylcholinesterase. This enzyme is critical for controlling nerve signals in the body. The damage to this enzyme kills pests and may cause unwanted side effects in

exposed humans. All organophosphates have a common mechanism of toxicity and can cause similar symptoms in humans who have too much exposure.

Because organophosphates are often sprayed on crops and plants, small particles of the chemical may be carried away from the field or yard before falling to the ground. After organophosphates are applied, they may be present in the soil, surface waters, and on the surface of the plants. They can move through the soil and contaminate ground water. Rain can wash organophosphates on soil and plant surfaces into surface waters.

Organophosphates are rapidly broken down into other chemicals, so they do not build up in the environment.

Symptoms of sudden poisoning by organophosphates start during or after exposure, depending on how the poison is contacted. Symptoms start fastest after organophosphates are breathed, and next by eating or drinking contaminated food or water or getting them on the skin. Some symptoms are headache, dizziness, weakness, diarrhea, nausea and vomiting, salivation, watery eyes, and small pupils. Severe symptoms are seizures, slow pulse, difficulty breathing, and coma. Long after exposure, people also can develop nervous system problems such as muscle weakness and numbness and tingling of the hands and feet (neuropathy).

Long-term exposure to organophosphates can cause confusion, anxiety, loss of memory, loss of appetite, disorientation, depression, and personality changes. Other symptoms such as weakness, headache, diarrhea, nausea and vomiting also may occur.

Some studies in adults and children have linked organophosphate exposure to lymphoma and leukemia. Home pesticide use overall has been linked to childhood cancers such as soft tissue sarcomas, leukemias, and cancer of the brain. The results of these studies are controversial. No studies have definitively linked these exposures with cancer because the exposure is not measured, and people usually are not exposed to just the one pesticide being studied. In experimental animals, studies of different organophosphates showed more adrenal, thyroid, and pancreatic tumours.

5.4 Aromatic amines

Human epidemiological evidence on the relation between aromatic amines and cancer risk has been reviewed by ATSDR and IARC. Cancer risk in humans resulting from exposure to aromatic amines from occupational sources and tobacco smoking was assessed with reference to ecologic, cohort, and case-control studies. Seven arylamines have been classified by the International Agency for Research on Cancer: benzidine-based dyes and MOCA (4,4'-methylene bis 2-choloroaniline) were considered 'probably' carcinogenic, Group 2A, because of a high level of evidence in experimental animals; two occupational chemicals (2-naphthylamine and benzidine), one drug (Chlornaphazine), and two manufacturing processes (manufacture of auramine and magenta) were included in Group 1 on the basis of 'sufficient' evidence of carcinogenicity in humans.

Occupational exposures to aromatic amines explain up to 25 percent of bladder cancers in some areas of Western countries; these estimates might be higher in limited areas of developing countries. Aromatic amines contaminate the ambient air as a component of environmental tobacco smoke. There is increasing evidence that the excess of bladder cancer in smokers is attributable to aromatic amines rather than to other contaminants of tobacco smoke such as polycyclic aromatic hydrocarbons (PAH). A modulating role in the risk of bladder cancer associated with exposure to aromatic amines is played by metabolic polymorphisms, such as the N-acetyltransferase genotype, raising important social and ethical issues. The consistent observation of a difference between men

and women in bladder cancer risk, after allowing for known risk factors, suggests consideration of gender-related biological determinants for future investigation.

5.5 Nitrosamines

N-Nitrosamines are a class of chemical compounds with the essential feature of the N–N=O structure; the R1 and R2 groups attached to the amine nitrogen may range from a simple hydrogen (H) atom to more complex chemical substituents (including ring structures that incorporate the nitrogen atom), as shown in the structures of individual nitrosamines.

Human exposure to nitrosamines can result from formation of N-nitroso compounds either in food during storage or preparation or in vivo, usually in the stomach. Individual nitrosamines are not found in isolation but occur in mixtures of various nitrosamines. Nitrosamines or their precursors occur in a wide variety of foods and manufactured and natural products, such as agricultural chemicals, tobacco, detergents, rust inhibitors, cutting fluids, rubber additives, solvents, drugs, plastics, tanned leather products, textiles, and cosmetics (ATSDR).

Nitrosamines generally are not intentionally added to foods or consumer products, but are formed from constituents of the foods or products that are either naturally present, such as the amines that are part of the structure of proteins in meat, or added during production (e.g., nitrates or nitrites added to meats as preservatives). Nitrosamines are formed when nitrites, which can be formed from nitrates, react with a secondary or tertiary amine. The concentration of nitrosamines tends to increase over time, and their formation is enhanced by high temperatures, such as occur while frying food, and high acidity, such as in stomach acid. Ascorbic acid or its isomers inhibit the formation of nitrosamines and often are added to food preparations to prevent nitrosamine formation.

Although food and tobacco products are important sources of external exposure to N-nitrosamines, exposure also occurs from nitrosamines produced internally in the digestive tract. About 5% of ingested nitrates are reduced to nitrites in saliva. These nitrites can subsequently react in solution with secondary and tertiary amines, as well as N-substituted amides, carbamates, and other related compounds, to form N-nitroso compounds within the gastrointestinal tract. This internal formation is a major source of human exposure to N-nitrosamines.

Occupational exposure may happen in many places including industries such as tanneries, pesticide manufacturing plants, rubber and tire manufacturing plants, alkylamine manufacture/use industries, fish processing industries, foundries, and dye manufacturing plants.

Nitrosamines may be very harmful to the liver of animals and humans. People who were intentionally poisoned on one or several occasions with unknown levels of N-nitrosamines in beverage or food died of severe liver damage accompanied by internal bleeding. Animals that ate food, drank water, or breathed air containing high levels over a period of days or several weeks also developed serious, non-cancerous, liver disease.

When rats, mice, hamsters, and other animals ate food, drank water, or breathed air containing lower levels of N-nitrosamines for periods more than several weeks, liver cancer and lung cancer as well non-cancerous liver damage occurred.

Although there are no reports of N-nitrosamines causing cancer in humans, it is reasonable to expect that exposure to N-nitrosamines by eating, drinking, or breathing could cause cancer in humans.

5.6 Halogenated hydrocarbons

Halogenated aliphatic compounds are moderately or very reactive. They generally become less reactive as more of their hydrogen atoms are replaced with halogen atoms. Halogenated acetylene compounds are unstable and should be treated as explosives. Low molecular weight haloalkanes are highly flammable and can react with some metals to form dangerous products. They are also peroxidizable and may polymerize violently. They may react violently with aluminum. Materials in this group are incompatible with strong oxidizing and reducing agents. Also, they are incompatible with many amines, nitrides, azo/diazo compounds, alkali metals, and epoxides.

Many halogenated hydrocarbons have moderate to high toxicity by inhalation. The brominated materials tend to be particularly toxic. Much of the toxicity is because these substances are not metabolized but persist and accumulate in fatty tissues (they tend to be fat-soluble). They cause chloracne in humans. The combustion of chlorinated organic compounds may produce poisonous phosgene gas (COCl2). Other materials formed by incomplete combustion are classes of chlorinated organic compounds, chlorodibenzodioxins and chlorodibenzofurans. These compounds cause cancer in laboratory tests.

5.7 Phenolics

Phenols, sometimes called phenolics, are a class of aromatic organic compounds consisting of one or more hydroxyl groups attached to an aromatic hydrocarbon group. Phenol is a benzene derivative and is the simplest member of the phenolic chemicals. Its chemical formula is C6H5OH and its structure is that of a hydroxyl group (-OH) bonded to a phenyl ring. Synonyms for phenol include carbolic acid, benzo phenol, and hydroxybenzene.

Phenol is produced naturally and synthesized as a manufactured chemical. Naturally, it is a constituent of coal tar and creosote, decomposing organic material, human and animal wastes, and as a compound found in many non-foods and foods. For example, salicylic acid is a natural phenolic compound found in willow bark. Salicylic acid is also synthesized from phenol as an intermediate in the industrial production of aspirin. Phenol is also formed during forest fires, and by atmospheric degradation of benzene in the presence of light. In addition, phenol is produced by the body and excreted as a metabolic product independent of external exposure or intake.

Phenolics are irritants to the skin, eyes and URT, and are toxic by inhalation, ingestion and skin absorption causing systemic phenolic poisoning.

5.8 Summary of health effects of mixtures

The limited data indicate that probable additive or synergistic effects exist between substances within mixtures; but the extent of these effects is not currently known or quantifiable. As noted above in the data from ATSDR and PubChem, the toxic effects of the most toxic compound in any mixture are assumed to be the minimum effects of the mixture.

Table 1: Summary of health effects of mixtures

Chemical groups	Health effects
Organo-chlorines	Acute: convulsions, headache, dizziness, nausea, vomiting, tremors, confusion, muscle weakness, slurred speech, salivation and sweating. Chronic: damage to the liver, kidney, central nervous system, thyroid and bladder. Many organo-chlorines have been linked to elevated rates of liver or kidney cancer in animals. Lindane and pentachlorophenol have been classified by the IARC as Group 1 – carcinogenic to humans causing non-Hodgkin lymphoma. There is some evidence indicating that organochlorine pesticides, including DDT, may also cause cancer in humans.
Organo-phosphates	Acute: headache, dizziness, weakness, diarrhea, nausea and vomiting, salivation, watery eyes, and small pupils. Severe symptoms are seizures, slow pulse, difficulty breathing, and coma. Long after exposure, people also can develop nervous system problems such as muscle weakness and numbness and tingling of the hands and feet (neuropathy). Long-term exposure: confusion, anxiety, loss of memory, loss of appetite, disorientation, depression, and personality changes. Other symptoms such as weakness, headache, diarrhea, nausea and vomiting also may occur. Some studies in adults and children have linked organophosphate exposure to lymphoma and leukemia.
Aromatic amines	Seven arylamines have been classified by the International Agency for Research on Cancer: benzidine-based dyes and MOCA (4,4'-methylene bis 2-choloroaniline) were considered 'probably' carcinogenic, Group 2A, because of a high level of evidence in experimental animals; two occupational chemicals (2-naphthylamine and benzidine), one drug (Chlornaphazine), and two manufacturing processes (manufacture of auramine and magenta) were included in Group 1 on the basis of 'sufficient' evidence of carcinogenicity in humans. Occupational exposures to aromatic amines explain up to 25 percent of bladder cancers.
Nitrosamines	Acute: irritants to the skin, eyes and URT; very harmful to the liver of animals and humans. Chronic: N-nitrosodiethylamine has been classified by the IARC as Group 2A – probably carcinogenic to humans.
Halogenated hydrocarbons	Acute: moderate to high toxicity by inhalation. The brominated materials tend to be particularly toxic. Chronic: These compounds cause chloracne in humans, and cancer in laboratory tests.
Phenolics	Phenolics are irritants to the skin, eyes and URT, and are toxic by inhalation, ingestion and skin absorption causing systemic phenolic poisoning.

6. STATEMENTS OF PRINCIPLES (SoP)

6.1 Statements of Principles (SoPs) determined by the Repatriation Medical Authority (RMA)

As stated in the previous report ARP1701, SoPs are legislative instruments and have the same legal effect as any legislation passed by Parliament. SoPs exclusively state what factors must exist to establish a causal connection between specific diseases, injuries or death, and service. In 1994 the Australian Government requested the Repatriation Commission, in consultation with veterans' organisations, to prepare legislation to reform the process of decision making about disease causation. The aim was to create a more equitable and consistent system of dealing with claims for disability pensions received from Australian veterans and their dependents. One of the outcomes of the legislative reform was the formation of the Repatriation Medical Authority (RMA) which is an independent statutory authority responsible to the Minister for Veterans' Affairs.

The RMA consists of a panel of five practitioners eminent in fields of medical science. Their role is to determine Statements of Principles (SoPs) for any disease, injury or death that could be related to military service, based on sound medical-scientific evidence. The SoPs state the factors which "must" or "must as a minimum" exist to cause a specific disease, injury or death.

It is important to note that there are two SoPs for each condition as explained on the RMA website. The legislation provides that claims for pension, and the SoPs used to determine claims, should be assessed at two different standards of proof.

6.2 Reasonable hypothesis standard

The more generous (beneficial) standard, known as the reasonable hypothesis standard, applies to veterans and serving members who have operational, or equivalent, service. This includes peacekeeping, hazardous and British nuclear test defence service under the Veterans' Entitlements Act 1986 (the VEA), and warlike and non-warlike service under the Military Rehabilitation and Compensation Act 2004 (the MRCA).

6.3 Balance of probabilities standard

The balance of probabilities standard is for veterans and serving members with non-operational service.

Therefore, for any given condition there are two SoPs. In most cases there are at least slight differences, and in many cases the more generous reasonable hypothesis version of the SoP will contain more causal factors. The legislation requires that the same body of evidence be interpreted differently for the two standards of proof. For the reasonable hypothesis standard, the sound medical-scientific evidence must indicate or point to a causal association between a risk factor and the disease in question. For the balance of probabilities standard, the sound medical-scientific evidence must show that it is more probable than not that there is a causal association between a risk factor and the disease.

Based on the assumption that the firefighters, whose presumed chemical exposures are the subject of this extended review, experienced their exposures during non-operational service in peace time, the **balance of probabilities** standard has been applied.

6.4 SoP with halogenated hydrocarbons as causal factors

The SoP for **Chloracne** lists halogenated hydrocarbons as causal factors:

> ***CHLORACNE No. 18 of 2012***
>
> ***Factors: 6.*** (a) inhaling, ingesting or having cutaneous contact with a polyhalogenated aromatic hydrocarbon from the specified list, or a chemical mixture containing a polyhalogenated aromatic hydrocarbon from the specified list, within the six weeks before the clinical onset of chloracne

6.5 SoP with irritants as causal factors

The SoP for **Conjunctivitis lists** irritants as causal factors:

> ***CONJUNCTIVITIS No. 2 of 2012***
>
> ***Factors: 6.*** *(s) having ocular or periocular exposure to an irritant substance within the 24 hours before the clinical worsening of conjunctivitis;*
>
> *"an irritant substance" means a chemical agent (including those contained in smokes, smog, aerosolised sprays and fumes) which causes an inflammatory effect on living tissue at the site of contact; "*

6.6 SoP with organo-chlorines and organo-phosphates as causal factors

The SoP for **Epileptic Seizure** lists organo-chlorines and organo-phosphates as causal factors:

> ***EPILEPTIC SEIZURE No. 78 of 2013***
>
> ***Factors: 6.*** *(dd) inhaling, ingesting or having cutaneous contact with a neurotoxic substance.*
>
> *a neurotoxic substance or a food or compound containing a neurotoxic substance" means: (g) organochlorine insecticide; (h) organophosphates.*

6.7 SoP with aromatic amines as causal factors

The SoP for **Malignant Neoplasm of the Bladder** lists aromatic amines as causal factors:

> ***MALIGNANT NEOPLASM OF THE BLADDER No. 97 of 2011***
>
> ***Factors: 6.*** *(d) inhaling fumes containing a high concentration of an aromatic amine from the specified list or ingesting or having cutaneous contact with an aromatic amine from the specified list.*

an aromatic amine from the specified list means: (a) 2-naphthylamine; (b) 4-aminobiphenyl; (c) benzidine; or (d) ortho-toluidine.

6.8 SoP with Lindane as a causal factor

The SoP for **Non-Hodgkin Lymphoma** lists Lindane (organo-chlorine) as a causal factor:

NON-HODGKIN LYMPHOMA No. 91 of 2018

Factors: 9. *(21) inhaling, ingesting or having cutaneous contact with lindane on more days than not for a cumulative period of at least one year, at least five years before the clinical onset of non-Hodgkin lymphoma.*

6.9 SoP with exposure to organophosphorous (organo-phosphate) as a causal factor

The SoP for **Parkinson's Disease and Secondary Parkinsonism** lists organophosphorous as a causal factor:

PARKINSON'S DISEASE AND SECONDARY PARKINSONISM No. 56 of 2016

Factors: 9. (*3) having an episode of acute cholinergic poisoning from exposure to an organophosphorus ester within the six weeks before the clinical worsening of Parkinson's disease or secondary parkinsonism;*

acute cholinergic poisoning means symptoms and signs due to the inhibition of acetylcholinesterase enzyme activity which occur within the 24 hours following exposure. These symptoms and signs are acute paralysis, overwhelming bronchial secretions, bradycardia, gastrointestinal distress, miosis, lacrimation or diarrhoea.

6.10 Summary of SoPs and firefighter chemicals in this extension review, combined with ARP1701

Based on both the ARP1701 report and this extension review, the occupation of firefighter is listed as a factor in only one SoP – mesothelioma. Smoke from fires is listed as a factor for bronchiectasis and chronic obstructive pulmonary disease, and smoke in an enclosed space is a factor in the SoP for fibrosing interstitial lung disease and malignant neoplasm of the lung. Inhalation of irritants is a factor for asthma, and exposure to irritants is a factor for conjunctivitis and irritant dermatitis.

Additionally, many of the contaminants listed in Appendix C of ARP1701, and in Attachments 2 and 3 of this extended review, are causal factors in a wide range of SoPs, but not in exposures experienced by firefighters. These contaminants include arsenic, benzene, carbon disulfide, cobalt, dioxins and furans, manganese, PAHs, vinyl chloride, and VOCs noted in ARP1701, and additional chemicals including aromatic amines, halogenated hydrocarbons, organo-chlorines and organo-phosphates.

Table 2: Tabulated summary of contaminants listed as factors, correlated with SoPs:

Factor	Statement of Principles (SoP)
Firefighting for a cumulative period of at least 1 000 hours before the clinical onset of mesothelioma, where the first exposure occurred at least 15 years before the clinical onset of mesothelioma.	MESOTHELIOMA No. 105 of 2015
Inhaling vapours, gases or fumes of a chemical agent including **smoke from fires**.	BRONCHIECTASIS No. 31 of 2017
Inhaling a respiratory tract irritant from the specified list including smoke from fires; inhaling smoke from the combustion of wood, charcoal, coal or other biomass or fossil fuel	CHRONIC OBSTRUCTIVE PULMONARY DISEASE No. 38 of 2014 and Amendment No. 129 of 2015
Inhalation of toxic gases or fumes including smoke	FIBROSING INTERSTITIAL LUNG DISEASE No. 54 of 2013
Inhaling smoke from the combustion of coal, wood, charcoal or another solid biomass fuel	MALIGNANT NEOPLASM OF THE LUNG No. 93 of 2014
Volatile organic compounds (VOC) as irritants in general	ASTHMA No. 61 of 2012 IRRITANT CONTACT DERMATITIS No. 111 of 2011 CONJUNCTIVITIS No. 2 of 2012
Volatile organic compounds (VOCs), in the form of benzene	ACUTE MYELOID LEUKAEMIA No 72 of 2015 APLASTIC ANAEMIA No. 51 of 2012 and Amendment No.32 of 2016 MYELODYSPLASTIC SYNDROME No. 74 of 2015
Volatile organic compounds (VOC) in the form of carbon disulfide and hexane	PERIPHERAL NEUROPATHY No. 75 of 2014
Volatile organic compounds (VOC) in the form of carbon disulfide	PARKINSON'S DISEASE AND SECONDARY PARKINSONISM No. 56 of 2016
Volatile organic compounds (VOC) in the form of vinyl chloride	MALIGNANT NEOPLASM OF THE LIVER No. 22 of 2011
Polycyclic aromatic hydrocarbons (PAH)	MALIGNANT NEOPLASM OF THE BLADDER No. 97 of 2011
Dioxins and furans	PERIPHERAL NEUROPATHY No. 75 of 2014 CHLORACNE No. 18 of 2012 MYELOMA No. 70 of 2012 – Amendment Statement of Principles concerning MYELOMA No. 73 of 2014 PORPHYRIA CUTANEA TARDA No. 44 of 2012 SOFT TISSUE SARCOMA No. 6 of 2015
Aromatic amines	MALIGNANT NEOPLASM OF THE BLADDER No. 97 of 2011
Halogenated hydrocarbons	CHLORACNE No. 18 of 2012
Organo-chlorines	EPILEPTIC SEIZURE No. 78 of 2013 NON-HODGKIN LYMPHOMA No. 91 of 2018

Factor	Statement of Principles (SoP)
Organo-phosphates	EPILEPTIC SEIZURE No. 78 of 2013 PARKINSON'S DISEASE AND SECONDARY PARKINSONISM No. 56 of 2016
Metals	
arsenic, beryllium, cadmium, chromium, nickel	MALIGNANT NEOPLASM OF THE LUNG No. 93 of 2014
arsenic	MALIGNANT NEOPLASM OF THE BLADDER No. 97 of 2011 MALIGNANT NEOPLASM OF THE RENAL PELVIS AND URETER No. 99 of 2011
cobalt	NON-MELANOTIC MALIGNANT NEOPLASM OF THE SKIN No. 8 of 2016
manganese	PERIPHERAL NEUROPATHY No. 75 of 2014 PARKINSON'S DISEASE AND SECONDARY PARKINSONISM No. 56 of 2016

7 LITERATURE REVIEW – ADDRESSING THE GAPS

7.1 Introduction

An additional literature review has been undertaken for this extension study to address the gaps in relation to the reported health effects arising from the contaminants identified in Attachments 2 and 3 that have not been listed specifically as factors in the SoPs. As in ARP1701, the resources of PubMed[3] were utilized in the literature search, and scientific publications were found by searching for "firefighters and exposures", "firefighters and health effects", and "firefighters and cancer", as in the preparation of ARP1701. The publications of most relevance to this review were those demonstrating probable causal relationships, and these have been summarised in the following sections.

7.2 Firefighter exposures

Abrand et al[1]: Firefighters have occupational exposure to toxic compounds during firefighting, and from surface contamination of equipment. This French study measured the surface load of benzo [a]pyrene (BaP), a carcinogenic polycyclic aromatic hydrocarbon, on the outer surface of fire jackets, personal protective equipment and tools used by firefighters after live fire training in a closed environment. The effectiveness of a standard jacket washing procedure on BaP contamination was assessed.

A single training session was responsible for a BaP deposit of 113.75 ± 45.03µg/m2 on exposed fire jacket material. After a single session, the deposit of BaP found on PPE and tools was measured on different surfaces ranged from 12 to 157 µg/m2. After multiple training sessions, a cumulative effect was suspected. The current PPE cleaning and maintenance procedures does not appear to reduce contamination effectively.

It was concluded that the estimated load of BaP on the outer surface of fire jackets could potentially have acute and chronic effects if absorbed by the firefighters.

Andersen et al[2]: Firefighting is regarded as possibly carcinogenic, although there are few mechanistic studies on genotoxicity in humans. The authors investigated exposure to polycyclic aromatic hydrocarbons (PAH), lung function, systemic inflammation and genotoxicity in peripheral blood mononuclear cells (PBMC) of 22 professional firefighters before and after a 24-h work shift.

Exposure was assessed by measurements of particulate matter (PM), PAH levels on skin, urinary 1-hydroxypyrene (1-OHP) and self-reported participation in fire extinguishing activities.

PM measurements indicated that use of personal protective equipment (PPE) effectively prevented inhalation exposure, but exposure to PM occurred when the environment was perceived as safe and the self-contained breathing apparatuses were removed. The level of PAH on skin and urinary 1-OHP concentration were similar before and after the work shift, irrespective of self-reported participation in fire extinction activities.

Post-shift, the subjects had reduced levels of oxidatively damaged DNA in PBMC, and increased plasma concentration of vascular cell adhesion molecule 1 (VCAM-1). The subjects reporting

participation in fire extinction activities during the work shift had a slightly decreased lung function, increased plasma concentration of VCAM-1, and reduced levels of oxidatively damaged DNA in PBMC.

It was concluded that the firefighters were not exposed to PM while using PPE, but exposure occurred when PPE was not used. The work shift was not associated with increased levels of genotoxicity. Increased levels of VCAM-1 in plasma were observed.

Fent et al[3]: In this study, the authors characterized the area and personal air concentrations of combustion byproducts produced during controlled residential fires with furnishings common in 21st century single family structures. Area air measurements were collected from the structure during active fire and overhaul (post suppression) and on the fireground where personnel were operating without any respiratory protection. Personal air measurements were collected from firefighters assigned to fire attack, victim search, overhaul, outside ventilation, and command/pump operator positions.

Two different fire attack tactics were conducted for the fires (6 interior and 6 transitional) and exposures were compared between the tactics. For each of the 12 fires, firefighters were paired up to conduct each job assignment, except for overhaul that was conducted by 4 firefighters.

Sampled compounds included polycyclic aromatic hydrocarbons (PAHs), volatile organic compounds (VOCs, e.g., benzene), hydrogen cyanide (HCN), and particulate (area air sampling only). Median personal air concentrations for the attack and search firefighters were generally well above applicable short-term occupational exposure limits, except for HCN measured from search firefighters. Area air concentrations of all measured compounds decreased after suppression.

Personal air concentrations of total PAHs and benzene measured from some overhaul firefighters exceeded exposure limits. Median personal air concentrations of HCN (16,300 ppb) exceeded the exposure limit for outside vent firefighters, with maximum levels (72,900 ppb) higher than the immediately dangerous to life and health (IDLH) level. Median air concentrations on the fireground (including particle count) were above background levels and highest when collected downwind of the structure and when ground-level smoke was the heaviest. No statistically significant differences in personal air concentrations were found between the 2 attack tactics.

It was concluded that the results supported the importance of wearing self-contained breathing apparatus when conducting overhaul or outside ventilation activities. Firefighters should also try to establish command upwind of the structure fire, and if this cannot be done, respiratory protection should be considered.

Stec et al[4]: This was the first UK study identifying firefighters exposure to PAH carcinogens. Wipe samples were collected from skin (jaw, neck, hands), personal protective equipment of firefighters, and work environment (offices, fire stations and engines) in two UK Fire and Rescue Service Stations.

Levels of 16 US Environmental Protection Agency (EPA) PAHs were quantified together with more potent carcinogens: 7,12-dimethylbenzo[a]anthracene, and 3-methylcholanthrene (3-MCA) (12 months post-initial testing).

Cancer slope factors, used to estimate cancer risk, indicate a markedly elevated risk. PAH carcinogens including benzo[a]pyrene (B[a]P), 3-MCA, and 7,12-dimethylbenz[a]anthracene PAHs

were determined on body surfaces (e.g., hands, throat), on PPE including helmets and clothing, and on work surfaces. The main exposure route appeared to be via skin absorption.

The authors concluded that their results suggested an urgent need to monitor exposures to firefighters in their occupational setting and conduct long-term follow-up regarding their health status.

Wingfors et al[5]: These authors stated that over the past 10 years, a number of safety measures for reducing firefighters' exposure to combustion particles have been introduced in Sweden. The most important measure was the reduction in the time firefighters wore suits and handled contaminated equipment after turn-outs involving smoke exposure. Their study was divided into two parts: one being to investigate the level of protection obtained by multiple garment layers, and the other to assess exposure during a standardized smoke diving exercise.

Realistic work protection factors (WPFs) were calculated by comparing air concentrations of the full suite of gaseous and particle-bound polycyclic aromatic hydrocarbons (PAHs) inside and outside structural ensembles, including jacket and thick base layer, during a tough fire extinguishing exercise using wood as the fuel.

Then, during a standardized firefighting exercise, exposure was assessed by measuring PAH skin deposition and levels of eight urinary PAH metabolites in 20 volunteer student firefighters before and after the exercise.

The average WPF for the sum of 22 PAHs was 146 ± 33 suggesting a relatively high protective capacity, but also indicating a substantial enrichment of contaminants with a risk of prolonged dermal exposure. Accordingly, in the second exercise, the median levels of skin-deposited Σ14-PAHs and urinary 1-hydroxypyrene significantly increased 5-fold (21 to 99 ng/wipe) and 8-fold (0.14 to 1.1 µmol mol-1 creatinine), respectively, post exposure.

Among the PAH metabolites investigated, 1-hydroxypyrene proved to be the most useful indicator of exposure, with significantly elevated urinary levels at both 6 h and 20 h after the exercise and with the strongest correlation to dermal exposure. Metabolites from two-ring PAH met the detection criteria.

The authors concluded that their results from correlation studies indicated that dermal uptake was a major route of exposure, and in accordance with previous findings. They also concluded that some of the newly adopted protective measures were correctly implemented and should continue to be followed and be more widely adopted.

Keir et al[6]: In this study, exposure to combustion emissions were examined in Ottawa Fire Service (OFS) firefighters. Paired urine and dermal wipe samples (i.e., pre- and post-event), personal air samples, and fire event questionnaires were collected from 27 male OFS firefighters. A total of 18 OFS office workers were used as additional controls.

Exposures to polycyclic aromatic hydrocarbons (PAHs) and other organic mutagens were assessed by quantification of urinary PAH metabolite levels, levels of PAHs in dermal wipes and personal air samples, and urinary mutagenicity using the Salmonella mutagenicity assay (Ames test). Urinary Clara Cell 16 (CC16) and 15-isoprostane F_{2t} (8-iso-$PGF_{2\alpha}$) levels were used to assess lung injury and overall oxidative stress, respectively.

The authors found significant 2.9- to 5.3-fold increases in average post-event levels of urinary PAH metabolites, depending on the PAH metabolite ($p < 0.0001$). Average post-event levels of urinary

mutagenicity showed a significant, event-related 4.3-fold increase ($p < 0.0001$). Urinary CC16 and 8-iso-$PGF_{2\alpha}$ did not increase. PAH concentrations in personal air and on skin accounted for 54% of the variation in fold changes of urinary PAH metabolites ($p < 0.002$).

It was concluded that emergency on-shift fire suppression was associated with significantly elevated exposures to combustion emissions.

7.2.1 Summary of firefighters' exposures

In summary, these studies on exposures, together with those cited in ARP1701, support the assumption that the contaminants found at the site of ADF firefighter training at Point Cook could have been present in the smoke to which the firefighters were exposed, and that such smoke exposures were toxic.

7.3 Firefighters and respiratory dysfunction

Slattery et al[7]: The authors of this study stated that, despite the known occupational hazards, it was not yet clear whether long-term career firefighting lead to a greater rate of decline in lung function than would normally be expected; and whether any rate of change was affected by firefighting exposures and other risk/protective factors.

A systematic search of online electronic databases was conducted to identify longitudinal studies reporting on the rate of change in the forced expiratory volume in one second (FEV_1) and forced vital capacity (FVC). Included studies were critically appraised to determine their risk of bias using the Research Triangle Institute Item Bank (RTI-IB) on Risk of Bias and Precision of Observational Studies.

Twenty-two studies were identified for inclusion, from four different countries, published between 1974 and 2016. Examined separately, studies were categorised by the type of firefighting exposure. Firefighters experienced variable rates of decline in lung function, which were particularly influenced by cigarette smoking. The influence of routine firefighting exposures was unclear and limited by the methods of measurement; but firefighters exposed to 'non-routine' severe exposures unanimously experienced accelerated declines.

Overall, the data provided an unclear picture of how the rate of change in lung function of firefighters related to routine exposures and how it compared to the rate of change expected in a working-age population. Non-smoking firefighters who routinely wore respiratory protection were more likely to have a normal rate of decline in lung function.

Exposure to catastrophic events significantly increased the rate of decline in firefighter lung function.

Gianniou et al[8]: This study was to assess the respiratory health, and airway and systemic inflammation, in professional forest firefighters after firefighting activities.

A total of 60 firefighters who participated in forest firefighting operations in Greece during 2008 were included in the study. Symptoms and exposure, pulmonary function, atopy, bronchial hyperresponsiveness, and markers of inflammation in induced sputum, serum, and bronchoalveolar lavage (BAL) fluid were assessed.

The authors reported that measurable eosinophilic and neutrophilic inflammation were induced in the bronchial airways after acute exposure during forest firefighting. This was associated with increased respiratory symptoms from the upper and lower respiratory tract, and pulmonary function impairment. Additionally, a measurable systemic inflammatory response was demonstrated.

The study showed that acute exposure during forest firefighting significantly augmented the intensity of airway and systemic inflammation in relation to the baseline inflammatory background due to chronic exposure.

It was concluded that the repeated acute exposures during firefighting, by increasing the burden of chronic airway and systemic inflammation, could lead to allergic sensitization of the airways and increased incidence of rhinitis and asthma after prolonged exposure.

Witt et al[9]: The authors stated that firefighters are exposed to toxic combustion products generated in fires, with the most frequent and the most toxic being: carbon monoxide, hydrogen cyanide, ammonia, and those resulting from PVC combustion - hydrochloride, phosgene and chloride. Additionally, fire-extinguisher powder can be inhaled. The aim of their study was to ascertain the influence of toxic agents present at the scene of fire on the lung tissue of firefighters, and also to study this on an animal model.

The study group consisted of firefighters who had a minimum of 10 years' service. After completing a questionnaire, their clinical status was ascertained based on a general examination, laboratory tests and lung function tests.

Questionnaire analysis showed a high percentage of pathological symptoms in the studied group. The incidence of the symptoms correlated with the duration of occupational exposure to toxic agents. Among other results, obstruction of flow in medium airways in about 30% of the studied individuals represented the most important finding.

Experimental tests were performed on male Wistar rats, aged 3 months. They were insufflated with the solution of powdered fire-extinguisher, after which morphology specimens of lung tissue were studied. Evidence for disseminated fibrosis was obtained, which supported the previous clinical findings in the firefighters.

It was concluded that the study demonstrated a correlation between occupational exposure and respiratory system involvement in firefighters. The authors recommended that firefighters should receive special medical care focused on prophylaxis, early detection and therapy for pulmonary diseases.

7.3.1 Summary of effects on firefighters' respiratory dysfunction

In summary, the above studies, and those previously cited in ARP1701, support the SoPs for bronchiectasis, chronic obstructive pulmonary disease, fibrosing interstitial lung disease, and asthma which all list smoke, in various exposures, as a causal factor. There were no publications providing probable causal links between firefighters and other non-cancer long-term health outcomes.

7.4 Firefighters and cancer

Muegge et al[10]: In this US study, the authors examined the odds of cancer and cardiovascular mortality of firefighters relative to a matched group of non-firefighters from the general population. Firefighter death records were matched to four non-firefighter death records on age at time of death, sex, race, ethnicity, and year of death. Exact odds ratios, 95% confidence intervals, and P-values were calculated using conditional logistic regression to compare groups.

The odds of death due to malignant cancers was significantly higher for firefighters than non-firefighters (OR: 1.19; 95%CI 1.08, 1.30). There was no difference in the odds of death for cardiovascular diseases, including ischemic heart disease, between the two groups.

The study concluded that there was a need for early and effective cancer prevention strategies among firefighters, including worksite health promotion programs and incumbent physical activity evaluation.

Kullberg et al[11]: These authors stated that previous studies on firefighters indicated an increased risk of cancer, although findings regarding which cancer sites were in excess have been inconsistent. The aim of their study was to investigate the cancer incidence among Swedish firefighters.

This updated cohort study included 1,080 men who worked at least 1 year as a firefighter in the city of Stockholm, Sweden during 1931-1983. First-time diagnoses of cancer were identified through the Swedish Cancer Registry from 1958 until 2012. Employment as a firefighter was determined from the annual fire station enrolment records. Standardized incidence ratios were calculated using the Stockholm population as reference.

Their results indicated that firefighters in Stockholm had a low overall risk of cancer (SIR = 0.81 95% CI 0.71-0.91). However, firefighters were at an increased risk of stomach cancer (SIR = 1.89 95% CI 1.25-2.75). Firefighters had significantly low risks for prostate cancer (SIR = 0.68 95% CI 0.52-0.87) and malignant melanoma of the skin (SIR = 0.30 95% CI 0.06-0.88).

There was a statistically significant trend of increasing overall risk of cancer with increasing employment duration.

It was concluded that Stockholm firefighters had an increased risk of stomach cancer but a low overall risk of cancer. The trend of increasing overall risk of cancer with increasing employment duration could potentially be related to the carcinogenic exposures at work.

7.4.1 Summary of firefighters' cancer risk

In summary, the above publications, and those cited in ARP1701, support the view that, on the balance of probabilities, exposures experienced by firefighters contribute materially to the subsequent development of cancers in general and to some specific malignancies: cancers of the bladder, brain, colon, kidney, lung, prostate, stomach and testes; and leukaemia, multiple myeloma, and non-Hodgkin's lymphoma.

7.5 References

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8 CONCLUSIONS

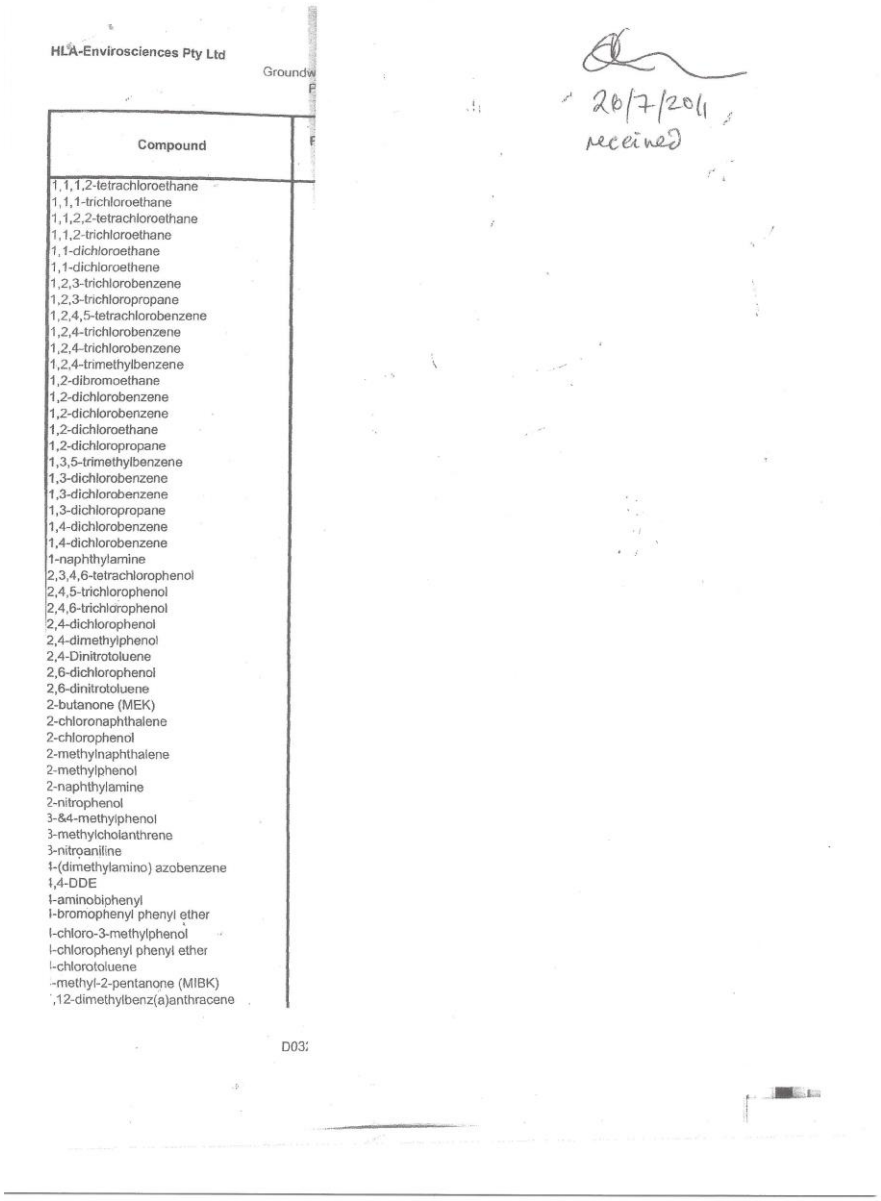
Overall, this Firefighter Chemical Review Extension and ARP1701, together with reviews of the SoPs and the relevant literature, concludes that **"firefighting"**, as in the current SoP for mesothelioma, should be considered as a factor in other SoPs as indicated in the following Table 3:

Table 3: Firefighter exposures as a factor in future SoPs

Factor	Statement of Principles (SoP)
Firefighting for a cumulative period before the clinical onset of the condition, where the first exposure occurred before the clinical onset of the condition	Acute myeloid leukaemia Adenocarcinoma of the kidney Aplastic anaemia Asthma Bronchiectasis Chloracne Chronic obstructive pulmonary disease Conjunctivitis Epileptic Seizure Fibrosing interstitial lung disease Irritant contact dermatitis Malignant neoplasm of the bladder Malignant neoplasm of the brain Malignant neoplasm of the colorectum Malignant neoplasm of the liver Malignant neoplasm of the lung Malignant neoplasm of the prostate Malignant neoplasm of the renal pelvis and ureter Malignant neoplasm of the testis Mesothelioma Myelodysplastic syndrome Myeloma Non-Hodgkin's lymphoma Non-melanotic malignant neoplasm of the skin Parkinson's disease and secondary parkinsonism Peripheral neuropathy Porphyria cutanea tarda Soft tissue sarcoma

9 ATTACHMENTS

9.1 Attachment 1 – List of chemicals supplied by Firefighters



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Groundw

F

20/7/2011
received

Compound	F
1,1,1,2-tetrachloroethane	
1,1,1-trichloroethane	
1,1,2,2-tetrachloroethane	
1,1,2-trichloroethane	
1,1-dichloroethane	
1,1-dichloroethene	
1,2,3-trichlorobenzene	
1,2,3-trichloropropane	
1,2,4,5-tetrachlorobenzene	
1,2,4-trichlorobenzene	
1,2,4-trichlorobenzene	
1,2,4-trimethylbenzene	
1,2-dibromoethane	
1,2-dichlorobenzene	
1,2-dichlorobenzene	
1,2-dichloroethane	
1,2-dichloropropane	
1,3,5-trimethylbenzene	
1,3-dichlorobenzene	
1,3-dichlorobenzene	
1,3-dichloropropane	
1,4-dichlorobenzene	
1,4-dichlorobenzene	
1-naphthylamine	
2,3,4,6-tetrachlorophenol	
2,4,5-trichlorophenol	
2,4,6-trichlorophenol	
2,4-dichlorophenol	
2,4-dimethylphenol	
2,4-Dinitrotoluene	
2,6-dichlorophenol	
2,6-dinitrotoluene	
2-butanone (MEK)	
2-chloronaphthalene	
2-chlorophenol	
2-methylnaphthalene	
2-methylphenol	
2-naphthylamine	
2-nitrophenol	
3-&4-methylphenol	
3-methylcholanthrene	
3-nitroaniline	
4-(dimethylamino) azobenzene	
4,4-DDE	
4-aminobiphenyl	
4-bromophenyl phenyl ether	
4-chloro-3-methylphenol	
4-chlorophenyl phenyl ether	
4-chlorotoluene	
4-methyl-2-pentanone (MIBK)	
7,12-dimethylbenz(a)anthracene	

D03

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Groundwa
Po

Compound	Pa
a-BHC	
Acenaphthene	
Acenaphthylene	
Acetophenone	
Aldrin	
Aniline	
Anthracene	
b-BHC	
Benz(a)anthracene	
Benzene	
Benzo(a) pyrene	
Benzo(g,h,i)perylene	
Bis(2-chloroethoxy) methane	
Bis(2-chloroisopropyl) ether	
Bis(2-ethylhexyl) phthalate	
Bromobenzene	
Bromodichloromethane	
Bromoform	
Bromomethane	
Butyl benzyl phthalate	
Carbon disulfide	
Carbon tetrachloride	
Chlorobenzene	
Chlorodibromomethane	
Chloroethane	
Chloroform	
Chloromethane	
Chrysene	
cis-1,2-dichloroethene	
cis-1,3-dichloropropene	
d-BHC	
DDD	
DDT	
Dibenz(a,h)anthracene	
Dibenzofuran	
Dibromomethane	
Dichlorodifluoromethane	<
Dieldrin	<
Diethylphthalate	<
Dimethyl phthalate	<
Di-n-butyl phthalate	<
Di-n-octyl phthalate	<
Diphenylamine	<
Endosulfan I	<
Endosulfan II	<
Endosulfan sulphate	<
Endrin	<
Endrin aldehyde	<
Endrin ketone	<

D032912_

[redacted]

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Groundv

Compound
Ethylbenzene
Fluoranthene
Fluorene
g-BHC (Lindane)
Heptachlor
Heptachlor epoxide
Hexachlorobenzene
Hexachlorobutadiene
Hexachlorobutadiene
Hexachlorocyclopentadiene
Hexachloroethane
Indeno(1,2,3-c,d)pyrene
Isopropylbenzene
Methoxychlor
Naphthalene
Naphthalene
Nitrobenzene
N-nitrosodi-n-butylamine
N-nitrosodi-n-propylamine
N-nitrosopiperidine
Pentachlorobenzene
Pentachloronitrobenzene
Pentachlorophenol
Phenanthrene
Phenol
Pyrene
Styrene
TCE
Tetrachloroethene
Toluene
TPH C 6 - C 9 Fraction
TPH C10 - C14 Fraction
TPH C15-C28 Fraction
TPH C29-C36 Fraction
trans-1,2-dichloroethene
trans-1,3-dichloropropene
Trichlorofluoromethane
Vinyl acetate
Vinyl chloride

9.2 Attachment 2 - List of chemicals requested for review – excluding those reviewed in ARP1701

Chemical Name	Comments
1,1,1,2-tetrachloroethane **VOC** Irritant to skin, eyes, URT and CNS. IARC: Group 3 – Not classifiable as to its carcinogenicity to humans.	**PubChem:** Clear colorless liquid. 1,1,1,2-tetrachloroethane is a member of chloroethanes. Exposure Routes: inhalation, ingestion, skin and/or eye contact. Symptoms: Irritation eyes, skin; lassitude (weakness, exhaustion), restlessness, irregular respiration, muscle incoordination. Target Organs: Eyes, skin, central nervous system, liver. **OSHA:** Possible human carcinogen. Basis for classification: Increased incidence of combined hepatocellular adenomas and carcinomas in female mice; inadequate evidence from human studies. human carcinogenicity data: Inadequate. Animal carcinogenicity data: Limited. Classification based on EPA guidelines. **IARC:** 1,1,1,2-Tetrachloroethane is not classifiable as to its carcinogenicity to humans (Group 3).
1,2,3-trichlorobenzene **VOC** Few data on human toxicity. Liver toxin in experimental animals. Not classified by IARC.	**ATSDR**: Trichlorobenzenes have been used as solvents. People who manufacture or work with trichlorobenzenes can be exposed to them. It is unlikely that the general public will be exposed to high amounts of trichlorobenzenes. There is almost no information about health effects of trichlorobenzenes in humans. Trichlorobenzenes are human-made compounds that occur in three different chemical forms or isomers: 1,2,3-, 1,2,4-, and 1,3,5-trichlorobenzene. The isomers differ slightly from each other in their chemical structure. 1,2,3-Trichlorobenzene and 1,3,5-trichlorobenzene are colorless solids, while 1,2,4 trichlorobenzene is a colorless liquid. Trichlorobenzenes have primarily been used as solvents and chemical intermediates to produce other compounds. 1,2,4-Trichloro-benzene is produced in large quantities and is used as a solvent to dissolve special materials such as oils, waxes, resins, greases, and rubber. It is also frequently used to produce dyes and textiles. 1,2,3-Trichlorobenzene and 1,3,5 trichlorobenzene are produced in lower quantities and have fewer uses. There is virtually no information regarding health effects of trichlorobenzenes in humans. However, based on results from studies in animals, it is reasonable to predict that humans exposed to high amounts of trichlorobenzenes may develop liver problems. Studies in animals indicate that oral administration of trichlorobenzenes for short or long periods produces mainly alterations in the liver and kidneys. Long term administration of 1,2,4-trichlorobenzene to rats did not affect their capacity

Chemical Name	Comments
	to have normal offspring. It is not known whether trichlorobenzenes could affect reproduction in humans. There are no studies of cancer in people exposed to trichlorobenzenes. Mice given 1,2,4-trichlorobenzene in the food for 2 years developed cancer of the liver. The EPA has stated that 1,2,4-trichlorobenzene is not classifiable as to human carcinogenicity. **OSHA**: Not listed as carcinogenic. **IARC:** Not classified.
1,2,3-trichloropropane **VOC** Irritant to skin, eyes, URT and CNS. Liver and kidney toxin in experimental animals. IARC: Group 2A – Probably carcinogenic to humans.	**ATSDR:** 1,2,3-Trichloropropane is a synthetic chemical that is also known as allyl trichloride, glycerol trichlorohydrin, and trichlorohydrin. It is a colorless, heavy liquid with a sweet but strong odour. It evaporates very quickly and small amounts dissolve in water. It is mainly used to make other chemicals. Some of it is also used as an industrial solvent, paint and varnish remover, and cleaning and degreasing agent. Very little information is available on the amounts manufactured and the specific uses. Exposure to 1,2,3-trichloropropane may occur from drinking water or from breathing air that is contaminated. This is most likely to occur near facilities that produce the chemical or near hazardous waste sites. People who are exposed to 1,2,3-trichloropropane can have eye and throat irritation. People exposed to 100 parts of 1,2,3-trichloropropane per million parts of air (ppm) felt irritation, and some people exposed to 50 ppm for an 8-hour workday also had throat and eye irritation. Rats and mice died after breathing air containing 1,2,3-trichloropropane at levels higher than in the environment. When rats breathed it at levels lower than those that irritated humans, they developed eye, nose, and lung irritation, and liver and kidney disease. The main health effect in both animals and people is damage to the respiratory system. When rats swallowed 1,2,3-trichloropropane at high levels, they died from liver and kidney damage. When exposed to moderate levels that did not cause death, the rats had minor liver and kidney damage, blood disorders, and stomach irritation. When it was applied to the skin of rabbits, it caused severe irritation followed by injury to internal organs. **OSHA:** Listed by OSHA as a carcinogen. **IARC:** There is inadequate evidence in humans for the carcinogenicity of 1,2,3-trichloropropane. There is sufficient

Chemical Name	Comments
	evidence in experimental animals for the carcinogenicity of 1,2,3-trichloropropane. 1,2,3-trichloropropane is probably carcinogenic to humans (Group 2A). In making the overall evaluation, the Working Group took into account the following evidence: (i) 1,2,3- trichloropropane causes tumours at multiple sites and at high incidence in mice and rats. (ii) The metabolism of 1,2,3-trichloropropane is qualitatively similar in human and rodent microsomes. (iii) 1,2,3- Trichloropropane is mutagenic to bacteria and to cultured mammalian cells and binds to DNA of animals treated in vivo.
1,2,4,5-tetrachlorobenzene **VOC** Irritant to skin, eyes, URT and CNS. Not classified by IARC.	**PubChem:** Symptoms of exposure to this compound may include irritation of the skin, eyes, mucous membranes and upper respiratory tract. It is harmful by inhalation, ingestion or skin absorption. It is an irritant of the skin, eyes, mucous membranes and upper respiratory tract. When heated to decomposition it emits highly toxic fumes. **OSHA:** Not listed as a carcinogen. **IARC:** Not classified.
1,2-dibromoethane **Halogenated hydrocarbon** Few data on human toxicity by inhalation, but toxic and corrosive by ingestion. IARC: Group 2A – Probably carcinogenic to humans.	**ATSDR:** 1,2-dibromoethane is a manufactured chemical. It also occurs naturally in small amounts in the ocean where it is formed, probably by algae and kelp. It is a colorless liquid with a mild, sweet odour. Other names for 1,2-dibromoethane are ethylene dibromide, EDB, and glycol bromide. 1,2-dibromoethane has been used as a pesticide in soil, and on citrus, vegetable, and grain crops. Most of these uses have been stopped by the Environmental Protection Agency (EPA) since 1984. Another major use was as an additive in leaded gasoline; however, since leaded gasoline is now banned, it is no longer used for this purpose. Uses today include treatment of logs for termites and beetles, control of moths in beehives, and as a preparation for dyes and waxes. Redness and inflammation, including skin blisters and mouth and stomach ulcers, can occur if large amounts are swallowed. One accidental swallowing caused death in a woman. It is highly unlikely that there would be a risk of death to people from low-level exposure. Although very little is known about the effects from breathing 1,2-dibromoethane over a long period of time, some male workers had reproductive effects including damage to their sperm. No other long-term effects are known in people.

Chemical Name	Comments
	In rats, death occurred from breathing high levels for a short time. Lower levels caused liver and kidney damage. When rats breathed air or ate food containing 1,2-dibromoethane for short or long periods of time, they were less fertile or had abnormal sperm. Changes in the brain and behaviour were also seen in young rats whose male parents had breathed 1,2-dibromoethane, and birth defects were observed in the young of animals that were exposed while pregnant. 1,2-dibromoethane is not known to cause birth defects in people. The Department of Health and Human Services has determined that 1,2-dibromoethane may reasonably be anticipated to be a carcinogen. There are no reports of cancer in workers or other people exposed to 1,2-dibromoethane for several years. However, rats and mice that breathed, swallowed, or touched it for long periods had cancer in many organs. **OSHA:** Not listed as a carcinogen. **IARC:** There is inadequate evidence in humans for the carcinogenicity of ethylene dibromide (1,2-dibromethane). There is sufficient evidence in experimental animals for the carcinogenicity of ethylene dibromide. Ethylene dibromide is probably carcinogenic to humans (Group 2A). In making the overall evaluation, the Working Group took into consideration that ethylene dibromide is genotoxic in a broad range of in-vitro and in-vivo assays and binds covalently with DNA in vivo.
1-naphthylamine **Aromatic amine** Irritant to skin, eyes and URT. Toxic by inhalation causing methaemoglobinaemia. IARC: Group 3 – Not classifiable as to its carcinogenicity to humans.	**PubChem:** 1-naphthylamine is a crystalline solid or a solid dissolved in a liquid. It is Insoluble in water and denser than water. Contact may slightly irritate skin, eyes and mucous membranes. May be slightly toxic by ingestion. It is used to make other chemicals. Inhalation may cause cyanosis resulting in blueness of lips and under finger nails. Contact with liquid causes local irritation of eyes. Neither ingestion nor contact with skin produces any recognized immediate effects. **OSHA:** Listed as a carcinogen. **IARC:** 1-Naphthylamine is not classifiable as to its carcinogenicity to humans (Group 3).
2,3,4,6-tetrachlorophenol	**ATSDR:** Chlorophenols are a group of chemicals in which chlorines (between one and five) have been added to phenol.

Chemical Name	Comments
Chlorinated phenolic Irritant to skin, eyes and URT. Symptoms of phenolic poisoning from inhalation and skin absorption. IARC: Group 2B – Possibly carcinogenic to humans.	Phenol is an aromatic compound derived from benzene, the simplest aromatic hydrocarbon, by adding a hydroxy group to a carbon to replace a hydrogen. There are five basic types of chlorophenols: mono[one]chlorophenols, di[two]chlorophenols, tri[three]chlorophenols, tetra[four]chlorophenols, and penta[five]chlorophenols. In all, there are 19 different chlorophenols. Eight are discussed by ATSDR in this review: 2-chlorophenol, 4-chlorophenol, 2,4-dichlorophenol, 2,4,5-trichlorophenol, 2,4,6- trichlorophenol, 2,3,4,5-tetrachlorophenol, 2,3,4,6- tetrachlorophenol, and 2,3,5,6-tetrachlorophenol. Except for 2-chlorophenol, which is a liquid at room temperature, all of the chlorophenols are solids. The chlorophenols have a strong medicinal taste and odour; small amounts (at parts per billion [ppb] to parts per million [ppm] concentrations) can be tasted in water. Very small amounts of chlorophenols can also make fish taste bad. All the compounds discussed are, or were, produced commercially. Chlorophenols with at least two chlorines either have been used directly as pesticides or converted into pesticides. Also, chlorophenols, especially 4- chlorophenol, have been used as antiseptics. In addition to being produced commercially, small amounts of some chlorophenols, especially the mono- and dichlorophenols, may be produced when waste water or drinking water is disinfected with chlorine, if certain contaminants are present in the raw water. They are also produced during the bleaching of wood pulp with chlorine when paper is being produced. Symptoms of exposure to these compounds may include irritation of the skin, eyes, nose, and pharynx; conjunctivitis, corneal injuries, and dermatitis with repeated skin contact. Symptoms of exposure to phenols (through ingestion or contact with the skin or mucous membranes) may include painless blanching or erythema, possible corrosion, profuse sweating, intense thirst, nausea and vomiting, diarrhea, cyanosis from methemoglobinemia, hyperactivity; stupor; blood pressure fall; hyperpnea; abdominal pain; haemolysis; convulsions; coma; and pulmonary edema followed by pneumonia. If death from respiratory failure is not immediate, jaundice and oliguria or anuria may occur. Skin sensitivity occasionally occurs. These compounds are toxic by ingestion and inhalation. When heated to decomposition they emit toxic fumes of chloride. **OSHA:** Chlorophenols, including dichlorophenols, are not listed as carcinogens.

Chemical Name	Comments
	IARC: There is limited evidence in humans for the carcinogenicity of combined exposures to polychlorophenols, including dichlorophenols, or to their sodium salts. There is evidence suggesting lack of carcinogenicity of 2,4-dichlorophenol in experimental animals. There is inadequate evidence in experimental animals for the carcinogenicity of 2,4,5-trichlorophenol. There is limited evidence in experimental animals for the carcinogenicity of 2,4,6 trichlorophenol. There is sufficient evidence in experimental animals for the carcinogenicity of pentachlorophenol. Overall evaluation: Combined exposures to polychlorophenols or to their sodium salts are possibly carcinogenic to humans (Group 2B).
2,4,5-trichlorophenol	See above, for the toxicity of 2,4,5-trichlorphenol is similar to that of all the polychlorophenols.
2,4,6-trichlorophenol	See above, for the toxicity of 2,4,6-trichlorphenol is similar to that of all the polychlorophenols.
2,4-dichlorophenol	See above, for the toxicity of 2,4-dichlorphenol is similar to that of all the polychlorophenols.
2,4-dimethylphenol **Phenolic** Irritant and corrosive to skin, eyes, URT and CNS. Highly toxic by inhalation, ingestion and skin absorption causing phenolic poisoning. Not classified by IARC.	**PubChem:** 2,4-dimethylphenol is a colorless crystal or clear, dark amber liquid. Symptoms of exposure to this compound may include severe irritation of the skin and eyes, dizziness, stomach pain, exhaustion and damage to the liver and kidneys. Other symptoms include headache, nausea and vomiting. It may cause severe burns of the eyes and skin, irritation of the respiratory tract and coma. It may also cause corrosion of tissue of the mucous membranes and upper respiratory tract, eyes and skin. Inhalation may result in burning sensation, coughing, wheezing, laryngitis and short ness of breath. Inhalation may be fatal as a result of spasm, inflammation and edema of the larynx and bronchi, chemical pneumonitis and pulmonary edema. Symptoms of exposure to this class of compounds include profuse sweating, skin sensitization, painless blanching or erythema of the skin, intense thirst diarrhea, cyanosis from methemoglobinemia, hyperactivity, stupor, fall in blood pressure, hyperpnea, abdominal pain, haemolysis and convulsions. If death from respiratory failure is not immediate, jaundice and oliguria or anuria may occur. This compound is highly toxic by ingestion, inhalation or skin absorption. It is a severe irritant of the skin and eyes. It is corrosive to the skin, eyes, mucous membranes and upper respiratory tract. When heated to decomposition it emits acrid

Chemical Name	Comments
	smoke, irritating fumes and toxic fumes of carbon monoxide and carbon dioxide. **OSHA:** Not listed as a carcinogen. **IARC:** Not classified.
2,4-dinitrotoluene **DNT** Toxic by inhalation causing lung damage in humans and experimental animals. IARC: Group 2B – Possibly carcinogenic to humans.	**ATSDR:** There are six forms of dinitrotoluenes (DNTs) which are called isomers. The names of the six isomers are 2,3-DNT, 2,4-DNT, 2,5-DNT, 2,6-DNT, 3,4-DNT, and 3,5-DNT. DNTs are not found naturally in the environment and are manufactured. DNTs are typically found as a mixture of two isomers: 2,4-DNT and 2,6-DNT. The other isomers (2,3-, 2,5-, 3,4-, and 3,5-DNT) are found in small amounts in this mixture. DNTs are primarily used as a chemical intermediate for the production of toluene diisocyanate. They are also used in the production of trinitrotoluene (TNT), dyes, and polyurethane foams. A study of workers reported a relationship between heart disease and long-term exposure to DNTs. Animal studies have shown that breathing DNTs can damage the lungs. Animal studies have also shown that ingesting DNTs during brief or long periods can cause anemia and damage to the nervous system, male reproductive system, and liver. Studies of workers have not shown conclusively that DNTs cause cancer. However, some studies of workers have found increased risk of kidney and bladder cancer associated with exposure to DNTs. Laboratory animals ingesting DNTs during most of their lives developed cancer of the liver and tumours in the kidneys. The EPA has classified the mixture of 2,4- and 2,6-DNT as a probable human carcinogen. **OSHA:** 2,4-dinitrotoluene is listed as a carcinogen. **IARC**: There is inadequate evidence in humans for the carcinogenicity of 2,4-, 2,6- and 3,5-dinitrotoluenes. There is sufficient evidence in experimental animals for the carcinogenicity of 2,4-dinitrotoluene and 2,6-dinitrotoluene. There is inadequate evidence in experimental animals for the carcinogenicity of 3,5-dinitrotoluene. Overall evaluation: 2,4- and 2,6-dinitrotoluenes are possibly carcinogenic to humans (Group 2B). 3,5-dinitrotoluene is not classifiable as to its carcinogenicity to humans (Group 3).

Chemical Name	Comments
2,6-dichlorophenol	See above as reviewed under 2,3,4,6-tetrachlorophenol, for the toxicity of 2,6-dichlorphenol is similar to that of all the polychlorophenols
2,6-dinitrotoluene	See above as reviewed under 2,4-dinitrotoluene, for the toxicity is similar.
2-butanone (MEK) **VOC** Irritant to skin, eyes, URT and CNS. Not classified by IARC.	**ATSDR:** 2-butanone is a manufactured chemical, but it is also present in the environment from natural sources. It is a colorless liquid with a sharp, sweet odour. It is also known as methyl ethyl ketone (MEK). 2-butanone is produced in large quantities. Nearly half of its use is in paints and other coatings because it will quickly evaporate into the air and it dissolves many substances. It is also used in glues and as a cleaning agent. 2-butanone occurs as a natural product. It is made by some trees and found in some fruits and vegetables in small amounts. It is also released to the air from car and truck exhausts. The known health effects to people from exposure to 2-butanone are irritation of the nose, throat, skin, and eyes. If 2-butanone is breathed along with other chemicals that damage health, it can increase the amount of damage that occurs. Serious health effects in animals have been seen only at very high levels. When breathed, these effects included birth defects, loss of consciousness, and death. When swallowed, rats had nervous system effects including drooping eyelids and uncoordinated muscle movements. There was no damage to the ability to reproduce. Mice who breathed low levels for a short time showed temporary behavioural effects. Mild kidney damage was seen in animals that drank water with lower levels of 2-butanone for a short time. There are no long-term studies with animals either breathing or drinking 2-butanone. The Department of Health and Human Services has not classified 2-butanone as to its human carcinogenicity. **OSHA:** Not listed as a carcinogen. **IARC:** Not classified.
2-chloronaphthalene **Chlorinated hydrocarbon** Irritant to skin, eyes and URT; repeated exposure causes chloracne and liver damage.	**PubChem:** 2-chloronaphthalene occurs as an off-white crystalline powder. Symptoms of chronic exposure to this class of compounds include chloracne, cysts, headache, fatigue, vertigo, anorexia and jaundice. It is a strong irritant. It may be absorbed through the skin. When heated to decomposition it emits toxic fumes of chlorides.

Chemical Name	Comments
Not classified by IARC.	**OSHA:** Not listed as a carcinogen. **IARC:** Not classified.
2-chlorophenol **Chlorinated phenolic** Toxic by inhalation causing chloracne and liver damage. Not classified by IARC.	**ATSDR:** Chlorophenols are a group of chemicals that are produced by adding chlorines to phenol. Phenol is an aromatic compound derived from benzene. There are 5 basic types of chlorophenols and 19 different chlorophenols. Most chlorophenols are solid at room temperature. They have a strong, medicinal taste and smell. Small amounts can be tasted in water. Some chlorophenols are used as pesticides. Others are used in antiseptics. Small amounts are produced when water is disinfected with chlorine. They are also produced while bleaching wood pulp with chlorine to make paper. Workers exposed to pesticides that contain chlorophenols have developed acne and mild injury to their livers. In laboratory studies, animals that received high levels of chlorophenols in food or water developed liver and immune system effects. They did not gain as much weight as animals not fed the compounds. Chlorophenols have not been shown to cause birth defects in animals. **OSHA:** Not listed as a carcinogen. **IARC:** Not classified.
2-methylphenol **(o-cresol)** **Cresol** Irritant and corrosive by inhalation and ingestion. Not classified by IARC.	**ATSDR:** 2-methylphenol is also known as o-cresol. Cresols are a widely occurring natural and manufactured group of chemicals. In their pure form, they are colorless solids and may be liquids if they are mixtures. Cresols smell like medicine. There are three forms of cresols that differ slightly in their chemical structure: ortho-cresol (o-cresol or 2-methylphenol), meta-cresol (m-cresol or 3-methylphenol), and para-cresol (p-cresol or 4-methylphenol). These forms occur separately or as a mixture. Cresols are used to dissolve other chemicals, as disinfectants and deodorizers, and to make other chemicals. Cresols may be formed normally in the body from other compounds. Cresols are found in many foods and in wood and tobacco smoke, crude oil, coal tar, and in chemical mixtures used as wood preservatives. Small organisms in soil and water produce cresols when they break down materials in the environment. Most of the cresols that are ingested will enter the blood stream, but less will enter the blood if there is contact with the skin.

Chemical Name	Comments
	Most exposures to cresols are at very low levels that are not harmful, but cresols breathed, ingested, or applied to the skin at very high levels, can be very harmful because they are corrosive substances. Inhalation of high levels of cresols for a short time results in irritation of the eyes, nose, and throat. Ingestion of high levels results in mouth and throat burns, abdominal pain, vomiting, kidney problems, and effects on the blood and nervous system. Skin contact with high levels of cresols can burn the skin and damage the kidneys, liver, blood, lungs, and brain. Death may occur in both cases. It is not known what the effects are from long-term ingestion or skin contact with low levels of cresols. Studies in animals have also found lesions inside the nose and thyroid gland damage in animals eating food containing mostly p-cresol or a mixture of m- and p-cresol. Animal studies suggest that cresols probably would not affect reproduction in humans. **OSHA:** Not listed as a carcinogen. **IARC:** Not classified.
2-naphthylamine (beta-naphthylamine) **Aromatic amine** Toxic by ingestion, inhalation and skin absorption. IARC: Group 1 – Carcinogenic to humans causing bladder cancer.	**PubChem:** 2-naphthylamine (2-aminonaphthalene) is a naphthalene derivative with carcinogenic action. It belongs to the family of naphthalenes. These are compounds contain two fused benzene rings. 2-naphthylamine is a white to reddish coloured solid in the form of flakes. Slightly soluble in hot water and denser than water. Toxic by ingestion, inhalation and skin absorption. Used to make dyes and agricultural chemicals. Inhalation, ingestion or skin contact with this compound may cause severe injury or death. Contact with molten substance may cause severe burns to skin and eyes. Effects of contact or inhalation may be delayed. Fire may produce irritating, corrosive and/or toxic gases. Runoff from fire control or dilution water may be corrosive and/or toxic and cause pollution. NIOSH considers 2-naphthylamine to be a potential occupational carcinogen. **OSHA:** 2-naphthylamine is listed as a carcinogen. **IARC:** There is evidence for carcinogenicity to humans (sufficient) Case reports and epidemiological studies conducted independently in the 1950s and 1960s showed that

Chemical Name	Comments
	occupational exposure to 2-naphthylamine, either alone or as an impurity in other compounds, is causally associated with the occurrence of bladder cancer. Two studies in the USA examined cancer incidence and mortality in a group of chemical workers exposed mainly to 2-naphthylamine. In one, a remarkable and significantly increased incidence of bladder cancer was found (13 observed, 3.3 expected), which was not explained by smoking habits. Two reports on one occupational population at a dyestuffs plant in Italy documented a very high bladder cancer risk linked specifically to 2-naphthylamine production (6 deaths observed, 0.04 expected) and a clear exposure-response relationship of the risk to exposures in the plant. Incidence studies from Japan dealing with exposure to both 2-naphthylamine and benzidine showed apparently increased risks of cancer of the urinary tract and bladder and, possibly, an increased occurrence of second primary cancers at several sites, including the liver. Case reports and ecological studies also documented the relationship between exposure to 2-naphthylamine, as well as to benzidine, and bladder cancer risk. 2-Naphthylamine was most probably involved in the exposure to aryl amines reported in a UK study as producing a significantly increased bladder cancer risk, which was not accounted for by smoking habits. There is also evidence for carcinogenicity to animals (sufficient). 2-naphthylamine was tested for carcinogenicity by oral administration in many animal species and by the mouse-lung adenoma bioassay. Following its oral administration, it induced bladder neoplasms in hamsters, dogs, and nonhuman primates; and liver tumours in mice. A low incidence of bladder carcinomas was observed in rats after its oral administration. In a lung adenoma bioassay in mice, 2-naphthylamine produced positive results. Overall evaluation: 2-Naphthylamine is carcinogenic to humans (Group 1).
2-nitrophenol **Chemical intermediate** No data on human toxicity. Not classified by IARC.	**ATSDR:** Nitrophenols include two chemicals, 2-nitrophenol and 4-nitrophenol, which are very similar. They are manufactured chemicals that do not occur naturally in the environment. The manufacture of one almost always produces a little of the other, so they are grouped together when discussing their properties and harmful effects. 2-nitrophenol is a light-yellow solid with a peculiar sweet smell. 4-nitrophenol is a colorless to light yellow solid with very little odour. 2-nitrophenol is used mainly to make dyes, paint colouring, rubber chemicals, and substances that kill moulds. 4-

Chemical Name	Comments
	nitrophenol is used mainly to make drugs, fungicides, dyes, and to darken leather. There are no studies that have looked at the effects of the nitrophenols in people. All toxicity information comes from studies in animals. Some studies in animals have shown that 4-nitrophenol is more harmful than 2-nitrophenol when given in high amounts over a short time. Rats that breathed moderate levels of 4-nitrophenol for two weeks developed a blood disorder that reduced the ability of the blood to carry oxygen to tissues and organs. However, these abnormalities disappeared a few days after exposure stopped. No other harmful effects to other systems or organs were seen. Skin irritation has been noted in animals that had large amounts of 4-nitrophenol applied to their skin, and eye irritation when it was applied to the eye. These effects are most likely due to the large amount used and not to a specific harmful effect of nitrophenols. No birth defects were seen in the offspring of animals that ingested large quantities of 4-nitrophenol. There is no information from animal studies on the effects of ingesting low levels of nitrophenols. The Department of Health and Human Services, and the Environmental Protection Agency (EPA) have not classified the nitrophenols as to their human carcinogenicity. An animal study found no evidence of cancer when 4-nitrophenol was applied to the skin of mice, and no studies in people are available. **OSHA:** Not listed as a carcinogen. **IARC**: Not classified.
3- & 4-methylphenol (meta- & para-cresol)	These compounds are cresols – see data above under 2-methylphenol (ortho- or o-cresol).
3-methylcholanthrene **PAH** Irritant to skin, eyes and URT. IARC: Group 1 – Carcinogenic to humans.	**ATSDR:** 3-methylcholanthrene is a polycyclic aromatic hydrocarbon (PAH). PAHs are a group of over 100 different chemicals that are formed during the incomplete burning of coal, oil and gas, garbage, or other organic substances like tobacco or charbroiled meat. PAHs are usually found as a mixture containing two or more of these compounds, such as soot. Some PAHs are manufactured. These pure PAHs usually exist as colorless, white, or pale yellow-green solids. PAHs are found in coal tar, crude oil, creosote, and roofing tar, but a few are used in medicines or to make dyes, plastics, and pesticides. PAHs enter the air mostly as releases from volcanoes, forest fires, burning coal, and automobile exhaust.

Chemical Name	Comments
	PAHs can occur in air attached to dust particles. Some PAH particles can readily evaporate into the air from soil or surface waters. PAHs can break down by reacting with sunlight and other chemicals in the air, over a period of days to weeks. PAHs enter water through discharges from industrial and wastewater treatment plants. Most PAHs do not dissolve easily in water. They stick to solid particles and settle to the bottoms of lakes or rivers. Microorganisms can break down PAHs in soil or water after a period of weeks to months. In soils, PAHs are most likely to stick tightly to particles; certain PAHs move through soil to contaminate underground water. PAH contents of plants and animals may be much higher than PAH contents of soil or water in which they live. Mice that were fed high levels of one PAH during pregnancy had difficulty reproducing and so did their offspring. These offspring also had higher rates of birth defects and lower body weights. It is not known whether these effects occur in people. Animal studies have also shown that PAHs can cause harmful effects on the skin, body fluids, and ability to fight disease after both short- and long-term exposure. The Department of Health and Human Services (DHHS) has determined that some PAHs may reasonably be expected to be carcinogens. Some people who have breathed or touched mixtures of PAHs and other chemicals for long periods of time have developed cancer. Some PAHs have caused cancer in laboratory animals when they breathed air containing them (lung cancer), ingested them in food (stomach cancer), or had them applied to their skin (skin cancer). **PubChem:** 3-methylcholanthrene is a highly carcinogenic polycyclic aromatic hydrocarbon produced by burning organic compounds at very high temperatures. The short notation often used is 3-MC or MCA. This compound forms pale yellow solid crystals when crystallized from benzene and ether. Methylcholanthrene is used in laboratory studies of chemical carcinogenesis. It is an alkylated derivative of benz[a]anthracene and has a similar UV spectrum. The most common isomer is 3-methylcholanthrene, Symptoms of exposure to this compound include strong irritation of the skin, eyes, mucous membranes and upper respiratory tract. This compound may be fatal by inhalation or ingestion. It is a powerful irritant of the skin, eyes, mucous membranes and upper respiratory tract. When heated to decomposition it emits acrid smoke, irritating fumes and toxic fumes.

Chemical Name	Comments
	OSHA: PAHs are listed with coal-tar pitch volatiles as carcinogens. **IARC:** Exposures to mixtures of PAHs in a wide range of occupations have been classified as carcinogenic to humans (Group 1).
3-nitroaniline **Aromatic amine** Irritant to skin, eyes, URT and CNS. Highly toxic by inhalation, ingestion and skin absorption causing methaemoglobinaemia. Not classified by IARC.	**PubChem:** 3-nitroaniline, also known as 'meta'-nitroaniline and m-nitroaniline, is a non-volatile stable solid commonly used as a raw material for dyes. 3-nitroaniline is an aniline carrying a nitro functional group in position 3. It is stable in neutral, acidic or alkaline solutions and is classified as "not readily biodegradable" with "low bioaccumulation potential" Symptoms of exposure to 3-nitroaniline may include cyanosis and liver damage. When inhaled or ingested, it may cause headache, flushing of the face, difficult breathing, nausea, vomiting, weakness, drowsiness, irritability and dermatitis. Structurally similar chemicals may cause methemoglobinemia. It is a highly toxic irritant. It may be fatal if inhaled or swallowed. It causes eye and skin irritation. When heated to decomposition this compound emits toxic fumes. **OSHA:** Not listed as a carcinogen. **IARC:** Not classified.
4-(dimethylamino) azobenzene (para-dimethylamino azobenzene) **Laboratory chemical** Toxic by inhalation, ingestion and skin absorption causing liver and kidney damage. IARC: Group 2B – Possibly carcinogenic to humans.	**PubChem:** 4-dimethylamino azobenzene (para-dimethylamino azobenzene) is a reagent used mainly to induce experimental liver cancer. 4-dimethylamino azobenzene is a yellow, crystalline solid compound. It was used as a dye for colouring polishes, wax products, polystyrene and soap, and was also used as a pH indicator, but is no longer used or produced in the United States. Exposure to this substance causes dermatitis. 4-dimethylaminoazobenzene is reasonably anticipated to be a human carcinogen. It is toxic by inhalation, skin absorption, ingestion, and skin and/or eye contact. Symptoms may include enlarged liver; liver, kidney disturbance; contact dermatitis; cough, wheezing, dyspnoea (breathing difficulty); bloody sputum; bronchial secretions; frequent urination, haematuria (blood in the urine), dysuria. Acute (short-term) dermal exposure to 4-dimethylamino azobenzene may result in contact dermatitis in humans. No information is available on the chronic (long-term),

Chemical Name	Comments
	reproductive, developmental, or carcinogenic effects of 4-dimethylamino azobenzene in humans. Animal studies have reported birth defects in the offspring of mice exposed to 4-dimethylamino azobenzene and tumours of the lung, liver, and bladder from oral exposure to 4-dimethylamino azobenzene. EPA has not classified 4-dimethylaminoazobenzene for carcinogenicity. NIOSH considers 4-dimethylaminoazobenzene to be a potential occupational carcinogen. **OSHA:** Not listed as a carcinogen. **IARC:** 4-dimethylamino azobenzene has been evaluated as possibly carcinogenic to humans (Group 2B).
4,4-DDD **4,4-DDE** **4,4-DDT** **Organo-chlorine** Toxic to CNS and liver by inhalation, ingestion and skin absorption. IARC: Group 2A – Probably carcinogenic to humans.	**ATSDR:** DDT (dichlorodiphenyl trichloroethane) is a pesticide once widely used to control insects in agriculture and insects that carry diseases such as malaria. DDT is a white, crystalline solid with no odor or taste. Its use in the U.S. was banned in 1972 because of damage to wildlife but is still used in some countries. DDE (dichlorodiphenyl dichloroethylene) and DDD (dichlorodiphenyl dichloroethane) are chemicals similar to DDT that contaminate commercial DDT preparations. DDE has no commercial use. DDD was also used to kill pests, but its use has also been banned. One form of DDD has been used medically to treat cancer of the adrenal gland. DDT affects the nervous system. People who accidentally swallowed large amounts of DDT became excitable and had tremors and seizures. These effects went away after the exposure stopped. No effects were seen in people who took small daily doses of DDT by capsule for 18 months. A study in humans showed that women who had high amounts of a form of DDE in their breast milk were unable to breast feed their babies for as long as women who had little DDE in the breast milk. Another study in humans showed that women who had high amounts of DDE in breast milk had an increased chance of having premature babies. In animals, short-term exposure to large amounts of DDT in food affected the nervous system, while long-term exposure to smaller amounts affected the liver. Also in animals, short-term oral exposure to small amounts of DDT or its breakdown products may also have harmful effects on reproduction. Studies in DDT-exposed workers did not show increases in cancer.

Chemical Name	Comments
	Studies in animals given DDT with the food have shown that DDT can cause liver cancer. The Department of Health and Human Services (DHHS) determined that DDT may reasonably be anticipated to be a human carcinogen. **OSHA:** DDT is listed as a carcinogen. **IARC:** The insecticide DDT was classified as probably carcinogenic to humans (Group 2A), based on sufficient evidence that DDT causes cancer in experimental animals and limited evidence of its carcinogenicity in humans. Epidemiological studies found positive associations between exposure to DDT and NHL, testicular cancer, and liver cancer. There was also strong experimental evidence that DDT can suppress the immune system and disrupt sex hormones. However, overall there was no association between breast cancer and DDT levels measured in samples of blood or fat.
4-aminobiphenyl **Aromatic amine** IARC: Group 1 – Carcinogenic to humans causing bladder cancer.	**PubChem:** 4-Aminobiphenyl is an organic compound with the formula $C_6H_5C_6H_4NH_2$. It is an amine derivative of biphenyl. It is a colorless solid, although aged samples can appear coloured. 4-Aminobiphenyl was commonly used in the past as a rubber antioxidant and an intermediate for dyes. Exposure to this aryl-amine can happen through contact with chemical dyes and from inhalation of cigarette smoke. Researches showed that 4-aminobiphenyl is responsible for bladder cancer in humans and dogs by damaging DNA. Due to its carcinogenic effects, commercial production of 4-aminobiphenyl ceased in the United States in the 1950s. **OSHA:** Listed as a carcinogen. **IARC:** There is sufficient evidence in humans for the carcinogenicity of 4-aminobiphenyl. 4-Aminobiphenyl causes cancer of the urinary bladder. There is sufficient evidence in experimental animals for the carcinogenicity of 4-aminobiphenyl. There is strong mechanistic evidence indicating that the carcinogenicity of 4-aminobiphenyl in humans operates by a genotoxic mechanism of action that involves metabolic activation, formation of DNA adducts, and induction of mutagenic and clastogenic effects. Metabolic activation to DNA-reactive intermediates occurs by multiple pathways including N-oxidation in the liver, O-acetylation in the bladder, and peroxidative activation in the mammary gland and other organs. 4-Aminobiphenyl is carcinogenic to humans (Group 1).

Chemical Name	Comments
4-bromophenyl phenyl ether **Halogenated hydrocarbon** Irritant and corrosive to skin, eyes and URT. Not classified by IARC.	**PubChem:** 4-bromophenyl phenyl ether is an aromatic ether that is diphenyl ether substituted at position 4 by a bromo group. It is an aromatic ether and an organobromine compound. Inhalation of this chemical may be harmful. Contact may cause burns to skin and eyes. Inhalation may have a damaging effect on the lungs. Fire may produce irritating, corrosive and/or toxic gases. Some liquids produce vapours that may cause dizziness or suffocation. **OSHA:** Not listed as a carcinogen. **IARC:** Not classified.
4-chloro-3-methylphenol **Chlorinated phenolic** Irritant to skin, eyes and URT. Not classified by IARC.	**NIOSH:** Occurs as white or slightly pink, hygroscopic crystals or crystalline powder. The substance decomposes on burning producing toxic and corrosive fumes including hydrogen chloride and phosgene . The substance can be absorbed into the body by inhalation and through the skin and by ingestion. Evaporation at 20°C is negligible; a harmful concentration of airborne particles can, however, be reached quickly. The substance is irritating to the eyes , the skin and the respiratory tract . Repeated or prolonged contact may cause skin sensitization. **OSHA:** Not listed as a carcinogen. **IARC:** Not classified.
4-chlorophenyl phenyl ether **Organochlorine** Irritant to skin, eyes and URT. Not classified by IARC.	**PubChem:** 4-chlorophenyl phenyl ether is an aromatic ether that is diphenyl ether substituted at position 4 by a chloro group. It is an aromatic ether and an organochlorine compound. Inhalation of this chemical may be harmful. Contact may cause burns to skin and eyes. Inhalation may have a damaging effect on the lungs. Fire may produce irritating, corrosive and/or toxic gases. Some liquids produce vapours that may cause dizziness or suffocation. **OSHA:** Not listed as a carcinogen. **IARC:** Not classified.

Chemical Name	Comments
4-chlorotoluene **VOC** Irritant to skin, eyes, URT and CNS. Not classified by IARC.	**PubChem:** 4-chlorotoluene is a member of monochlorobenzenes. The major hazards encountered in the use and handling of 4-chlorotoluene stem from its toxicologic properties, and flammability. Exposure may occur at sites where 4-chlorotoluene is manufactured or used as a solvent, disinfectant, or as an intermediate for organic chemicals and dyes. This colorless liquid may exert its strong irritant properties upon dermal contact or inhalation. On combustion, it forms toxic gases including carbon monoxide, hydrogen chloride, and possibly phosgene. **OSHA:** Not listed as a carcinogen. **IARC:** Not classified.
7,12-dimethylbenz(a)anthracene **PAH** Irritant to skin, eyes and URT. IARC: Group 1 – PAHs from "coal-tar pitch volatiles" are carcinogenic to humans.	**PubChem:** 7, 12-dimethylbenz[a]anthracene, also known as DMBA or 1, 4-Dimethyl-2, 3-benzphenanthrene, is classified as a phenanthrene or phenanthrene derivative. Phenanthrenes are polycyclic aromatic hydrocarbon (PAH) compounds. Symptoms of exposure to this compound include irritation of the skin, eyes and gastrointestinal tract. It may also cause acetonemia. It is harmful by ingestion, inhalation or skin absorption. It is an irritant of the skin, eyes and gastrointestinal tract. When heated to decomposition it emits acrid smoke, irritating fumes and toxic fumes NIOSH considers phenanthrenes in coal tar pitch volatiles to be potential occupational carcinogens. **OSHA:** Phenanthrenes in coal tar pitch volatiles are listed as carcinogens. **IARC**: Not classified.
a-BHC (a-hexachlorocyclohexane or a-HCH) **b-BHC (b-hexachlorocyclohexane or b-HCH)** **d-BHC (d-hexachlorocyclohexane or d-HCH)**	**ATSDR:** Hexachlorocyclohexane (HCH), formerly known as benzene hexachloride (BHC), is a synthetic chemical that exists in eight chemical forms called isomers. The different isomers are named according to the position of the hydrogen atoms in the structure of the chemical. One of these forms, gamma-HCH (or g-HCH, commonly called Lindane), is produced and used as an insecticide on fruit, vegetables, and forest crops, and animals and animal premises. It is a white solid whose vapour may evaporate into the air. The vapour is colourless and has a slight musty odour when it is present at 12 or more parts HCH per million parts air (ppm). g-HCH has not been produced in the United States since 1976. However, imported

Chemical Name	Comments
g-BHC (g-hexachlorocyclohexane or g-HCH) Lindane **Organo-chlorine** All BHCs are toxic by inhalation and ingestion to CNS. IARC: Group 1 – g-BHC (Lindane) is carcinogenic to humans. IARC: Group 2B – Other BHCs are possibly carcinogenic to humans.	g-HCH is available in the United States for insecticide use as a dust, powder, liquid, or concentrate. It is also available as a prescription medicine (lotion, cream, or shampoo) to treat and/or control scabies (mites) and head lice in humans. Technical-grade HCH, a mixture of several chemical forms of HCH, was also once used as an insecticide and typically contained about 10–15% of g-HCH as well as the a-, b-, d-, and e- forms of HCH. Virtually all of the insecticidal properties reside in the g- isomer. Technical-grade HCH has not been produced or used in the United States for more than 20 years. Some people who breathed contaminated workplace air during manufacturing of pesticides, including g-HCH, had blood disorders, dizziness, headaches, and changes in the levels of sex hormones. People who swallowed large amounts had seizures and some died. Animals fed g- and a-HCH have had convulsions, and animals fed b-HCH have become comatose. All isomers can produce liver and kidney effects. Reduced ability to fight infection was reported in animals fed g-HCH, and injury to the ovaries and testes was reported in animals given g-HCH or b-HCH. Long-term oral administration of a-HCH, b-HCH, g-HCH, or technical-grade HCH to laboratory rodents produced liver cancer. The Department of Health and Human Services (DHHS) has determined that HCH (all isomers) may reasonably be anticipated to cause cancer in humans. The EPA has determined that there is suggestive evidence that lindane (g-HCH) is carcinogenic, but the evidence is not sufficient to assess its human carcinogenic potential. The EPA has additionally classified technical HCH and a-HCH as probable human carcinogens, b-HCH as a possible human carcinogen, and g- and e-HCH as not classifiable as to human carcinogenicity. **OSHA:** Only g-BHC (Lindane) is listed as a carcinogen. **IARC:** Hexachlorocyclohexanes as a group were evaluated as possibly carcinogenic to humans (Group 2B) because of the possible carcinogenicity of g-BHC (lindane). However, there is now sufficient evidence in humans for the carcinogenicity of lindane for non-Hodgkin lymphoma (NHL). Lindane (g-BHC) has been re-classified as carcinogenic to humans (Group 1).
Acetophenone	**PubChem:** Acetophenone is a flavouring ingredient used in fruit flavours and as a leavening agent. Acetophenone is a raw

Chemical Name	Comments
Food and cigarette additive Non-toxic. Not classified by IARC.	material for the synthesis of some pharmaceuticals and is also listed as an approved excipient by the US FDA. Acetophenone has been listed as one of the 599 additives to cigarettes. Acetophenone is an organic compound with the formula C6H5C(O)CH3. It is the simplest aromatic ketone. This colourless, viscous liquid is a precursor to useful resins and fragrances No toxicity expected from inhalation or ingestion except slight narcotic effect. Liquid can cause eye and skin irritation on contact. **OSHA:** Acetophenone is listed as a carcinogen. **IARC:** Not classified.
Aldrin and Dieldrin **Organo-chlorine** Toxic to CNS by inhalation, ingestion and skin absorption. IARC: Group 3 – Not classifiable as to their carcinogenicity to humans.	**ATSDR:** Aldrin and dieldrin are insecticides with similar chemical structures. They are discussed together because aldrin quickly breaks down to dieldrin in the body and in the environment. Pure aldrin and dieldrin are white powders with a mild chemical odour. The less pure commercial powders have a tan colour. Neither substance occurs naturally in the environment From the 1950s until 1970, aldrin and dieldrin were widely used pesticides for crops like corn and cotton. Because of concerns about damage to the environment and potentially to human health, US EPA banned all uses of aldrin and dieldrin in 1974, except to control termites. In 1987, EPA banned all uses. People who intentionally or accidentally ingested large amounts of aldrin or dieldrin suffered convulsions and some died. Health effects may also occur after a longer period of exposure to smaller amounts because these chemicals build up in the body. Some workers exposed to moderate levels in the air for a long time had headaches, dizziness, irritability, vomiting, and uncontrolled muscle movements. Workers removed from the source of exposure rapidly recovered from most of these effects. Animals exposed to high amounts of aldrin or dieldrin also had nervous system effects. In animals, oral exposure to lower levels for a long period also affected the liver and decreased their ability to fight infections. Studies in animals have given conflicting results about whether aldrin and dieldrin affect reproduction in male animals and whether these chemicals may damage the sperm. There is no conclusive evidence that aldrin or dieldrin cause cancer in humans.

Chemical Name	Comments
	Aldrin and dieldrin have been shown to cause liver cancer in mice. The EPA has determined that aldrin and dieldrin are probable human carcinogens. **OSHA:** Aldrin and dieldrin are listed as carcinogens. **IARC:** Aldrin and dieldrin are not classifiable as to their carcinogenicity to humans (Group 3).
Aniline **Aromatic amine** Irritant to skin, eyes, URT and CNS. Toxic by inhalation, ingestion and skin absorption causing methaemoglobinaemia, and CNS toxicity. IARC: Group 3 – Not classifiable as to its carcinogenicity to humans.	**ATSDR:** Aniline is a clear to slightly yellow liquid with a characteristic odour. It does not readily evaporate at room temperature. Aniline is slightly soluble in water and mixes readily with most organic solvents. Aniline is used to make a wide variety of products such as polyurethane foam, agricultural chemicals, synthetic dyes, antioxidants, stabilizers for the rubber industry, herbicides, varnishes and explosives. Aniline can be toxic if ingested, inhaled, or by skin contact. Aniline damages haemoglobin, a protein that normally transports oxygen in the blood. This condition is known as methaemoglobinaemia and its severity depends on exposure. Methaemoglobinaemia is the most prominent symptom of aniline poisoning in humans, resulting in cyanosis (a purplish-blue skin colour) following acute high exposure to aniline. Dizziness, headaches, irregular heartbeat, convulsions, coma, and death may also occur. Direct contact with aniline can also produce skin and eye irritation. Long-term exposure to lower levels of aniline may cause symptoms similar to those experienced in acute high-level exposure. Studies in animals have not demonstrated reproductive toxicity for aniline. The available studies in humans are inadequate to determine whether exposure to aniline can increase the risk of developing cancer. Rats that ate food contaminated with aniline for life developed cancer of the spleen. The EPA has determined that aniline is a probable human carcinogen. **OSHA:** Aniline is listed as a carcinogen. **IARC:** Aniline is not classifiable as to its carcinogenicity to humans (Group 3).
Bis(2-chloroethoxy) methane	**PubChem:** Bis(2-chloroethoxy) methane is a colourless liquid used as a solvent. May be toxic by ingestion or inhalation.

Chemical Name	Comments
VOC Irritant to skin, eyes, URT and CNS. Not classified by IARC.	Severely irritates skin, eyes, and mucous membranes. It is a strong irritant. **OSHA:** Not listed as a carcinogen. **IARC:** Not classified.
Bis(2-chloroisopropyl) ether **VOC** Irritant to skin, eyes and URT. Toxic to liver and kidneys by inhalation and ingestion. IARC: Group 3 – Not classifiable as to its carcinogenicity to humans.	**PubChem:** Bis(2-chloroisopropyl) ether [syn: bis(2-chloro-1-methylethyl) ether] is a colourless to light brown liquid. It has been produced as a solvent and soil fumigant and is also formed in large quantities as a by-product in some propylene oxide/propylene glycol production processes. Low levels have been found in water. Symptoms of exposure to this compound include toxic effects to the liver and kidneys. It may cause skin and respiratory tract irritation. It is an irritant of the eyes and respiratory tract. It may be absorbed through the skin. It is a corrosive material. When heated to decomposition it emits highly toxic fumes. **OSHA:** Not listed as a carcinogen. **IARC:** No epidemiological data relevant to the carcinogenicity of bis(2-chloroisopropyl) ether were available. There is limited evidence in experimental animals for the carcinogenicity of bis(2-chloroisopropyl) ether. Overall evaluation: Bis(2-chloroisopropyl) ether is not classifiable as to its carcinogenicity to humans (Group 3).
Bis(2-ethylhexyl) phthalate [DEHP] **Phthalate** Low human toxicity, but carcinogenic in animal studies. IARC: Group 2B – Possibly carcinogenic to humans.	**ATSDR:** Bis(2-ethylhexyl) phthalate [DEHP] is a manufactured chemical that is commonly added to plastics to make them flexible. DEHP is a colorless liquid with almost no odour. DEHP is present in plastic products such as wall coverings, tablecloths, floor tiles, furniture upholstery, shower curtains, garden hoses, swimming pool liners, rainwear, baby pants, dolls, some toys, shoes, automobile upholstery and tops, packaging film and sheets, sheathing for wire and cable, medical tubing, and blood storage bags. At the levels found in the environment, DEHP is not expected to cause harmful health effects in humans. Most of what is known about the health effects of DEHP comes from studies of rats and mice given high amounts of DEHP. Harmful effects in animals generally occurred only with high amounts of DEHP or with prolonged exposures. Moreover, absorption and breakdown of DEHP in humans is different than in rats or mice, so the effects seen in rats and mice may not occur in humans.

Chemical Name	Comments
	Rats that breathed DEHP in the air showed no serious harmful effects. Their lifespan and ability to reproduce were not affected. Brief oral exposure to very high levels of DEHP damaged sperm in mice. Although the effect reversed when exposure ceased, sexual maturity was delayed in the animals. High amounts of DEHP damaged the liver of rats and mice. Whether or not DEHP contributes to human kidney damage is unclear. Skin contact with products containing DEHP will probably cause no harmful effects because it cannot be taken up easily through the skin. The Department of Health and Human Services (DHHS) has determined that DEHP may reasonably be anticipated to be a human carcinogen. The EPA has determined that DEHP is a probable human carcinogen. These determinations were based entirely on liver cancer in rats and mice. **OSHA:** DEHP is listed as a carcinogen. **IARC:** There is sufficient evidence in experimental animals for the carcinogenicity of DEHP. DEHP is possibly carcinogenic to humans (Group 2B).
Butyl benzyl phthalate **Phthalate** Irritant to skin, eyes and URT. Few data on human toxicity. IARC: Group 3 – Not classifiable as to its carcinogenicity to humans.	**PubChem:** Butyl benzyl phthalate (benzyl butyl phthalate) is a clear colourless liquid with a mild odour. Primary hazard is to the environment. Immediate steps should be taken to limit spread to the environment. Easily penetrates the soil to contaminate groundwater and nearby waterways. Prolonged contact with liquid causes some irritation of eyes and skin. Irritating vapours of unburned chemical may form in fires. **OSHA:** Not listed as a carcinogen. **IARC:** There is inadequate evidence in humans for the carcinogenicity of butyl benzyl phthalate. There is limited evidence in experimental animals for the carcinogenicity of butyl benzyl phthalate. Overall evaluation: Butyl benzyl phthalate is not classifiable as to its carcinogenicity to humans (Group 3).
Chlorodibromomethane (Dibromochloromethane) **Trihalomethane (THM)**	**ATSDR:** Chlorodibromomethane (dibromochloromethane) is a colourless to yellow, heavy, non-flammable, liquid with a sweet odour. Small amounts are formed naturally by plants in the ocean. They are somewhat soluble in water and readily evaporate into the air. Most of the chlorodibromomethane

Chemical Name	Comments
No known human toxicity. IARC: Group 3 – Not classifiable as to its carcinogenicity to humans.	that enters the environment is formed as a by-product when chlorine is added to drinking water to kill bacteria. Eating or breathing a large amount of chlorodibromomethane slows down the normal brain activities and causes sleepiness. Exposure to very high amounts may cause unconsciousness and even death. No studies are available about health effects in people exposed to chlorodibromomethane. Animals exposed to high amounts developed liver and kidney injuries. Exposure to low levels do not appear to seriously affect the brain, liver, or kidneys. There is no conclusive evidence that chlorodibromomethane causes cancer in humans because no cancer studies of humans exposed exclusively to these chemicals are available. Studies in animals indicate that long-term intake can cause liver and kidney cancer. The EPA classified chlorodibromomethane as a possible human carcinogen. **OSHA:** Not listed as a carcinogen. **IARC:** No epidemiological data relevant to the carcinogenicity of chlorodibromomethane were available. There is limited evidence in experimental animals for the carcinogenicity of chlorodibromomethane. Overall evaluation: Chlorodibromomethane is not classifiable as to its carcinogenicity to humans (Group 3).
Cis-1,3-dichloropropene (Cis-1,3-dichloropropylene) **Organo-chlorine** Irritant to skin, eyes and URT. Toxic in experimental animal studies. IARC: Group 2B – Possibly carcinogenic to humans.	**ATSDR:** There are five different types (or isomers) of dichloropropene (dichloropropylene) molecules: 1,1-dichloropropene; 1,2-dichloropropene; 1,3-dichloropropene; 2,3-dichloropropene; and 3,3-dichloropropene. 1,3-Dichloropropene is a colorless liquid with a sweet smell. It is used mainly in farming as a pesticide. Much less is known about the other dichloropropenes. 2,3-Dichloropropene is used in industry to make other chemicals. No uses were found for 1,1-, 1,2-, or 3,3-dichloropropene. Because 1,3-dichloropropene is produced and used in much higher amounts than the other isomers and because it is released to the environment as a pesticide, most of the data available are for 1,3-dichloropropene. Therefore, the focus of this summary is the 1,3-dichloropropene isomer. Most of the 1,3- and 2,3-dichloropropene that is inhaled or ingested will rapidly enter the bloodstream. Rats and mice that inhaled 1,3-dichloropropene or 2,3-dichloropropene repeatedly had damage to the lining of the nose. Damage to the urinary bladder and anemia were also seen in animals inhaling 1,3-dichloropropene for a long time.

Chemical Name	Comments
	Damage to the stomach lining and anemia were seen in animals orally exposed to 1,3-dichloropropene. Skin and eye irritation are seen in animals after 1,3-dichloropropene gets on their skin or in their eyes. A few workers who had skin contact with pesticides containing 1,3-dichloropropene developed blisters and an allergic reaction on their skin. The Department of Health and Human Services (DHHS) has determined that 1,3-dichloropropene may reasonably be anticipated to be a carcinogen. The EPA has classified 1,3-dichloropropene as a probable human carcinogen. **OSHA:** 1,3-dichloropropene is listed as a carcinogen. **IARC:** No epidemiological data relevant to the carcinogenicity of 1,3-dichloropropene were available. There is sufficient evidence in experimental animals for the carcinogenicity of mixed isomers of 1,3-dichloropropene (technical grade). Overall evaluation: 1,3-Dichloropropene (technical-grade) is possibly carcinogenic to humans (Group 2B).
Dibenzofuran **Furan** Few data on human toxicity. Not classified by IARC.	**PubChem:** Dibenzofuran is an organic heterotricyclic chemical. Exposure to dibenzofuran may occur through inhalation and dermal contact at sites where coal tar, coal tar derivatives, or creosote are handled. The general population may be exposed to dibenzofuran through contact with creosote-treated wood or inhalation of fly ash particulates and emissions from municipal waste incinerators. Since dibenzofuran is a contaminant often found in waste dumps and in water supplies, exposure through ingestion of contaminated food products, e.g., fish, may also occur. Despite significant human exposure, very little information on the toxicity of dibenzofuran was found in the available literature. This limited information suggests that dibenzofuran may not exhibit “dioxin-like” behaviour. Inhalation of material may be harmful. Contact may cause burns to skin and eyes. Fire may produce irritating, corrosive and/or toxic gases. **OSHA:** Not listed as a carcinogen. **IARC:** Not classified.
Dibromomethane **Halogenated hydrocarbon**	**PubChem:** Dibromomethane is a member of the class of bromomethanes. It is produced by marine algae. It has a role as a marine metabolite and an algal metabolite. It is a member of bromomethanes and a bromohydrocarbon.

Chemical Name	Comments
May be toxic to CNS by inhalation. Not classified by IARC.	It is a colourless liquid with a pleasant odour, and is insoluble in water and denser than water. May be toxic by ingestion. Used as a solvent and as a motor fuel. Inhalation causes anaesthetic effects, nausea and drunkenness. Contact with skin and eyes causes irritation of skin, eyes and nose. **OSHA:** Not listed as a carcinogen. **IARC:** Not classified.
Dichlorodifluoromethane **Halogenated hydrocarbon** May be toxic to CNS by inhalation. Not classified by IARC.	**PubChem:** Dichlorodifluoromethane is a direct contact freezing agent for foods. It has been used as a refrigerant, and aerosol spray propellant. Dichlorodifluoromethane was usually sold under the brand name Freon-12 and is a chlorofluorocarbon halomethane (CFC). Complying with the Montreal Protocol, its manufacture was banned in the United States along with many other countries in 1994 due to concerns about damage to the ozone layer. It is soluble in many organic solvents. Inhalation results in some narcosis when 10% in air is breathed. **OSHA:** Dichlorodifluoromethane is listed as a carcinogen. **IARC:** Not classified.
Dieldrin and aldrin	See aldrin and dieldrin above.
Diethyl phthalate **Phthalate** Irritant to skin, eyes and URT. Few data on human toxicity. Not classified by IARC.	**ATSDR:** Diethyl phthalate is a colorless liquid that has a bitter, disagreeable taste. This synthetic substance is commonly used to make plastics more flexible. Products in which it is found include toothbrushes, automobile parts, tools, toys, and food packaging. Diethyl phthalate can be released fairly easily from these products, as it is not part of the chain of chemicals (polymers) that makes up the plastic. Diethyl phthalate is also used in cosmetics, insecticides, and aspirin. No information is available regarding possible effects caused by diethyl phthalate after breathing, eating, or drinking it, or if it touches the skin. Very high oral doses of diethyl phthalate have caused death in animals, but brief oral exposures to lower doses caused no harmful effects. Weight gain was decreased in animals that ate high doses of diethylphthalate for a long time.

Chemical Name	Comments
	Diethyl phthalate placed directly on the skin of rats daily for 2 years was not carcinogenic. Liver tumours were seen in mice that had diethyl phthalate placed directly on their skin daily for 2 years. This type of tumour is common in mice, and the smallest dose resulted in a similar number of tumours as the largest dose. **OSHA:** Diethyl phthalate is listed as a carcinogen. **IARC:** Not classified.
Dimethyl phthalate **Phthalate** Irritant to skin, eyes and URT. Few data on human toxicity. Not classified by IARC.	**PubChem:** Dimethyl phthalate is an organic compound. The methyl ester of phthalic acid, it is a colourless liquid that is soluble in organic solvents. Dimethyl phthalate is used as an insect repellent for mosquitoes and flies. It is also an ectoparasiticide and has many other uses, including in solid rocket propellants, and plastics. Acute (short-term) exposure to dimethyl phthalate, via inhalation in humans and animals, results in irritation of the eyes, nose, and throat. No information is available on the chronic (long-term), reproductive, developmental, or carcinogenic effects of dimethyl phthalate in humans. Animal studies have reported slight effects on growth and on the kidney from chronic oral exposure to the chemical. EPA has classified dimethyl phthalate as a Group D, not classifiable as to human carcinogenicity. **OSHA:** Dimethyl phthalate is listed as a carcinogen. **IARC:** Not classified.
Di-n-butyl phthalate **Phthalate** Irritant to skin, eyes and URT. Few data on human toxicity. Not classified by IARC.	**ATSDR:** Di-n-butyl phthalate is a manufactured chemical that does not occur naturally. It is an odourless and oily liquid that is colorless to faint yellow in colour. It is slightly soluble in water and does not evaporate easily. Di-n-butyl phthalate is used to make plastics more flexible and is also in carpet backings, paints, glue, insect repellents, hair spray, nail polish, and rocket fuel. Di-n-butyl phthalate has relatively low toxicity. Adverse effects have not been reported in humans as a result of exposure to di-n-butyl phthalate. In laboratory animals, studies show that eating large amounts of di-n-butyl phthalate can affect their ability to reproduce. Sperm production can decrease but returns to near normal levels when exposure stops. Large amounts of di-n-butyl phthalate repeatedly applied to the skin for a long time can cause mild irritation.

Chemical Name	Comments
	There have been no cancer studies in humans and the one study in laboratory animals is inadequate. The EPA has determined that di-n-butyl phthalate is not classifiable as to human carcinogenicity based on inadequate evidence in both humans and animals. **OSHA:** Not listed as a carcinogen. **IARC:** Not classified.
Di-n-octyl phthalate **Phthalate** Irritant to skin, eyes and URT. Few data on human toxicity. Not classified by IARC.	**ATSDR:** Di-n-octyl phthalate is a colourless, odourless, oily liquid that doesn't evaporate easily. It is a manufactured substance used to keep plastics soft or more flexible. This type of plastic can be used for medical tubing and blood storage bags, wire and cables, carpet-back coating, floor tile, and adhesives. It is also used in cosmetics and pesticides. Little information is known about the health effects that might be caused by di-n-octyl phthalate. Some rats and mice that were given very high doses of di-n-octyl phthalate by mouth died. Mildly harmful effects have been seen in the livers of some rats and mice given very high doses of di-n-octyl phthalate by mouth for short (14 days or less) or intermediate periods (15 to 365 days) of time, but lower doses given for short periods of time generally caused no harmful effects. No information is available on the health effects of having di-n-octyl phthalate in contact with human skin. It can be mildly irritating when applied to the skin of animals. Di-n-octyl phthalate is not known to cause cancer in humans or animals. Di-n-octyl phthalate has not been classified as to its carcinogenicity by the Department of Health and Human Services (DHHS), or the EPA. **OSHA:** Not listed as a carcinogen. **IARC:** Not classified.
Diphenylamine **Aromatic amine** Irritant to skin, eyes and URT. Not classified by IARC.	**PubChem:** Diphenylamine is found in coriander. Diphenylamine is used for control of superficial scald in stored apples Diphenylamine is the organic compound with the formula (C6H5)2NH. It is a colourless solid, but samples are often yellow due to oxidized impurities. In humans, it may be irritating to mucous membranes. Methemoglobinemia has been produced experimentally. In veterinary use, it is one of active ingredients in topical agents for prevention and treatment of screwworm infestation.

Chemical Name	Comments
	Inhalation may irritate mucous membranes. Overexposure, including ingestion of solid or skin contact, may cause fast pulse, hypertension, and bladder trouble. Contact with dust irritates eyes. **OSHA:** Diphenylamine is listed as a carcinogen. **IARC:** Not classified.
Endosulfan I **Endosulfan II** **Endosulfan sulphate** **Organo-chlorine** Toxic to CNS by inhalation and ingestion. Not classified by IARC.	**ATSDR:** Endosulfan is a restricted-use pesticide. It is particularly effective against aphids, fruit worms, beetles, leafhoppers, moth larvae, and white flies on a wide variety of crops. Endosulfan is sold as a mixture of two different forms of the same chemical (referred to as Î±- and Î²-endosulfan). Technical grade endosulfan also contains endosulfan sulphate. It is a cream-to-brown-coloured solid that may appear crystalline or in flakes. It has a distinct odour similar to turpentine. Endosulfan is applied to crops by aerial or ground-level foliar spray. The use of endosulfan is being restricted to certain crops and is scheduled to be cancelled for all uses by 2016 in the US. The main target of endosulfan toxicity is the nervous system. Exposure to high amounts of endosulfan induces hyperactivity and convulsions, regardless of the route of exposure. Severe poisoning may result in death. There are no studies of people exposed to low levels of endosulfan for long periods of time (i.e., years). Studies in animals have shown that swallowing endosulfan in contaminated food for long periods of time affects mainly the kidneys. Studies of occupational and environmental exposure of humans have not provided conclusive evidence that endosulfan can cause cancer. Endosulfan did not cause cancer in animal studies. The Department of Health and Human Services (DHHS), and the EPA have not classified endosulfan as to its ability to cause cancer. **OSHA:** Endosulfan is listed as a carcinogen. **IARC:** Not classified.
Endrin **Endrin aldehyde** **Endrin ketone**	**ATSDR:** Endrin is an organochloride with the chemical formula $C_{12}H_8Cl_6O$ that was first produced in 1950. It was primarily used as an insecticide, as well as a rodenticide and piscicide. It is a colourless, odourless solid, although commercial samples are often off-white. Endrin was manufactured as an

Chemical Name	Comments
Organo-chlorine Toxic to CNS by inhalation and ingestion. Not classified by IARC.	emulsifiable solution known commercially as Endrex. The compound became infamous as a persistent organic pollutant and for this reason it is banned in many countries. Little is known about the properties of endrin aldehyde (an impurity and breakdown product of endrin) or endrin ketone (a product of endrin when it is exposed to light). Exposure to endrin can cause various harmful effects including death and severe central nervous system (brain and spinal cord) injury. Swallowing large amounts of endrin may cause convulsions and death in a few minutes or hours. Symptoms that may result from endrin poisoning are headaches, dizziness, nervousness, confusion, nausea, vomiting, and convulsions. No long-term health effects have been noted in workers who have been exposed to endrin by breathing or touching it. Studies in animals confirm that endrin's main target is the nervous system. In studies using rats, mice, and dogs, endrin did not produce cancer. However, most of these studies did not accurately evaluate the ability of endrin to cause cancer. No significant excess of cancer has been found in exposed factory workers. The EPA has determined that endrin is not classifiable as to its human carcinogenicity because there is not enough information to allow classification. **OSHA:** Endrin is listed as a carcinogen. **IARC:** Not classified.
Heptachlor **Heptachlor epoxide** **Organo-chlorine** Few data on human toxicity. IARC: Group 2B – Possibly carcinogenic to humans.	**ATSDR:** Heptachlor is a manufactured chemical and does not occur naturally. Pure heptachlor is a white powder that smells like camphor (mothballs). The less pure grade is tan. Heptachlor was used extensively in the past for killing insects in homes, buildings, and on food crops. These uses stopped in 1988. Currently it can only be used for fire ant control in underground power transformers. Heptachlor epoxide is also a white powder. Bacteria and animals break down heptachlor to form heptachlor epoxide. The epoxide is more likely to be found in the environment than heptachlor. There is no reliable information on health effects in humans. Liver damage, excitability, and decreases in fertility have been observed in animals ingesting heptachlor. The effects are worse when the exposure levels were high or when exposure lasted many weeks.

Chemical Name	Comments
	Although there is very little information on heptachlor epoxide, it is likely that similar effects would also occur after exposure to this compound. Lifetime exposure to heptachlor resulted in liver tumours in animals. EPA has classified heptachlor as a possible human carcinogen. EPA also considers heptachlor epoxide as a possible human carcinogen. **OSHA:** Heptachlor and heptachlor epoxide are listed as carcinogens. **IARC:** There is inadequate evidence in humans for the carcinogenicity of heptachlor. There is sufficient evidence in experimental animals for the carcinogenicity of heptachlor. Overall evaluation: Heptachlor is possibly carcinogenic to humans (Group 2B).
Hexachlorobenzene (HCB) **Organo-chlorine** Toxic to CNS by inhalation and ingestion. IARC: Group 2B – Possibly carcinogenic to humans.	**ATSDR:** Hexachlorobenzene is a fungicide that was used in the United States until 1984. It has not been commercially produced in the United States since the late 1970s. Hexachlorobenzene is a white crystalline solid that does not occur naturally in the environment. Although not currently manufactured in the United States, it is formed as a waste product during the manufacture of other chemicals such as trichloroethylene and tetrachloroethylene, and is a contaminant in some pesticides, such as pentachloronitrobenzene and pentachlorophenol. Small amounts can also be produced during combustion of municipal waste Brief exposure to very high levels of hexachlorobenzene may cause adverse effects on the nervous system such as weakness, tremors, and convulsions; skin sores; and liver and thyroid effects. Long-term exposure can cause damage to the liver and reproductive system and can cause developmental effects. Because hexachlorobenzene accumulates in body fat, including breast tissue where it can remain for long periods, long-term exposure can result in a build-up of hexachlorobenzene in the body. Therefore, long-term exposure may be more serious than acute or short-term exposure. Studies in animals suggest that eating food with hexachlorobenzene for a long time can cause cancer of the liver, kidney, and thyroid. There is no strong evidence that hexachlorobenzene causes cancer in humans.

Chemical Name	Comments
	The U.S. Department of Health and Human Services (DHHS) considers hexachlorobenzene as reasonably anticipated to be a human carcinogen. EPA has indicated that hexachlorobenzene is a probable human carcinogen. **OSHA:** Hexachlorobenzene is listed as a carcinogen. **IARC:** There is inadequate evidence in humans for the carcinogenicity of hexachlorobenzene. There is sufficient evidence in experimental animals for the carcinogenicity of hexachlorobenzene. Overall evaluation: Hexachlorobenzene is possibly carcinogenic to humans (Group 2B).
Hexachlorobutadiene **Organo-chlorine** Few data on human toxicity. IARC: Group 3 – Not classifiable as to its carcinogenicity to humans.	**ATSDR:** Hexachlorobutadiene is a colourless liquid with a turpentine-like odour. It is also called perchlorobutadiene. Hexachlorobutadiene is not found naturally in the environment. It is formed when other chemicals are made. It is a chlorinated aliphatic diene with niche applications but is most commonly used as a solvent for other chlorine-containing compounds. It is mainly used to make rubber compounds. It is also used as a solvent, and to make lubricants, in gyroscopes, as a heat transfer liquid, and as a hydraulic fluid. There are no studies that have looked at the effects of hexachlorobutadiene in humans. All toxicological information has come from studies in animals. Studies in mice have shown irritation of the nose when large amounts were breathed over a short time. The only other effect noted in animals from breathing hexachlorobutadiene was a reduction in the body weights of foetuses when their mothers breathed high levels of the chemical. There are no studies which looked at animals breathing low levels of hexachlorobutadiene over a long time. Rats and mice that drank low levels of hexachlorobutadiene over both short and long periods had kidney and liver damage. Studies in rabbits found kidney and liver damage from contact with the chemical on the skin for a short time. The Environmental Protection Agency (EPA) has determined that hexachlorobutadiene is a possible human carcinogen. An animal study found kidney tumours in rats exposed to low levels of hexachlorobutadiene. **OSHA:** Hexachlorobutadiene is listed as a carcinogen. **IARC:** There is inadequate evidence in humans for the carcinogenicity of hexachlorobutadiene.

Chemical Name	Comments
	There is limited evidence in experimental animals for the carcinogenicity of hexachlorobutadiene. Overall evaluation: Hexachlorobutadiene is not classifiable as to its carcinogenicity to humans (Group 3).
Hexachlorocyclopentadiene (HCCPD) **Organo-chlorine** Irritant to skin, eyes, URT and CNS. Not classified by IARC.	**ATSDR:** Hexachlorocyclopentadiene (HCCPD) is a manufactured chemical that does not occur naturally. It is a light, lemon-yellow liquid that has a sharp musty odour. It easily evaporates into the air; the vapour looks like a blue haze. HCCPD is used in the manufacture of certain pesticides. Most of the HCCPD in the environment results from releases during its production and disposal. It is also used to make flame retardants, resins that won't burn, shock-proof plastics, esters, ketones, fluorocarbons, and dyes. Collectively, the pesticides derived from hexachlorocyclopentadiene are called the cyclodienes. Inhalation of high levels of HCCPD vapours, may cause a sore throat or shortness of breath and chest discomfort. Inhalation may result in a headache, and liver and kidney effects. Skin contact can be irritating and corrosive. Animal studies show that when HCCPD is inhaled, it caused bleeding, swelling, and fluid retention in the lungs. Exposure to large amounts caused breathing difficulty and death. Other studies found that swallowing HCCPD caused lung, liver, kidney, brain and heart damage; most of the animals died during the exposure. There is no information available to show whether HCCPD causes cancer in humans. A study in rats and mice did not show an increase in tumours. The EPA has determined that HCCPD is not classifiable as to human carcinogenicity. **OSHA:** Hexachlorocyclopentadiene (HCCPD) is listed as a carcinogen. **IARC:** Not classified.
Methoxychlor **Organo-chlorine** Few data on human toxicity. Toxic to CNS in experimental animals.	**ATSDR:** Methoxychlor is a synthetic organochloride insecticide, now obsolete. Methoxychlor is a manufactured chemical that does not occur naturally in the environment. Pure methoxychlor is a pale-yellow powder with a slight fruity or musty odour. Methoxychlor was used as an insecticide against flies, mosquitoes, cockroaches, and a wide variety of other insects. It was used on agricultural crops and livestock, and in animal feed, barns, grain storage bins, home garden, and on pets. Methoxychlor is also known as DMDT

Chemical Name	Comments
IARC: Group 3 – Not classifiable as to its carcinogenicity to humans.	There is very little information on how methoxychlor affects human health. Animals exposed to very high amounts of methoxychlor suffered tremors and convulsions and seizures. Because methoxychlor is broken down quickly in the body, humans are not likely to experience these effects unless exposed to very high levels. Animal studies show that exposure to methoxychlor in food or water harms the ovaries, uterus, and mating cycle in females, and the testes and prostate in males. Fertility is decreased in both male and female animals. These effects can occur both in adult and in developing animals and could also occur following inhalation or skin contact. These effects are caused by a breakdown product of methoxychlor which acts as a natural sex hormone. These effects have not been reported in humans. Most of the information available from human and animal studies suggests that methoxychlor does not cause cancer. The EPA has determined that methoxychlor is not classifiable as to its carcinogenicity to humans. **OSHA:** Methoxychlor is listed as a carcinogen. **IARC:** The IARC has concluded that methoxychlor is not classifiable as to its carcinogenicity to humans (Group3).
Nitrobenzene **Aromatic amine** Irritant to skin, eyes and URT. Toxic by inhalation and ingestion causing methaemoglobinaemia and CNS toxicity. IARC: Group 2B – Possibly carcinogenic to humans.	**ATSDR:** Nitrobenzene is an industrial chemical. It is an oily yellow liquid with an almond-like odour. It dissolves only slightly in water and will evaporate to air. It is produced in large quantities for use in industry. Most of the nitrobenzene produced is used to manufacture a chemical called aniline. Nitrobenzene is also used to produce lubricating oils such as those used in motors and machinery. A small amount of nitrobenzene is used in the manufacture of dyes, drugs, pesticides, and synthetic rubber. A small amount of nitrobenzene may cause mild irritation if it contacts the skin or eyes directly. Repeated exposures to a high concentration of nitrobenzene can result in methemoglobinemia, a condition in which the blood's ability to carry oxygen is reduced. This results in the skin turning a bluish colour and may also cause nausea, vomiting, and shortness of breath. Effects such as headache, irritability, dizziness, weakness, and drowsiness may also occur. There is also some evidence that breathing high concentrations of nitrobenzene may damage the liver. Animal studies have reported effects on the blood and liver from exposure to nitrobenzene. A single dose of nitrobenzene

Chemical Name	Comments
	fed to male rats resulted in damage to the testicles and decreased levels of sperm. No studies are available on whether nitrobenzene causes cancer in humans. In animals, breathing nitrobenzene resulted in an increase in liver, thyroid, and kidney tumours. **OSHA:** Nitrobenzene is listed as a carcinogen. **IARC:** There is inadequate evidence in humans for the carcinogenicity of nitrobenzene. There is sufficient evidence in experimental animals for the carcinogenicity of nitrobenzene. Overall evaluation: Nitrobenzene is possibly carcinogenic to humans (Group 2B).
N-nitrosodi-n-butylamine **Nitrosamine** Irritant to skin and eyes. IARC: Group 2B – Possibly carcinogenic to humans.	**PubChem:** N-nitrosodi-n-butylamine is a pale-yellow liquid. Inhalation of material may be harmful. Contact may cause burns to skin and eyes. Fire may produce irritating, corrosive and/or toxic gases. **OSHA:** Not listed as a carcinogen. **IARC:** No adequate human studies of the relationship between exposure to N-nitrosodi-n-butylamine and human cancer have been reported N-Nitrosodi-n-butylamine is reasonably anticipated to be a human carcinogen based on sufficient evidence of carcinogenicity in experimental animals. Overall evaluation: N-nitrosodi-n-butylamine is possibly carcinogenic to humans (Group 2B).
N-nitrosodi-n-propylamine **Nitrosamine** Laboratory chemical with few data on human toxicity. IARC: Group 2B – Possibly carcinogenic to humans.	**ATSDR:** N-nitrosodi-n-propylamine is a chemical produced by industry in small amounts for research. It is a yellow liquid at room temperature. Small amounts of n-nitrosodi-n-propylamine are produced as a side reaction during some manufacturing processes, as a contaminant in some weed killers, and during the manufacture of some rubber products. No information is available on the effects of n-nitrosodi-n-propylamine in humans. Studies in animals have shown effects on the liver, lung, stomach, kidneys, and heart at very high doses. No studies are available on whether or not n-nitrosodi-n-propylamine causes cancer in humans. Animal studies have shown an increase in cancer of the liver, nose, and stomach from n-nitrosodi-n-propylamine exposure. The Department of Health and Human Services (DHHS) has

Chemical Name	Comments
	determined that n-nitrosodi-n-propylamine may reasonably be anticipated to be a human carcinogen. **OSHA:** Not listed as a carcinogen. **IARC:** N-nitrosodi-n-propylamine has been evaluated as being possibly carcinogenic to humans (Group 2B).
N-nitrosopiperidine **Nitrosamine** Laboratory chemical with few data on human toxicity. IARC: Group 2B – Possibly carcinogenic to humans.	**PubChem:** N-nitrosopiperidine is a nitrosamine. It is one of the many carcinogens detected in cigarette smoke, and is also found in meat, cheese and spices that have been treated with the preservative sodium nitrite. It has a role as a carcinogenic agent, an apoptosis inducer, a mutagen and an environmental contaminant. It is a nitrosamine and a piperidine. When heated to decomposition this compound emits highly toxic fumes. **OSHA:** Not listed as a carcinogen. **IARC:** N-nitrosopiperidine has been evaluated as being possibly carcinogenic to humans (Group 2B).
Pentachlorobenzene **Organo-chlorine** Irritant to skin, eyes and URT. Not classified by IARC.	**PubChem:** Pentachlorobenzene is a member of the class of pentachlorobenzenes that are benzene with five of the hydrogens being replaced by chlorines. Now classed as a persistent organic pollutant under the Stockholm Convention. It has a role as a persistent organic pollutant. Inhalation of material may be harmful. Contact may cause burns to skin and eyes. Fire may produce irritating, corrosive and/or toxic gases. **OSHA:** Not listed as a carcinogen. **IARC:** Not classified.
Pentachloronitrobenzene (Quintozene) **Organo-chlorine** Irritant and sensitiser to skin, eyes, URT and CNS. Inhalation and ingestion causes CNS and liver toxicity.	**PubChem**: Pentachloronitrobenzene is a C-nitro compound, that is nitrobenzene in which every hydrogen has been replaced by a chlorine. It is a fungicide used on a variety of crops, including cotton, rice and seed grains, but it is no longer approved for use within the European Union. It has a role as an antifungal agrochemical. It is a member of pentachlorobenzenes and an aromatic fungicide. It is a crystalline pale yellow to white solid or powder with a musty moth ball odour. Symptoms of exposure to this compound may include irritation of the skin and eyes.

Chemical Name	Comments
IARC: Group 3 – Not classifiable as to its carcinogenicity to humans.	Skin contact may result in erythema, itching, edema and formation of small vesicles. Skin sensitization may also occur. Eye contact may result in conjunctivitis and corneal injury. Kidney and liver damage may occur. Vomiting may also occur. Exposure to this type of compound can cause central nervous system stimulation, vomiting, diarrhea, paraesthesiae, excitement, giddiness, fatigue, tremors, convulsions, coma, pulmonary edema, hypothermia and liver, kidney and myocardial toxicity. Respiration may be initially accelerated and then later depressed. Chronic exposure to this type of compound leads to headache, loss of appetite, muscular weakness, fine tremors and apprehensive mental state. When heated to decomposition it emits toxic fumes. No information is available on the chronic (long-term), reproductive, developmental, or carcinogenic effects of pentachloronitrobenzene in humans. Chronic exposure of dogs to pentachloronitrobenzene in their diet has been observed to result in damage to the liver. EPA has classified pentachloronitrobenzene as a Group C, possible human carcinogen. **OSHA:** Pentachloronitrobenzene is listed as a carcinogen. **IARC:** Quintozene (pentachloronitrobenzene) was tested in a preliminary study by the oral route in two strains of mice and produced an increased incidence of hepatomas in males of one strain. A feeding study in rats was considered inadequate. Application of quintozene followed by croton oil to mouse skin gave positive results which could not be interpreted due to a lack of adequate controls. No epidemiological studies were available. Overall evaluation: Pentachloronitrobenzene is not classifiable as to its carcinogenicity to humans (Group 3).
Pentachlorophenol (PCP) **Organo-chlorine** Inhalation and ingestion causes systemic toxicity in humans. IARC: Group 1 – Carcinogenic to humans causing non-Hodgkin's lymphoma.	**ATSDR:** Pentachlorophenol is an organochlorine compound used as a pesticide and a disinfectant. First produced in the 1930s, it is marketed under many trade names. Pentachlorophenol is a manufactured chemical that does not occur naturally. Pure pentachlorophenol exists as colorless crystals. Impure pentachlorophenol (the form usually found at hazardous waste sites) is dark gray to brown and exists as dust, beads, or flakes. Humans are usually exposed to impure pentachlorophenol (also called technical grade pentachlorophenol). Pentachlorophenol was widely used as a pesticide and wood preservative. Since 1984, the purchase and use of

Chemical Name	Comments
	pentachlorophenol has been restricted to certified applicators. It is no longer available to the general public. It is still used industrially as a wood preservative for utility poles, railroad ties, and wharf pilings. Studies in workers show that exposure to high levels of pentachlorophenol can cause the cells in the body to produce excess heat. When this occurs, a person may experience a very high fever, profuse sweating, and difficulty breathing. The body temperature can increase to dangerous levels, causing injury to various organs and tissues, and even death. Liver effects and damage to the immune system have also been observed in humans exposed to high levels of pentachlorophenol for a long time. Damage to the thyroid and reproductive system has been observed in laboratory animals exposed to high doses of pentachlorophenol. Some of the harmful effects of pentachlorophenol are caused by the other chemicals present in technical grade pentachlorophenol. Some studies have found an increase in cancer risk in workers exposed to high levels of technical grade pentachlorophenol for a long time, but other studies have not found this. Increases in liver, adrenal gland, and nasal tumours have been found in laboratory animals exposed to high doses of pentachlorophenol. The EPA has determined that pentachlorophenol is a probable human carcinogen. **OSHA:** Pentachlorophenol is listed as a carcinogen. **IARC:** The IARC changed its classification of PCP in 2016 from Group 2B (possibly carcinogenic to humans) to Group 1 – carcinogenic to humans: The insecticide pentachlorophenol (PCP) is classified as a persistent organic pollutant under the Stockholm Convention. PCP is a multipurpose pesticide that has mainly been used as a wood preservative. It has also been used as a biocide in the leather and textile industries. In Europe and North America, the sale to consumers of products containing PCP has been restricted since the 1990s. PCP was re-classified by IARC as carcinogenic to humans (Group 1), based on sufficient evidence that PCP causes non-Hodgkin lymphoma in humans. In all of the available epidemiological studies, exposure to PCP was positively associated with non-Hodgkin lymphoma.
Phenol	**ATSDR:** Phenol is both a manufactured chemical and a natural substance. It is a colorless-to-white solid when pure. The

Chemical Name	Comments
Phenolic Irritant to skin, eyes, URT and CNS. Very toxic by inhalation, ingestion and skin absorption causing liver and heart damage in humans. IARC: Group 3 – Not classifiable as to its carcinogenicity to humans.	commercial product is a liquid. Phenol has a distinct odour that is sickeningly sweet and tarry. Phenol is used primarily in the production of phenolic resins and in the manufacture of nylon and other synthetic fibres. It is also used in chemicals that kill bacteria and fungi in slimes, as a disinfectant and antiseptic, and in medicinal preparations such as mouthwash and sore throat lozenges. It is mildly acidic and requires careful handling due to its propensity to cause chemical burns. Short-term exposure to phenol in the air can cause respiratory irritation, headaches, and burning eyes. Skin exposure to high amounts of phenol causes skin burns, liver damage, dark urine, irregular heartbeat, and may be fatal. Ingestion of high concentrations of phenol has resulted in internal burns and death. In animals, breathing air with high levels of phenol resulted in irritation of the lungs. Repeated exposures induced muscle tremors and loss of coordination. Exposure to high concentrations of phenol in the air for several weeks caused paralysis and severe injury to the heart, liver, kidneys, and lungs, and in some cases, death. Some animals that drank water with very high concentrations of phenol suffered muscle tremors and loss of coordination. Phenol can have beneficial effects when used medically as an antiseptic or anaesthetic. The EPA has determined that phenol is not classifiable as to its carcinogenicity to humans. **OSHA:** Phenol is listed as a carcinogen. **IARC:** There is inadequate evidence in humans for the carcinogenicity of phenol. There is inadequate evidence in experimental animals for the carcinogenicity of phenol. Overall evaluation: Phenol is not classifiable as to its carcinogenicity to humans (Group 3).
Trichlorofluoromethane **Halogenated hydrocarbon** Low toxicity for humans. Not classified by IARC.	**PubChem:** Trichlorofluoromethane is a clear light-coloured, nearly odourless, liquid. It is denser than water. It poses a low acute health hazard to humans. The primary hazard is to the environment. Immediate steps should be taken to limit spread to the environment as it easily penetrates the soil to contaminate groundwater and nearby waterways. Breathing concentrations approaching 10% in air will cause dizziness and drowsiness. Contact with tissues may cause frostbite.

Chemical Name	Comments
	OSHA: Trichlorofluoromethane is listed as a carcinogen. **IARC:** Not classified.
Vinyl acetate **Chemical intermediate** Irritant to skin, eyes, URT and CNS. IARC: Group 2B – Possibly carcinogenic to humans.	**ATSDR:** Vinyl acetate is an industrial chemical that is produced in large amounts in the United States. It is a clear, colourless liquid with a sweet, fruity smell. It is very flammable and may be ignited by heat, sparks, or flames. Vinyl acetate is used to make other industrial chemicals. These chemicals are used mainly to make glues for the packaging and building industries. They are also used to make paints, textiles, and paper. Vinyl acetate is also used as a coating in plastic films for food packaging and as a modifier of food starch. The major effects experienced from breathing high levels of vinyl acetate for a short time are irritated eyes, nose, and throat. Vinyl acetate has caused skin irritation and blisters in workers who accidentally spilled it on their skin. Eye irritation has also been seen when people were exposed to vinyl acetate in the air or through accidents when the chemical went into their eyes. Long-term animal studies show a reduced ability of animals to fight infection when rats and mice ingested high levels of the chemical. Birth defects were not seen in the offspring of animals that were exposed to vinyl acetate in drinking water during their pregnancies. There are no human studies on the carcinogenicity of vinyl acetate. Animal studies have shown mixed results; one study showed an increase in tumours of the noses of rats who breathed vinyl acetate, while another study did not show an increase in tumours in rats who drank water containing the chemical. **OSHA:** Vinyl acetate is listed as a carcinogen. **IARC:** The available data were too limited to form the basis for an evaluation of the carcinogenicity of vinyl acetate to humans. Vinyl acetate was tested in one experiment in mice and in one experiment in rats by inhalation. No treatment-related increase in tumour incidence was observed in mice; in rats, an increased incidence of nasal cavity tumours was found in animals of each sex. No increase in tumour incidence was found in rats administered vinyl acetate in the drinking-water in utero and then for life. Vinyl acetate is rapidly metabolized by esterases in human blood and animal tissues to acetaldehyde and acetic acid.

Chemical Name	Comments
	Vinyl acetate irritates the eye and respiratory system. Respiratory distress is seen after sub-chronic exposure by inhalation. Other effects included nasal irritation, nasal mucosal metaplasia, tracheal metaplasia and bronchitis or bronchiolitis. After chronic exposure by inhalation, changes were observed in the lung. Non-neoplastic effects, atrophic and regenerative changes, were seen in the nasal cavity. After chronic exposure via the drinking-water, the only effects observed were decrements in body weight at high doses. Vinyl acetate induced sperm abnormalities and sister chromatid exchange in rodents exposed in vivo; micronuclei were induced in bone marrow but not in meiotic cells. No DNA binding was seen in rat hepatocytes. In human lymphocytes in vitro, vinyl acetate produced chromosomal aberrations, micronuclei, sister chromatid exchange and DNA cross-links. It enhanced viral transformation and sister chromatid exchange in mammalian cells in vitro, and it induced DNA-protein cross-links in rat nasal epithelial cells in vitro. Vinyl acetate did not induce mutation in bacteria but induced DNA-protein cross-links in plasmid DNA. The primary metabolite of vinyl acetate, acetaldehyde, is genotoxic in a wide range of assays. Overall: There is inadequate evidence in humans for the carcinogenicity of vinyl acetate. There is limited evidence in experimental animals for the carcinogenicity of vinyl acetate. Overall evaluation: Vinyl acetate is possibly carcinogenic to humans (Group 2B).

9.3 Attachment 3 – additional chemicals identified, excluding those in Attachment 2 and those reviewed in ARP1701

Chemical Name	Comments
1,1-dichloropropene **Cis-1,3-dichloropropene** **Trans-1,3-dichloropropene** **Dichloropropenes** Irritant and sensitiser to skin. IARC Group 2B – possibly carcinogenic to humans.	**ATSDR:** Dichloropropenes are synthetic chemicals, and isomers are 1,1-dichloropropene 1,2-dichloropropene 1,3-dichloropropene 2,3-dichloropropene and 3,3-dichloropropene. 1,3-Dichloropropene is a colorless liquid with a sweet smell. It dissolves in water and evaporates easily. It is used mainly in farming as a pesticide. Much less is known about the other dichloropropenes. 2,3-Dichloropropene is used in industry to make other chemicals. No uses were found for 1,1-, 1,2-, or 3,3-dichloropropene. Because1,3-dichloropropene is produced and used in much higher amounts than the other isomers and because it is released to the environment as a pesticide, most of the data available are for 1,3-dichloropropene. Therefore, the focus of this summary is the 1,3-dichloropropene isomer. Exposure to 1,3-dichloropropene occurs mainly in farms where it is used to treat crops or in factories where it is made. Exposure to other dichloropropenes is much more limited. Dichloropropenes cause irritation at the point of contact. Most of the 1,3- and 2,3-dichloropropene that is inhaled or ingested will rapidly enter the bloodstream. Rats and mice that inhaled 1,3-dichloropropene or 2,3-dichloropropene repeatedly had damage to the lining of the nose. Damage to the urinary bladder and anemia were also seen in animals inhaling 1,3-dichloropropene for a long time. Damage to the stomach lining and anemia were seen in animals orally exposed to 1,3-dichloropropene. Skin and eye irritation are seen in animals after 1,3-dichloropropene gets on their skin or in their eyes. A few workers who had skin contact with pesticides containing 1,3-dichloropropene developed blisters and an allergic reaction on their skin. The Department of Health and Human Services (DHHS) has determined that 1,3-dichloropropene may reasonably be anticipated to be a carcinogen. The EPA has classified 1,3-dichloropropene as a probable human carcinogen. **OSHA:** 1,3-dichloropropene is listed as a carcinogen. **IARC**: No epidemiological data relevant to the carcinogenicity of 1,3-dichloropropene were available. There is sufficient evidence in experimental animals for the carcinogenicity of mixed isomers of 1,3-dichloropropene (technical grade). 1,3-Dichloropropene (technical-grade) is possibly carcinogenic to humans (Group 2B).

Chemical Name	Comments
1,2-dibromo-3-chloropropane **Halogenated hydrocarbon** Few data on human toxicity. IARC Group 2B – possibly carcinogenic to humans.	**ATSDR:** 1,2-dibromo-3-chloropropane is a manufactured chemical and is not found naturally in the environment. It is a colorless liquid with a sharp smell. It can be tasted in water at very low concentrations. Some industries use it to make another chemical that is used to make materials that resist burning. Large amounts of 1,2-dibromo-3-chloropropane were used in the past on certain farms to kill pests that harmed crops. The main effect from breathing high levels of 1,2-dibromo-3-chloropropane is damage to the male's ability to reproduce. Studies on workers have shown that men may produce fewer sperm, produce sperm that results in more girl than boy babies, and eventually become unable to father children. It can also cause headaches, nausea, lightheadedness, and weakness in workers. Animals breathing high levels of the chemical were not able to reproduce and had damaged stomachs, livers, kidneys, brains, spleens, blood, and lungs. Breathing low to moderate levels also caused damage to the reproductive system. The ability of people to reproduce was not affected by drinking water contaminated with low levels of 1,2-dibromo-3-chloropropane and there was no increase in the number of birth defects. Rats exposed to high levels did, however, have an increase in birth defects. It can also cause skin and eye damage from direct contact. The Department of Health and Human Services has determined that 1,2-dibromo-3-chloropropane may reasonably be anticipated to be a carcinogen. Animal studies found cancer of the nose in animals exposed by breathing the chemical, cancer of the stomach and kidney in animals that ingested the chemical, and cancer of the stomach and skin in animals who had skin contact with the chemical. **OSHA:** Listed as a carcinogen. **IARC:** There is inadequate evidence in humans for the carcinogenicity of 1,2-dibromo-3-chloropropane. There is sufficient evidence in experimental animals for the carcinogenicity of 1,2-dibromo-3-chloropropane. 1,2-dibromo-3-chloropropane is possibly carcinogenic to humans (Group 2B).
1,4-dinitrobenzene **Aromatic amine** Inhalation may cause anaemia.	**PubChem:** Dinitrobenzenes are chemical compounds composed of a benzene ring and two nitro group substituents. The three possible arrangements of the nitro groups afford three isomers, 1,2-dinitrobenzene, 1,3-dinitrobenzene, and 1,4-dinitrobenzene.

Chemical Name	Comments
Not classified by IARC.	1,3-dinitrobenzene is the most common isomer and it is used in the manufacture of explosives. **ATSDR:** Waste discharges from Army ammunitions plants or other chemical manufacturers are the primary sources for release of both compounds to air, water, and soil. 1,3-Dinitrobenzene and 1,4-dinitrobenzene are suspected to cause similar health effects. Exposure to high concentrations of 1,3-dinitrobenzene can reduce the ability of blood to carry oxygen and can cause the skin to become bluish in colour. If exposed to 1,3-dinitrobenzene for a long time a reduction in the number of red blood cells (anemia) may occur. Other symptoms of 1,3-dinitrobenzene exposure include headache, nausea, and dizziness. It is not known if there are any long-term health effects from exposure to dinitrobenzenes, or if these chemicals cause birth defects in humans. Results of studies in animals show that effects of 1,3-di-nitrobenzene on the blood are similar to the effects seen in people. Results from animal studies also show some other effects of 1,3-dinitrobenzene exposure, such as behavioural changes and male reproductive system damage. The EPA has determined that these compounds are not classifiable as to their carcinogenicity in humans. **OSHA:** Not listed as a carcinogen. **IARC:** Not classified.
2-hexanone (MBK) **VOC** Inhalation causes CNS toxicity. Not classified by IARC.	**ATSDR:** 2-hexanone is also known as methyl n-butyl ketone, MBK, or propyl acetone. It is a clear, colorless liquid with a sharp odour. It dissolves very easily in water and can evaporate easily into the air as a vapour. It was used in the past in paint and paint thinner, to make other chemical substances, and to dissolve oils and waxes. It is no longer made or used in the United States because it has harmful health effects. It is formed as a waste product resulting from industrial activities such as making wood pulp and producing gas from coal, and in oil shale operations. Breathing 2-hexanone can harm the nervous system. Workers who were exposed to 2-hexanone in the air for almost a year felt weakness, numbness, and tingling in the skin of the hands and feet. Similar effects were seen in different animals that ate or breathed high levels of 2-hexanone. Animal studies have shown that ingesting high levels of 2-hexanone harms the nervous system. Also, animals that ingested

Chemical Name	Comments
	2-hexanone experienced decreased body weight and effects on reproduction. The Department of Health and Human Services has not classified 2-hexanone as to human carcinogenicity. **OSHA:** 2-hexanone is listed as a carcinogen. **IARC:** Not classified.
2-nitroaniline **Aromatic amine** Inhalation and ingestion causes methaemoglobinaemia, CNS toxicity, and liver damage. Not classified by IARC.	**PubChem**: 2-nitroaniline is an orange solid with a musty odour. It sinks and mixes slowly with water. Inhalation or ingestion causes headache, nausea, methaemo-globinemia, vomiting, weakness, and stupor; cyanosis caused by contact usually develops in 4-6 hrs.; prolonged and excessive exposure may also cause liver damage. Contact with eyes or skin causes irritation; continued exposure may cause same symptoms as inhalation or ingestion. On combustion, forms toxic fumes of nitrogen oxides. Reacts with strong acids, strong oxidants and strong reducing agents. Reacts with organic materials in the presence of moisture. This generates fire hazard. **OSHA:** Not listed as a carcinogen. **IARC:** Not classified.
2-pentanone **(methyl propyl ketone)** **VOC** Irritant to skin, eyes and URT (upper respiratory tract). Not classified by IARC.	**PubChem:** 2-pentanone (methyl propyl ketone) is found in apples and can be isolated from soya oil, pineapple and other plant sources. It is a colourless liquid ketone with an odour resembling that of acetone. It is sometimes used in very small amounts as a flavouring food additive. Two other ketones, 3-pentanone and methyl isopropyl ketone, are isomers of 2-pentanone Exposure can cause irritation of eyes, nose and throat. **OSHA:** Not listed as a carcinogen. **IARC:** Not classified.
4-bromofluorobenzene **Halogenated hydrocarbon** No data on human toxicity. Not classified by IARC.	**PubChem:** 4-Bromofluorobenzene is a halogenated aromatic organic compound with the formula C_6H_4BrF. It is a derivative of benzene, with a bromine atom bonded para to a fluorine atom. It has uses as a precursor to some pharmaceuticals, as an agrochemical intermediate, and in organic synthesis. **OSHA:** Not listed as a carcinogen. **IARC:** Not classified.

Chemical Name	Comments
4-chloroaniline **Aromatic amine** Inhalation and ingestion causes methaemoglobinaemia, CNS toxicity, and liver damage. Irritant to eyes and URT. IARC: Group 2B – possibly carcinogenic to humans.	**PubChem:** 4-chloroaniline (p-chloroaniline) is a white or pale-yellow solid. Melting point 69.5°C. 4-chloroaniline is a chloroaniline in which the chloro atom is para to the aniline amino group. It is a chloroaniline and a member of monochlorobenzenes. Inhalation or ingestion causes bluish tint to fingernails, lips, and ears indicative of cyanosis; headache, drowsiness, and nausea, followed by unconsciousness. Liquid can be absorbed through skin and cause similar symptoms. Contact with eyes causes irritation. Irritating and toxic hydrogen chloride and oxides of nitrogen may form in fires. **OSHA:** Listed as a carcinogen. **IARC:** para-chloroaniline was tested for carcinogenicity in mice and rats by administration in the diet and by gavage. It produced haemangiosarcomas in male and female mice in different organs after administration in the diet. It induced haemangiosarcomas of the spleen and liver and hepatocellular adenomas and carcinomas in male mice after administration by gavage. It induced sarcomas of the spleen and splenic capsule in male rats in both studies. para-chloroaniline causes methaemoglobinaemia and is metabolized similarly in humans and experimental animals. Evaluation: There is inadequate evidence in humans for the carcinogenicity of para-chloroaniline. There is sufficient evidence in experimental animals for the carcinogenicity of para-chloroaniline. Overall evaluation: para-chloroaniline is possibly carcinogenic to humans (Group 2B).
4-nitroaniline **Aromatic amine** Inhalation and ingestion causes methaemoglobinaemia, CNS toxicity, and liver damage. Not classified by IARC.	**PubChem:** 4-nitroaniline (p-nitroaniline or 1-amino-4-nitrobenzene) is an organic compound with the formula $C_6H_6N_2O_2$. It consists of a benzene ring in which an amino group is para to a nitro group. This chemical is commonly used as an intermediate in the synthesis of dyes, antioxidants, pharmaceuticals, gasoline, gum inhibitors, poultry medicines, and as a corrosion inhibitor. Inhalation or ingestion causes headache, drowsiness, shortness of breath, nausea, methemoglobinemia, and unconsciousness; fingernails, lips, and ears become bluish; prolonged and excessive exposures may also cause liver damage. Contact with eyes causes irritation and possible corneal damage. Contact with skin causes irritation; continued exposure may cause same symptoms as inhalation or ingestion.

Chemical Name	Comments
	OSHA: Not listed as a carcinogen. **IARC:** Not classified.
5-nitro-o-toluidine **Aromatic amine** Inhalation and ingestion causes methaemoglobinaemia, CNS toxicity, and liver damage. Irritant to eyes and URT. IARC: Group 3 – not classifiable as to its carcinogenicity to humans.	**PubChem:** 5-nitro-o-toluidine is a C-nitro compound in which the nitro compound is meta to the amino group and para to the methyl group of o-toluidine. Symptoms of exposure to this chemical include methemoglobinemia and respiratory distress. This compound is an irritant and an experimental carcinogen. It may be absorbed through the skin. When heated to decomposition this compound emits toxic fumes. 5-Nitro-ortho-toluidine is used as an intermediate in the production of a wide assortment of pigments and azo dyes. No data on occupational exposure levels were available. **OSHA:** Not listed as a carcinogen. **IARC:** 5-nitro-ortho-toluidine was tested for carcinogenicity by oral administration in one strain of mice and in one strain of rats. It produced an increase in the incidence of hepatocellular tumours in mice of each sex and a marginal increase in the incidence of hepatocellular carcinomas in male rats. No human carcinogenicity data were available. Overall evaluation: There is limited evidence for the carcinogenicity of 5-nitro-ortho-toluidine in experimental animals (Group 3).
Azinophos methyl **O-P (organo-phosphate)** Very toxic by inhalation, ingestion and skin absorption due to cholinesterase inhibition. Not classified by IARC.	**PubChem:** Azinophos-methyl (also known as Guthion), is an organophosphate pesticide that was used on many crops, especially apples, pears, cherries, peaches, almonds, and cotton. Many of its former uses have been cancelled by the US EPA, and its few remaining uses are currently in the process of being phased out. Guthion is a synthetic substance and does not occur naturally. Pure Guthion is a colourless to white odourless crystalline solid that melts at about 72-74ºC . Technical-grade Guthion is a cream to yellow-brown granular solid. Guthion is poorly soluble in water. It is extremely toxic. Probable oral lethal dose in humans is 5-50 mg/kg, or between 7 drops and 1 teaspoon for a 70 kg person. It is a potent cholinesterase inhibitor which can cause death. **OSHA:** Listed as a carcinogen. **IARC:** Not classified.
Azobenzene	**PubChem:** Azobenzene is a chemical compound composed of two phenyl rings linked by a N=N double bond. It is the simplest

Chemical Name	Comments
VOC Irritant to skin, eyes and URT. Inhalation causes CNS toxicity, liver and kidney damage. IARC: Group 3 – not classifiable as to its carcinogenicity to humans.	example of an aryl azo compound. The term azobenzene or simply azo is often used to refer to a wide class of similar compounds. These azo compounds are considered as derivatives of diazene and are sometimes referred to as diazenes. The diazenes absorb light strongly and are common dyes. Symptoms of exposure to this compound may include irritation of the skin, eyes and respiratory tract; liver and kidney damage; and possible blood disorders. Symptoms of exposure to azobenzene may include cyanosis, headache, shallow respiration, dizziness, confusion, jaundice, pain on urination, anemia, weight loss, weakness, irritability, blood pressure fall, lethargy, stupor, convulsions, coma, and possible death. The nervous system, liver, kidneys, and bone marrow may be affected after chronic exposure. This compound irritates the skin, eyes, and respiratory tract, and can be absorbed through the skin. It is a positive animal carcinogen. When heated to decomposition it emits toxic fumes. **OSHA:** Not listed as a carcinogen. **IARC:** Not classifiable as to its carcinogenicity to humans (Group 3).
Benzyl alcohol **VOC** Irritant to skin, eyes, URT and CNS. Not classified by IARC.	**PubChem:** Benzyl alcohol is a colourless liquid with a sharp burning taste and slight odour. It is used as a local anaesthetic and to reduce pain associated with local anaesthetic injection. Also, it is used in the manufacture of other benzyl compounds, as a pharmaceutical aid, and in a wide variety of cosmetic formulations as a fragrance component, preservative, solvent, and viscosity-decreasing agent. Inhalation of vapor may cause irritation of upper respiratory tract. Prolonged or excessive inhalation may result in headache, nausea, vomiting, and diarrhoea. In severe cases, respiratory stimulation followed by respiratory and muscular paralysis, convulsions, narcosis and death may result. Ingestion may produce severe irritation of the gastrointestinal tract, followed by nausea, vomiting, cramps and diarrhoea; tissue ulceration may result. Contact with eyes causes local irritation. Benzyl alcohol can be absorbed through skin with anaesthetic or irritant effect. **OSHA:** Not listed as a carcinogen. **IARC:** Not classified.

Chemical Name	Comments
Carbazole **Aromatic compound** Irritant to skin, eyes, URT and CNS. IARC: Group 3 – not classifiable as to its carcinogenicity to humans.	**PubChem:** Carbazole occurs as white crystals, plates, leaflets or light tan powder. Sublimes readily. Exhibits strong fluorescence and long phosphorescence on exposure to ultraviolet light. Symptoms of exposure to this compound may include irritation. It may cause allergic reactions. It may also cause dermatitis, bronchitis, coughing, dyspnoea and respiratory distress. Carbazole may be harmful by ingestion, inhalation and skin absorption. It may cause irritation. When heated to decomposition it emits toxic fumes. **OSHA:** Not listed as a carcinogen. **IARC:** No epidemiological data relevant to the carcinogenicity of carbazole were available. There is limited evidence in experimental animals for the carcinogenicity of carbazole. Overall evaluation: Carbazole is not classifiable as to its carcinogenicity to humans (Group 3).
Chlorpyrifos **O-P** Very toxic by inhalation, ingestion and skin absorption due to cholinesterase inhibition. Not classified by IARC.	**ATSDR:** Chlorpyrifos is an organophosphate pesticide that is a white crystal-like solid with a strong odour. It does not mix well with water, so it is usually mixed with oily liquids before it is applied to crops or animals. It may also be applied to crops in a capsule form. Chlorpyrifos has been widely used in homes and on farms. In the home, it is used to control cockroaches, fleas, and termites; it is also used in some pet flea and tick collars. On the farm, it is used to control ticks on cattle and as a spray to control crop pests. Breathing the air in an area in which chlorpyrifos has recently been sprayed may produce a variety of effects on the nervous system including headaches, blurred vision, watering of the eyes, excessive salivation, runny nose, dizziness, confusion, muscle weakness or tremors, nausea, diarrhea, and sudden changes in heart rate. The effect depends on the amount in the air and length of time exposed. Ingesting chlorpyrifos orally through contaminated food containers may cause similar symptoms. Exposure to high levels may cause severe sweating, loss of bowel control, severe muscle tremors, seizures, loss of consciousness (coma), or death. Animal studies have not shown that chlorpyrifos causes cancer. The EPA has classified chlorpyrifos as a possible human carcinogen. **OSHA:** Chlorpyrifos is listed as a carcinogen. **IARC:** Not classified.

Chemical Name	Comments
Cis-chlordane **Mixture of organo-chlorines** Toxic by inhalation, ingestion, and skin absorption causing CNS toxicity and liver damage. IARC: Group 2B – possibly carcinogenic to humans.	**ATSDR:** Chlordane is a manufactured chemical that was used as a pesticide in the United States from 1948 to 1988. Chlordane is not a single chemical, but is a mixture of many related chemicals, of which about 10 are major components. Some of the major components are trans-chlordane, cis-chlordane, ß-chlordene, heptachlor, and trans-nonachlor. It does not occur naturally in the environment. It is a thick liquid whose colour ranges from colourless to amber. Chlordane has a mild, irritating smell. Some of its trade names are Octachlor and Velsicol 1068. Until 1983, chlordane was used as a pesticide on crops like corn and citrus and on home lawns and gardens. Because of concern about damage to the environment and harm to human health, the Environmental Protection Agency (EPA) banned all uses of chlordane in 1983 except to control termites. In 1988, EPA banned all uses. Chlordane affects the nervous system, the digestive system, and the liver in people and animals. Headaches, irritability, confusion, weakness, vision problems, vomiting, stomach cramps, diarrhoea, and jaundice have occurred in people who breathed air containing high concentrations of chlordane or accidentally swallowed small amounts of chlordane. Large amounts of chlordane taken by mouth can cause convulsions and death in people. Long-term skin contact with soil containing high levels of chlordane may cause convulsions. Workers who used chlordane over a long period of time had minor changes in liver function. Animals given high levels of chlordane by mouth for short periods died or had convulsions. Long-term exposure caused harmful effects in the liver of test animals. **OSHA:** Chlordane is listed as a carcinogen. **IARC:** There is inadequate evidence in humans for the carcinogenicity of chlordane. There is sufficient evidence in experimental animals for the carcinogenicity of chlordane. Overall evaluation: Chlordane is possibly carcinogenic to humans (Group 2B).
Coumaphos **O-P**	**PubChem:** Coumaphos is an organothiophosphate insecticide, an organic thiophosphate, and an organochlorine compound. It has a role as an agrochemical, an acaricide, an antinematode drug, an avicide, and a cholinesterase inhibitor. Coumaphos is very toxic, with a probable oral lethal dose of 50-500 mg/kg.

Chemical Name	Comments
Very toxic by inhalation, ingestion and skin absorption due to cholinesterase inhibition. Not classified by IARC.	It may be fatal if inhaled, swallowed, or absorbed through skin. Contact may cause burns to skin and eyes. The symptoms of poisoning are due to the toxicity of all organophosphate chemicals, and are associated with cholinesterase inhibition: excessive salivation, sweating, rhinorrhoea and tearing; muscle twitching, weakness, tremor, incoordination; headache, dizziness, nausea, vomiting, abdominal cramps, diarrhoea; respiratory depression, tightness in chest, wheezing, productive cough, fluid in lungs; and pin-point pupils, sometimes with blurred or dark vision. In severe cases: seizures, incontinence, respiratory depression, loss of consciousness. **OSHA:** Not listed as a carcinogen. **IARC:** Not classified.
Demeton-O **Demeton-S** **O-P** Very toxic by inhalation, ingestion and skin absorption due to cholinesterase inhibition. Not classified by IARC.	**PubChem:** Demeton-O and Demeton-S were phosphonothioate insecticides with the chemical formula $C_8H_{19}O_3PS_2$. While they were previously used as insecticides, they are largely obsolete due to their relatively high toxicity to humans. The chemical structure of demeton is closely related to military nerve agents. Exposures may be fatal if inhaled, swallowed, or absorbed through skin. Contact may cause burns to skin and eyes. The symptoms of poisoning are due to the toxicity of all organophosphate chemicals, and are associated with cholinesterase inhibition: excessive salivation, sweating, rhinorrhoea and tearing; muscle twitching, weakness, tremor, incoordination; headache, dizziness, nausea, vomiting, abdominal cramps, diarrhoea; respiratory depression, tightness in chest, wheezing, productive cough, fluid in lungs; and pin-point pupils, sometimes with blurred or dark vision. In severe cases: seizures, incontinence, respiratory depression, loss of consciousness. **OSHA:** Not listed as a carcinogen. **IARC:** Not classified.
Diazinon **O-P** Very toxic by inhalation, ingestion and skin absorption due to cholinesterase inhibition.	**ATSDR:** Diazinon is the common name of an organophosphate pesticide used to control pest insects in soil, on ornamental plants, and on fruit and vegetable field crops. It was formerly used as the active ingredient in household and garden products used to control pests such as flies, fleas, and cockroaches. Diazinon is a synthetic chemical, it does not occur naturally in the environment.

Chemical Name	Comments
IARC: Group 2A – Probably carcinogenic to humans causing non-Hodgkin's lymphoma.	Pure diazinon is a colorless and practically odourless oil. Preparations used in agriculture and by exterminators contain 85-90% diazinon and appear as a pale to dark-brown liquid. Diazinon preparations sold in the past for home and garden use contained 1-5% diazinon in a liquid or as solid granules. Most diazinon used is in liquid form, but it is possible to be exposed to the solid form. Diazinon does not dissolve easily in water and does not burn easily. Most diazinon that is ingested will enter the bloodstream, but very little will enter the bloodstream if there is skin contact with it. Most cases of unintentional diazinon poisoning in people have resulted from short exposures to very high concentrations of the material. These very high levels have occasionally resulted in death. Diazinon affects mainly the nervous system regardless of the route of exposure. Some mild signs and symptoms of poisoning include headache, dizziness, weakness, feelings of anxiety, constriction of the pupils, and blurred vision. More severe symptoms include nausea and vomiting, abdominal cramps, slow pulse, diarrhea, pinpoint pupils, difficulty breathing, coma, and possibly death. These effects also occur in animals exposed to high doses of diazinon. There is no evidence that long-term exposure to low levels of diazinon causes harmful effects in humans. Diazinon has not been shown to cause cancer in humans or in animals. The Department of Health and Human Services (DHHS), and the EPA have not classified diazinon as to its carcinogenicity. **OSHA:** Diazinon is listed as a carcinogen. **IARC:** For the insecticide diazinon, there was limited evidence of carcinogenicity in humans for non-Hodgkin lymphoma and lung cancer. The evidence in humans was from studies of agricultural exposures in the USA and Canada published since 2001. The classification of diazinon in Group 2A was also based on strong evidence that diazinon induced DNA or chromosomal damage. Diazinon is classified as probably carcinogenic to humans (Group 2A).
Dichlorvos **Organo-chlorine** Inhalation and ingestion causes CNS toxicity.	**ATSDR:** Dichlorvos is an insecticide that is a dense colorless liquid. It has a sweetish smell and readily mixes with water. Dichlorvos used in pest control is diluted with other chemicals and used as a spray. It can also be incorporated into plastic that slowly releases the chemical. Dichlorvos is used for insect control in food storage areas, green houses, and barns, and control of insects on livestock. It is not generally used on outdoor crops. Dichlorvos is sometimes used

Chemical Name	Comments
IARC: Group 2B – possibly carcinogenic to humans.	for insect control in workplaces and in the home. Veterinarians use it to control parasites on pets. The major effect of dichlorvos is on the nervous system. Studies on people who were exposed to dichlorvos by breathing air in the workplace containing low levels of dichlorvos have not shown any harmful effects. Animal studies have shown that breathing high levels can cause nervous system effects. Ingesting large doses may cause nausea and vomiting, restlessness, sweating, and muscle tremors, while very large doses may cause coma, inability to breathe, and death. Animal studies have also shown effects on the nervous system when animals drank water or ate food containing dichlorvos. It is not known whether dichlorvos causes cancer in people. A study in rats and mice reported that rats had an increase in cancer of the pancreas and in leukemia, and female mice had an increase in stomach cancer after they were fed dichlorvos for 2 years. The Department of Health and Human Services (DHHS) has determined that dichlorvos may reasonably be anticipated to be a carcinogen. The EPA has determined that dichlorvos is a probable human carcinogen. **OSHA:** Dichlorvos is listed as a carcinogen. **IARC:** There is inadequate evidence in humans for the carcinogenicity of dichlorvos. There is sufficient evidence in experimental animals for the carcinogenicity of dichlorvos. Overall evaluation: Dichlorvos is possibly carcinogenic to humans (Group 2B).
Dimethoate **O-P** Very toxic by inhalation, ingestion and skin absorption due to cholinesterase inhibition. Not classified by IARC.	**PubChem:** Dimethoate is a widely used organophosphate insecticide and acaricide. It was patented and introduced in the 1950s. Like other organophosphates, dimethoate is an acetylcholinesterase inhibitor which disables cholinesterase, an enzyme essential for central nervous system function. It acts both by skin contact and ingestion. It is readily absorbed and distributed throughout plant tissues and is degraded relatively rapidly. Dimethoate is very toxic with the probable oral lethal dose in humans being between 50-500 mg/kg. Dimethoate is a cholinesterase inhibitor, meaning it affects the central nervous system. The symptoms of poisoning are due to the toxicity common to all organophosphate chemicals, and are associated with cholinesterase inhibition: excessive salivation, sweating, rhinorrhoea and tearing; muscle twitching, weakness, tremor, incoordination; headache, dizziness, nausea, vomiting,

Chemical Name	Comments
	abdominal cramps, diarrhoea; respiratory depression, tightness in chest, wheezing, productive cough, fluid in lungs; and pin-point pupils, sometimes with blurred or dark vision. In severe cases: seizures, incontinence, respiratory depression, loss of consciousness. Death is due to respiratory arrest arising from failure of respiratory centre, paralysis of respiratory muscles, intense bronchoconstriction or all three. Dimethoate has been found to be highly carcinogenic in Osborne-Mendel rats. Neoplasms at all sites, as well as malignant neoplasms, were increased in both low and high doses of dimethoate-treated male rats in the National Cancer Institute study. The malignant neoplasms were both carcinomas and sarcomas. Neoplasms of the endocrine organs, particularly carcinomas, were increased in male and female rats given dimethoate. These carcinomas were observed in the adrenal, thyroid, and pituitary glands. Neoplasms were also increased in the liver of male and female rats and in the reproductive organs of female rats given dimethoate. Male and female rats treated with dimethoate developed monocytic leukemia. There also were toxic changes in rats. Male rats had atrophy of the testes, chronic renal disease, parathyroid hyperplasia, and polyarteritis. Wistar male and female rats given dimethoate by gavage or intramuscularly developed a significant increase in malignant neoplasms, mainly sarcomas, and granulocytic leukemia. AB male and female mice also had an increased incidence of malignant neoplasms and granulocytic leukemia after dermal applications of dimethoate. **OSHA:** Not listed as a carcinogen. **IARC:** Not classified.
Disulfoton **O-P** Very toxic by inhalation, ingestion and skin absorption due to cholinesterase inhibition. Not classified by IARC.	**ATSDR:** Disulfoton is an organophosphate acetylcholinesterase inhibitor used as an insecticide. Disulfoton is a manufactured substance used as a pesticide to control a variety of harmful pests that attack many field and vegetable crops. It does not occur naturally. Pure disulfoton is a colourless oil with an unidentifiable characteristic odour and taste. The technical product is dark yellowish, with an aromatic odour. Although it is used mostly in agriculture, small quantities are used on home and garden plants, and for mosquito control in swamps. The use of disulfoton has decreased in recent years. Disulfoton is a cholinesterase inhibitor, meaning it affects the central nervous system. The symptoms of poisoning are due to the toxicity common to all organophosphate chemicals, and are associated with cholinesterase inhibition: excessive salivation, sweating, rhinorrhoea and tearing; muscle twitching, weakness,

Chemical Name	Comments
	tremor, incoordination; headache, dizziness, nausea, vomiting, abdominal cramps, diarrhoea; respiratory depression, tightness in chest, wheezing, productive cough, fluid in lungs; and pin-point pupils, sometimes with blurred or dark vision. In severe cases: seizures, incontinence, respiratory depression, loss of consciousness. Death is due to respiratory arrest arising from failure of respiratory centre, paralysis of respiratory muscles, intense bronchoconstriction or all three. Ingesting high levels of disulfoton can cause similar nervous system (neurologic) effects in animals. Animals that ingested disulfoton for long periods became nearsighted, and the structures of their eyes were damaged. The Department of Health and Human Services (DHHS, and the EPA have not classified disulfoton as to its ability to cause cancer. **OSHA:** Disulfoton is listed as a carcinogen. **IARC:** Not classified.
EPN **(Ethyl p-nitrophenyl benzenethiophosphonate)** **O-P** Very toxic by inhalation, ingestion and skin absorption due to cholinesterase inhibition. Not classified by IARC.	**PubChem:** EPN (ethyl p-nitrophenyl benzenethiophosphonate) is an organothiophosphorus cholinesterase inhibitor that is used as an insecticide and as a acaricide. This material may be fatal if swallowed. It is poisonous if inhaled and extremely hazardous by skin contact. Repeated exposure may, without symptoms, be increasingly hazardous. The estimated fatal oral dose is 0.3 grams for a 70 kg person. The symptoms of poisoning are due to the toxicity common to all organophosphate chemicals, and are associated with cholinesterase inhibition: excessive salivation, sweating, rhinorrhoea and tearing; muscle twitching, weakness, tremor, incoordination; headache, dizziness, nausea, vomiting, abdominal cramps, diarrhoea; respiratory depression, tightness in chest, wheezing, productive cough, fluid in lungs; and pin-point pupils, sometimes with blurred or dark vision. In severe cases: seizures, incontinence, respiratory depression, loss of consciousness. Death is due to respiratory arrest arising from failure of respiratory centre, paralysis of respiratory muscles, intense bronchoconstriction or all three. Decomposes on heating. This produces toxic and corrosive fumes including nitrogen oxides, phosphorus oxides and sulphur oxides. **OSHA:** EPN is listed as a carcinogen. **IARC:** Not classified.

Chemical Name	Comments
Ethoprop (Ethoprophos) **O-P** Very toxic by inhalation, ingestion and skin absorption due to cholinesterase inhibition. Not classified by IARC.	**PubChem:** Ethoprop (Ethoprophos) is an organophosphate acetylcholinesterase inhibitor used as an insecticide. It is an organic thiophosphate and an organothiophosphate. This material is extremely toxic, with the probable oral lethal dose for humans being 5-50 mg/kg. The symptoms of poisoning are due to the toxicity common to all organophosphate chemicals, and are associated with cholinesterase inhibition: excessive salivation, sweating, rhinorrhoea and tearing; muscle twitching, weakness, tremor, incoordination; headache, dizziness, nausea, vomiting, abdominal cramps, diarrhoea; respiratory depression, tightness in chest, wheezing, productive cough, fluid in lungs; and pin-point pupils, sometimes with blurred or dark vision. In severe cases: seizures, incontinence, respiratory depression, loss of consciousness. Death is due to respiratory arrest arising from failure of respiratory centre, paralysis of respiratory muscles, intense bronchoconstriction or all three. Gives off irritating or toxic fumes or gases in a fire. **OSHA:** Not listed as a carcinogen. **IARC:** Not classified.
Ethyl methanesulfonate **Research chemical** Irritant to skin, eyes, URT and CNS. IARC: Group 2B – Possibly carcinogenic to humans.	**PubChem:** Ethyl methanesulfonate is a sulfonoxyalkane with carcinogenic and teratogenic properties. Ethyl methanesulfonate ethylates DNA, thereby damaging DNA and leading to genetic mutations, single-stranded breaks in DNA, and chromosomal aberrations. Ethyl methanesulfonate may be used experimentally in biomedical research. It is clear colourless liquid denser than water. Symptoms of exposure to this compound may include irritation of the skin, eyes, respiratory tract and mucous membranes, dermatitis, nausea, vomiting, central nervous system depression and fibrosis. It may cause decreased visual acuity. This compound is an irritant of the skin, eyes and mucous membranes. When heated to decomposition it emits toxic fumes of sulphur oxides. **OSHA:** Not listed as a carcinogen. **IARC:** Ethyl methanesulfonate (EM) is carcinogenic in mice and rats following subcutaneous or intraperitoneal injection, being the only species and routes tested. It produced mainly lung and kidney tumours in both species. It is carcinogenic following administration of a single dose. No case reports or epidemiological studies were available.

Chemical Name	Comments
	Overall evaluation: Ethyl methanesulfonate is possibly carcinogenic to humans (Group 2B).
Fenitrothion **O-P** Very toxic by inhalation, ingestion and skin absorption due to cholinesterase inhibition. Not classified by IARC.	**PubChem:** Fenitrothion is an organothiophosphate cholinesterase inhibitor that is used as an insecticide. It is a brownish-yellow oil. Used as a selective acaricide and a contact and stomach insecticide against chewing and sucking insects on rice, orchard fruits, vegetables, cereals, cotton and forest. Also used against flies, mosquitoes, and cockroaches. This compound is an organophosphate insecticide. It is a highly toxic cholinesterase inhibitor, that acts on the nervous system. Does not cause delayed neurotoxicity and contact produces little irritation. The symptoms of poisoning are due to the toxicity common to all organophosphate chemicals, and are associated with cholinesterase inhibition: excessive salivation, sweating, rhinorrhoea and tearing; muscle twitching, weakness, tremor, incoordination; headache, dizziness, nausea, vomiting, abdominal cramps, diarrhoea; respiratory depression, tightness in chest, wheezing, productive cough, fluid in lungs; and pin-point pupils, sometimes with blurred or dark vision. In severe cases: seizures, incontinence, respiratory depression, loss of consciousness. Death is due to respiratory arrest arising from failure of respiratory centre, paralysis of respiratory muscles, intense bronchoconstriction or all three. **OSHA:** Not listed as a carcinogen. **IARC:** Not classified.
Fensulfothion **O-P** Very toxic by inhalation, ingestion and skin absorption due to cholinesterase inhibition. Not classified by IARC.	**PubChem:** Fensulfothion is an insecticide and nematicide. It is highly toxic and listed as an extremely hazardous substance. It is widely used on corn, onions, rutabagas, pineapple, bananas, sugar cane, sugar beets, and pea nuts. It is an organic thiophosphate, a sulfoxide and an organothiophosphate and an acetylcholinesterase inhibitor. It displays cholinesterase inhibiting properties. The symptoms of poisoning are due to the toxicity common to all organophosphate chemicals, and are associated with cholinesterase inhibition: excessive salivation, sweating, rhinorrhoea and tearing; muscle twitching, weakness, tremor, incoordination; headache, dizziness, nausea, vomiting, abdominal cramps, diarrhoea; respiratory depression, tightness in chest, wheezing, productive cough, fluid in lungs; and pin-point pupils, sometimes with blurred or dark vision. In severe cases: seizures, incontinence, respiratory depression, loss of consciousness.

Chemical Name	Comments
	Death is due to respiratory arrest arising from failure of respiratory centre, paralysis of respiratory muscles, intense bronchoconstriction or all three. **OSHA:** Fensulfothion is listed as a carcinogen. **IARC:** Not classified.
Fenthion **O-P** Very toxic by inhalation, ingestion and skin absorption due to cholinesterase inhibition. Not classified by IARC.	**PubChem:** Fenthion is an organothiophosphate insecticide, avicide, and acaricide. Like most other organophosphates, its mode of action is via cholinesterase inhibition. Due to its relatively low toxicity towards humans and mammals, fenthion is listed as moderately toxic compound in U.S. Environmental Protection Agency and World Health Organization toxicity class. The symptoms of poisoning are due to the toxicity common to all organophosphate chemicals, and are associated with cholinesterase inhibition: excessive salivation, sweating, rhinorrhoea and tearing; muscle twitching, weakness, tremor, incoordination; headache, dizziness, nausea, vomiting, abdominal cramps, diarrhoea; respiratory depression, tightness in chest, wheezing, productive cough, fluid in lungs; and pin-point pupils, sometimes with blurred or dark vision. In severe cases: seizures, incontinence, respiratory depression, loss of consciousness. Decomposes on heating producing toxic fumes including phosphorus oxides and sulphur oxides. **OSHA:** Fenthion is listed as a carcinogen. **IARC:** Not classified.
Hexachloropropene **Organo-chlorine** Very toxic causing multiple systemic effects by inhalation, ingestion and skin absorption. Not classified by IARC.	**PubChem:** Hexachloropropene is a clear colorless liquid. Insoluble in water. It is used as a plasticizer and hydraulic fluid. It is highly toxic, and may be fatal if inhaled, swallowed or absorbed through skin. Skin contact should be avoided. Effects of contact or inhalation may be delayed. Fire may produce irritating, corrosive and/or toxic gases. Runoff from fire control, or dilution water, may be corrosive and/or toxic and cause pollution. **OSHA:** Not listed as a carcinogen. **IARC:** Not classified.
Isophorone	**ATSDR:** Isophorone is a clear liquid that smells like peppermint. It can be dissolved in water and evaporates faster than water. It is an industrial chemical used as a solvent in some printing inks,

Chemical Name	Comments
Industrial and naturally occurring chemical Low toxicity but irritant to skin, eyes and URT. Not classified by IARC.	paints, lacquers, and adhesives. It is also used as an intermediate in the production of certain chemicals. Although isophorone is an industrial chemical, it also occurs naturally in cranberries. The only effects of isophorone reported by people who have been exposed are irritation of the skin, eyes, nose, and throat, and dizziness and fatigue. These effects have occurred in workers who breathed vapours of isophorone and other chemicals in the printing industry. Short-term exposure of animals to high levels of isophorone has caused inactivity and coma. Some animal studies suggest that isophorone may cause birth defects and slower growth in the offspring of rats and mice that breathed the vapours during pregnancy. When rats and mice were given high doses of isophorone in food or water for a long time, the male rats developed kidney disease. No studies are available on whether isophorone causes cancer in people. In male rats, isophorone caused an increase in tumours of the kidney, liver, and lymph and reproductive glands when they were exposed to it by ingestion. There was no increase in tumours in female rats or mice. The EPA has determined that isophorone is a possible human carcinogen, based on adequate evidence in animals and inadequate evidence in people. **OSHA:** Isophorone is listed as a carcinogen. **IARC:** Not classified.
Isosafrole **Fragrance chemical** Few data on human toxicity. IARC: Group3 – Not classifiable as to its carcinogenicity to humans.	**PubChem:** Isosafrole is an organic compound that is used in the fragrance industry. Structurally, the molecule is related to phenylpropene, a type of aromatic organic chemical. Its fragrance is reminiscent of anise or liquorice. It is found in small amounts in various essential oils but is most commonly obtained by isomerizing the plant oil safrole. It exists as two geometric isomers, cis-isosafrole and trans-isosafrole. It is used in small quantities in root beer and sarsaparilla flavours. Isosafrole is a member of benzodioxoles. The toxicological effects of isosafrole have not been thoroughly studied. The EPA's Office of Health and Environmental Assessment has designated isosafrole as a group B2 chemical. As a group B2 chemical, isosafrole is considered probably carcinogenic to humans.

Chemical Name	Comments
	OSHA: Not listed as a carcinogen. **IARC:** Isosafrole is carcinogenic in mice and rats producing liver tumours following oral administration. No case reports or epidemiological studies were available. Overall evaluation: Isosafrole is not classifiable as to its carcinogenicity to humans (Group 3).
Malathion **O-P** Very toxic by inhalation, ingestion and skin absorption due to cholinesterase inhibition. IARC: Group 2A – Probably carcinogenic to humans.	**ATSDR:** Malathion is an organophosphate insecticide of relatively low human toxicity. It does not occur naturally. Pure malathion is a colourless liquid, and technical-grade malathion, which contains >90% malathion and impurities in a solvent, is a brownish-yellow liquid that smells like garlic. Malathion is used to kill insects on farm crops and in gardens, to treat lice on humans, and to treat fleas on pets. Malathion is also used to kill mosquitos and Mediterranean fruit flies (medflies) in large outdoor areas. On the basis of studies in humans, dermal exposure occurring occupationally and oral exposure via the diet are important routes of exposure to malathion. The symptoms of poisoning are due to the toxicity common to all organophosphate chemicals, and are associated with cholinesterase inhibition: excessive salivation, sweating, rhinorrhoea and tearing; muscle twitching, weakness, tremor, incoordination; headache, dizziness, nausea, vomiting, abdominal cramps, diarrhoea; respiratory depression, tightness in chest, wheezing, productive cough, fluid in lungs; and pin-point pupils, sometimes with blurred or dark vision. In severe cases: seizures, incontinence, respiratory depression, loss of consciousness. There is no conclusive proof that malathion causes cancer in humans, although some studies have found increased incidence of some cancers in people who are regularly exposed to pesticides, such as farmers and pesticide applicators. **OSHA:** Malathion is listed as a carcinogen. **IARC:** There is limited evidence in humans for the carcinogenicity of malathion. Positive associations have been observed with non-Hodgkin lymphoma and cancer of the prostate. There is sufficient evidence in experimental animals for the carcinogenicity of malathion. Overall evaluation: Malathion is probably carcinogenic to humans (Group 2A).
Methyl methanesulfonate	**PubChem:** Methyl methanesulfonate is a stable, colorless, combustible liquid that emits toxic fumes of sulfoxide when heated to decomposition. Methyl methanesulfonate is used for

Chemical Name	Comments
Laboratory chemical Irritant to skin, eyes and URT. IARC: Group 2A – Probably carcinogenic to humans.	laboratory purposes as a catalyst in chemical synthesis and has been tested clinically as a cancer chemotherapeutic agent. This substance is an alkylating agent and acts as a mutagen by altering and damaging DNA and is reasonably anticipated to be a human carcinogen. Symptoms of exposure to methyl methanesulfonate may include irritation of the eyes, skin, mucous membranes, nose and respiratory tract. It can cause dermatitis and nausea. Large doses ingested over nearly a year produced gastrointestinal and hepatic toxic effects. It is corrosive and cause eye, nasal, respiratory and mucous membrane irritation. It is harmful if swallowed, inhaled or absorbed through the skin. When heated to decomposition it emits toxic fumes. **OSHA:** Not listed as a carcinogen. **IARC:** No epidemiological data relevant to the carcinogenicity of methyl methanesulfonate were available. There is sufficient evidence in experimental animals for the carcinogenicity of methyl methanesulfonate. Overall evaluation: Methyl methanesulfonate is probably carcinogenic to humans (Group 2A). In making the overall evaluation, the IARC took into consideration that methyl methanesulfonate is a direct-acting methylating agent which is mutagenic in a wide range of in-vivo and in-vitro test systems.
Methyl parathion **Parathion** **O-P** Very toxic by inhalation, ingestion and skin absorption due to cholinesterase inhibition. IARC: Group 3 – Not classifiable as to its carcinogenicity to humans.	**ATSDR:** Methyl parathion is an is an organophosphate insecticide and acaricide. It does not occur naturally in the environment. Pure methyl parathion exists as white crystals. Impure methyl parathion is a brownish liquid that smells like rotten eggs. Methyl parathion is used to kill insects on farm crops, especially cotton. The EPA now restricts how methyl parathion can be used and applied. Methyl parathion interferes with the normal way that the nerves and brain function. The symptoms of poisoning are due to the toxicity common to all organophosphate chemicals, and are associated with cholinesterase inhibition: excessive salivation, sweating, rhinorrhoea and tearing; muscle twitching, weakness, tremor, incoordination; headache, dizziness, nausea, vomiting, abdominal cramps, diarrhoea; respiratory depression, tightness in chest, wheezing, productive cough, fluid in lungs; and pin-point pupils, sometimes with blurred or dark vision. In severe cases: seizures, incontinence, respiratory depression, loss of consciousness, and death.

Chemical Name	Comments
	Changes in mental state may last several months after exposure to high levels of methyl parathion has ended. If people are exposed to levels of methyl parathion below those that affect nerve function, few or no health problems seem to occur. A reduced ability to fight infections has also been seen in some animal studies; There is no evidence that methyl parathion causes cancer in people who are regularly exposed, such as farmers and pesticide applicators, or in animals. The EPA has determined that methyl parathion is not classifiable as to human carcinogenicity. **OSHA:** Methyl parathion is listed as a carcinogen. **IARC:** Methyl parathion was tested adequately by oral administration in the diet of mice and rats. There was no increase in tumour incidence over that in controls Overall evaluation: Methyl parathion is not classifiable as to its carcinogenicity to humans (Group 3).
Mevinphos (Phosdrin) **O-P** Very toxic by inhalation, ingestion and skin absorption due to cholinesterase inhibition. Not classified by IARC.	**PubChem:** Mevinphos is an organophosphate cholinesterase inhibitor that is used as an insecticide. This material is very toxic, with the oral lethal dose for humans being less than 5 mg/kg. It has direct and immediate effects whether it is swallowed, inhaled, or absorbed through the skin. Mevinphos interferes with the normal way that the nerves and brain function. The symptoms of poisoning are due to the toxicity common to all organophosphate chemicals, and are associated with cholinesterase inhibition: excessive salivation, sweating, rhinorrhoea and tearing; muscle twitching, weakness, tremor, incoordination; headache, dizziness, nausea, vomiting, abdominal cramps, diarrhoea; respiratory depression, tightness in chest, wheezing, productive cough, fluid in lungs; and pin-point pupils, sometimes with blurred or dark vision. In severe cases: seizures, incontinence, respiratory depression, loss of consciousness, and death. It decomposes on heating. This produces toxic and corrosive fumes including phosphoric acid and phosphorus oxides. **OSHA:** Mevinphos is listed as a carcinogen. **IARC:** Not classified.
Naled (Dibrom)	**PubChem:** Naled is an organophosphate cholinesterase inhibitor that is used as an insecticide and as an acaricide.

Chemical Name	Comments
O-P Very toxic by inhalation, ingestion and skin absorption due to cholinesterase inhibition. Not classified by IARC.	Naled is a white solid that may be dissolved in a liquid organic carrier. It has a pungent odour. The symptoms of poisoning are due to the toxicity common to all organophosphate chemicals, and are associated with cholinesterase inhibition: excessive salivation, sweating, rhinorrhoea and tearing; muscle twitching, weakness, tremor, incoordination; headache, dizziness, nausea, vomiting, abdominal cramps, diarrhoea; respiratory depression, tightness in chest, wheezing, productive cough, fluid in lungs; and pin-point pupils, sometimes with blurred or dark vision. In severe cases: seizures, incontinence, respiratory depression, loss of consciousness, and death. It decomposes on heating and on contact with acids and oxidants. This produces toxic and corrosive fumes. **OSHA:** Naled is listed as a carcinogen. **IARC:** Not classified.
N-nitrosodiethylamine **Nitrosamine** Irritant to the skin, eyes and URT. IARC: Group 2A – Probably carcinogenic to humans.	**PubChem:** N-nitrosodiethylamine is a nitrosamine derivative with alkylating, carcinogenic, and mutagenic properties. N-nitrosodiethylamine is a clear slightly yellow liquid. It can reasonably be anticipated to be a carcinogen. It is used as a gasoline and lubricant additive and as an antioxidant and stabilizer in plastics. Contact can irritate the skin and eyes. The vapours cause respiratory tract irritation. When heated to decomposition this compound emits toxic fumes of nitrogen oxides. **OSHA:** Not listed as a carcinogen. **IARC:** There is sufficient evidence of a carcinogenic effect of N-nitrosodiethylamine in many experimental animal species. Although no epidemiological data were available, N-nitrosodiethylamine should be regarded for practical purposes as if it were carcinogenic to humans. Overall evaluation: N-nitrosodiethylamine is probably carcinogenic to humans (Group 2A).
N-nitrosomorpholine **Nitrosamine** Few data on human toxicity.	**PubChem:** N-nitrosomorpholine is a yellow, crystalline nitrosamine that is sensitive to light. N-nitrosomorpholine is not used or produced commercially in the US. This substance has been found as a contaminant in rubber products, including rubber nipples for baby bottles, and is also found in several vegetables, cheeses, alcoholic beverages and fruits.

Chemical Name	Comments
IARC: Group 2B – Possibly carcinogenic to humans.	No information is available on the acute (short-term), chronic (long-term), reproductive, developmental, or carcinogenic effects of N-nitrosomorpholine in humans. Animal studies have reported effects on the liver from chronic exposure as well as tumours of the liver, nasal cavity, lung, and kidneys from oral exposure to N-nitrosomorpholine. When heated to decomposition this compound emits toxic fumes of nitrogen oxides. The EPA has not classified N-nitrosomorpholine for carcinogenicity. **OSHA:** Not listed as a carcinogen. **IARC:** N-nitrosomorpholine is carcinogenic in mice, rats, Syrian golden, Chinese and European hamsters and various fish. Following its oral administration, it produces benign and malignant tumours of the liver and lung in mice, of the liver, kidney and blood vessels in rats, and of the liver in hamsters. After its subcutaneous injection it produces tumours of the upper digestive and respiratory tracts in hamsters; it is carcinogenic after its administration in single doses. It produces liver tumours in rats following its intravenous injection. It produces liver tumours in various fish following its administration in tank-water. A study in hamsters has been reported in which a dose-response relationship was established. No case reports or epidemiological studies were available. Overall evaluation: There is sufficient evidence for a carcinogenic effect of N-nitrosomorpholine in several experimental animal species. Although no epidemiological data were available, N-nitrosomorpholine should be regarded as possibly carcinogenic to humans (Group 2B).
N-nitrosopyrrolidine **Nitrosamine** Irritant to the skin, eyes and URT. IARC: Group 2B – Possibly carcinogenic to humans.	**PubChem:** N-nitrosopyrrolidine is a clear, yellow, oily, liquid nitrosamine. It is used in laboratory research to induce tumours in experimental animals. This substance may be formed during cooking of foods that contain sodium nitrite as a preservative, including meat, fish and cheese. Exposure to N- nitrosopyrrolidine irritates the skin and eyes and can damage the liver and kidneys. This substance is reasonably anticipated to be a human carcinogen. It decomposes when exposed to light and emits toxic fumes of nitrogen oxides when heated to decomposition. **OSHA:** Not listed as a carcinogen.

Chemical Name	Comments
	IARC: N-nitrosopyrrolidine has been evaluated as being possibly carcinogenic to humans (Group 2B).
o-toluidine **Aromatic amine** Highly toxic by inhalation, ingestion and skin absorption causing methaemoglobinaemia and CNS toxicity. IARC: Group 1 – Carcinogenic to humans causing cancer of the urinary bladder.	**PubChem:** There are three isomers of toluidine, which are organic compounds. These isomers are o-toluidine, m-toluidine, and p-toluidine. All three are aryl amines whose chemical structures are similar to aniline except that a methyl group is substituted onto the benzene ring. The difference between these three isomers is the position where the methyl group is bonded to the ring relative to the amino functional group. The chemical properties of the toluidines are quite similar to those of aniline and toluidines have properties in common with other aromatic amines. None of the toluidines is very soluble in pure water but will become soluble if the aqueous solution is acidic due to formation of ammonium salts, as usual for organic amines. At room temperature and pressure, o- and m-toluidines are viscous liquids, but p-toluidine is a flaky solid. o-toluidine is primarily used in the manufacture of dyes. o-toluidine is highly toxic to humans when absorbed through the skin, inhaled as vapor, or swallowed. Acute (short-term) exposure of humans to o-toluidine affects the blood (i.e., methemoglobinemia), with clinical signs of central nervous system depression. The chronic (long-term) effects in workers exposed to o-toluidine include anemia, anorexia, weight loss, skin lesions, central nervous system depression, cyanosis, and methemoglobinemia. Animal studies indicate that chronic exposure to o-toluidine causes effects on the spleen, liver, urinary bladder, and blood. Occupational exposure to dyestuffs (including o-toluidine) is associated with an increased risk of bladder cancer. o-Toluidine has been classified by EPA as a Group B2, probable human carcinogen. **OSHA:** o-toluidine is listed as a carcinogen. **IARC:** There is sufficient evidence in humans for the carcinogenicity of ortho-toluidine (o-toluidine). It causes cancer of the urinary bladder. There is sufficient evidence in experimental animals for the carcinogenicity of o-toluidine. There is moderate mechanistic evidence indicating that the carcinogenicity of o-toluidine involves metabolic activation, formation of DNA adducts, and induction of DNA-damaging effects. Overall evaluation: o-toluidine is carcinogenic to humans (Group 1).

Chemical Name	Comments
Parathion	See methyl parathion above.
Pentachloroethane **VOC** Irritant to skin, eyes, URT and CNS. Inhalation causes CNS toxicity. IARC: Group 3 – Not classifiable as to its carcinogenicity to humans.	**PubChem:** Pentachloroethane is a non-flammable but toxic chemical compound of chlorine, hydrogen, and carbon. It is used as a solvent for oil and grease, in metal cleaning, and in the separation of coal from impurities. It can cause Irritation of skin, lungs, eyes, and mucous membranes. Repeated or heavy inhalation causes depression of central nervous system with toxicity similar to tetrachloroethanes. In a fire it decomposes and produces toxic gases. **OSHA:** Pentachloroethane is listed as a carcinogen. **IARC:** No epidemiological data relevant to the carcinogenicity of pentachloroethane were available. There is limited evidence in experimental animals for the carcinogenicity of pentachloroethane. Overall evaluation: Pentachloroethane is not classifiable as to its carcinogenicity to humans (Group 3).
Phenacetin **Pharmaceutical** Toxic by ingestion causing methaemoglobinaemia and nephropathy. IARC: Group 1 – Carcinogenic to humans causing cancer of the renal pelvis and ureter.	**PubChem:** Phenacetin is a pain-relieving and fever-reducing drug, which was widely used between its introduction in 1887 and the ban imposed by the U.S. Food and Drug Administration in 1983. It is a phenylacetamide that caused nephropathy and methemoglobinemia leading to its withdrawal from the market. Symptoms following exposure to this compound may include weakness, dizziness, depression, collapse, cyanosis, sweating, gastric irritation, chills, fall in blood pressure, jaundice, coma, convulsions, weight loss, insomnia, shortness of breath, aplastic anemia, and damage to the liver, kidneys, heart and central nervous system. When heated to decomposition it emits toxic fumes. **OSHA:** Not listed as a carcinogen. **IARC:** There is sufficient evidence in humans for the carcinogenicity of analgesic mixtures containing phenacetin. Such mixtures cause cancer of the renal pelvis and ureter. There is limited evidence in experimental animals for the carcinogenicity of analgesic mixtures containing phenacetin. There is sufficient evidence in humans for the carcinogenicity of phenacetin. Phenacetin causes cancer of the renal pelvis and ureter. There is sufficient evidence in experimental animals for the carcinogenicity of phenacetin. Overall evaluations:

Chemical Name	Comments
	Analgesic mixtures containing phenacetin are carcinogenic to humans (Group 1). Phenacetin is carcinogenic to humans (Group 1).
Phorate **O-P** Very toxic by inhalation, ingestion and skin absorption due to cholinesterase inhibition. Not classified by IARC.	**PubChem:** Phorate is a clear liquid with an objectionable odour. It is used as an insecticide and acaricide and applied to plants and soil. It is an organophosphate chemical and a cholinesterase inhibitor. Phorate is one of the more toxic organophosphate insecticides with toxicity similar to parathion. The probable oral lethal dose for humans is less than 5 mg/kg. The symptoms of poisoning are due to the toxicity common to all organophosphate chemicals, and are associated with cholinesterase inhibition: excessive salivation, sweating, rhinorrhoea and tearing; muscle twitching, weakness, tremor, incoordination; headache, dizziness, nausea, vomiting, abdominal cramps, diarrhoea; respiratory depression, tightness in chest, wheezing, productive cough, fluid in lungs; and pin-point pupils, sometimes with blurred or dark vision. In severe cases: seizures, incontinence, respiratory depression, loss of consciousness, and death. It decomposes on heating and on contact with acids and oxidants. This produces toxic and corrosive fumes. **OSHA:** Not listed as a carcinogen. **IARC:** Not classified.
p-isopropyl toluene (P-Cymene) **VOC** Irritant to skin, eyes and URT. Not classified by IARC.	**ATSDR:** p-isopropyl toluene (P-Cymene) is a monoterpene that is toluene substituted by an isopropyl group at position 4. It has a role as a plant metabolite, a volatile oil component, and a human urinary metabolite. It is a member of toluenes and a monoterpene. Inhalation causes impairment of coordination, headache. Contact with liquid causes mild irritation of eyes and skin. Ingestion causes irritation of mouth and stomach. **OSHA:** Not listed as a carcinogen. **IARC:** Not classified.
Profenofos **O-P**	**PubChem:** Profenofos is a corrosive pale-yellow liquid with garlic-like odour. It is used as an insecticide. Profenofos is an organic thiophosphate, an organophosphate insecticide, an organochlorine insecticide and a member of monochlorobenzenes. It has a role as an acetylcholinesterase inhibitor, an acaricide and an agrochemical.

Chemical Name	Comments
Very toxic by inhalation, ingestion and skin absorption due to cholinesterase inhibition. Not classified by IARC.	It is highly toxic, may be fatal if inhaled, swallowed or absorbed through skin. Contact with molten substance may cause severe burns to skin and eyes. Avoid any skin contact. Effects of contact or inhalation may be delayed. The symptoms of poisoning are due to the toxicity common to all organophosphate chemicals, and are associated with cholinesterase inhibition: excessive salivation, sweating, rhinorrhoea and tearing; muscle twitching, weakness, tremor, incoordination; headache, dizziness, nausea, vomiting, abdominal cramps, diarrhoea; respiratory depression, tightness in chest, wheezing, productive cough, fluid in lungs; and pin-point pupils, sometimes with blurred or dark vision. In severe cases: seizures, incontinence, respiratory depression, loss of consciousness, and death. Fire may produce irritating, corrosive and/or toxic gases. Runoff from fire control or dilution water may be corrosive and/or toxic and cause pollution. **OSHA:** Not listed as a carcinogen. **IARC:** Not classified.
Prothiofos **O-P** Very toxic by inhalation, ingestion and skin absorption due to cholinesterase inhibition. Not classified by IARC.	**PubChem:** Prothiofos is similar to Profenofos, being an organophosphate that is the 2,4-dichlorophenyl ester of O-ethyl S-propyl dithiophosphoric acid. It has a role as an acetylcholinesterase inhibitor, and cholinesterase inhibitor, an agrochemical and an insecticide. It is also an organic thiophosphate, a dichlorobenzene and an organosulfur compound. The symptoms of poisoning are due to the toxicity common to all organophosphate chemicals, and are associated with cholinesterase inhibition: excessive salivation, sweating, rhinorrhoea and tearing; muscle twitching, weakness, tremor, incoordination; headache, dizziness, nausea, vomiting, abdominal cramps, diarrhoea; respiratory depression, tightness in chest, wheezing, productive cough, fluid in lungs; and pin-point pupils, sometimes with blurred or dark vision. In severe cases: seizures, incontinence, respiratory depression, loss of consciousness, and death. Fire may produce irritating, corrosive and/or toxic gases. Runoff from fire control or dilution water may be corrosive and/or toxic and cause pollution. **OSHA:** Not listed. **IARC:** Not classified.

Chemical Name	Comments
Ronnel (Fenchlorfos) **O-P** Very toxic by inhalation, ingestion and skin absorption due to cholinesterase inhibition. Not classified by IARC.	**PubChem:** Ronnel (Fenchlorfos) is a white to light-tan crystalline solid. It is used as a biocidal, being toxic to all animal life in differing degrees. It acts as a cholinesterase inhibitor. It degrades readily in the environment by hydrolysis and oxidation. The symptoms of poisoning are due to the toxicity common to all organophosphate chemicals, and are associated with cholinesterase inhibition: excessive salivation, sweating, rhinorrhoea and tearing; muscle twitching, weakness, tremor, incoordination; headache, dizziness, nausea, vomiting, abdominal cramps, diarrhoea; respiratory depression, tightness in chest, wheezing, productive cough, fluid in lungs; and pin-point pupils, sometimes with blurred or dark vision. In severe cases: seizures, incontinence, respiratory depression, loss of consciousness, and death. **OSHA:** Ronnel is listed as a carcinogen. **IARC:** Not classified.
Safrole **Natural chemical** Excess ingestion causes CNS toxicity. IARC: Group 2B – Possibly carcinogenic to humans.	**PubChem:** Safrole is found in anise and nutmeg but banned by FDA for use in food. Safrole is formerly used as a food flavour. It is a precursor in the synthesis of the insecticide synergist piperonyl butoxide and the recreational drug MDMA (Ecstacy). Safrole is a natural plant constituent, found in oil of sassafras and certain other essential oils. It is a member of a group of compounds extensively used as insecticide synergists. A major source of human exposure to safrole is through consumption of spices, such as nutmeg, cinnamon and black pepper, in which safrole is a constituent. This compound can cause vomiting, shock, cyanosis, delirium and probably convulsions. It will cause severe irritation if ingested. **OSHA:** Not listed as a carcinogen. **IARC:** Safrole is a liver carcinogen for the mouse and the rat when administered orally or subcutaneously. No epidemiological data are available on the effects of human exposure. Overall evaluation: Safrole is possibly carcinogenic to humans (Group 2B).
Stirophos (Tetrachlorvinphos) **O-P**	**PubChem:** Stirophos (tetrachlorvinphos) is an organophosphate cholinesterase inhibitor that is used as an insecticide. The symptoms of poisoning are due to the toxicity common to all organophosphate chemicals, and are associated with cholinesterase inhibition: excessive salivation, sweating,

Chemical Name	Comments
Very toxic by inhalation, ingestion and skin absorption due to cholinesterase inhibition. IARC: Group 2B – Possibly carcinogenic to humans.	rhinorrhoea and tearing; muscle twitching, weakness, tremor, incoordination; headache, dizziness, nausea, vomiting, abdominal cramps, diarrhoea; respiratory depression, tightness in chest, wheezing, productive cough, fluid in lungs; and pin-point pupils, sometimes with blurred or dark vision. In severe cases: seizures, incontinence, respiratory depression, loss of consciousness, and death. **OSHA:** Not listed as a carcinogen. **IARC:** There is inadequate evidence in humans for the carcinogenicity of tetrachlorvinphos (Stirophos). There is sufficient evidence in experimental animals for the carcinogenicity of tetrachlorvinphos. Overall evaluation: Tetrachlorvinphos (Stirophos) is possibly carcinogenic to humans (Group 2B).
Sulfotepp (Dithion or TEDP) **O-P** Very toxic by inhalation, ingestion and skin absorption due to cholinesterase inhibition. Not classified by IARC.	**PubChem:** Sulfotepp (tetraethyl dithiopyrophosphate, TEDP or Dithion) is an organic thiophosphate and an organothiophosphate insecticide. It has a role as an acetylcholinesterase and cholinesterase inhibitor, an acaricide and an agrochemical. Sulfotepp is very toxic with oral lethal dose in humans being less than 5 mg/kg. The symptoms of poisoning are due to the toxicity common to all organophosphate chemicals, and are associated with cholinesterase inhibition: excessive salivation, sweating, rhinorrhoea and tearing; muscle twitching, weakness, tremor, incoordination; headache, dizziness, nausea, vomiting, abdominal cramps, diarrhoea; respiratory depression, tightness in chest, wheezing, productive cough, fluid in lungs; and pin-point pupils, sometimes with blurred or dark vision. In severe cases: seizures, incontinence, respiratory depression, loss of consciousness, and death. **OSHA:** Not listed as a carcinogen. **IARC:** Not classified.
tert-butylbenzene (2-methyl-2-phenylpropane) **VOC**	**ATSDR, PubChem, OSHA, IARC and other databases were searched** No toxicological date were available. Not listed or classified as a carcinogen.
Tributylmethylether (TBME) (Methyl-tert-butylether (MTBE))	**ATSDR:** MTBE is the common name for a synthetic chemical called methyl-tert-butyl ether or tributylmethylether. It is a flammable liquid made from combinations of chemicals like

Chemical Name	Comments
VOC Irritant to skin, eyes, URT and CNS. IARC: Group 3 – Not classifiable as to its carcinogenicity to humans.	isobutylene and methanol. It has a distinctive odour that most people find disagreeable. It was first introduced as an additive for unleaded gasolines in the 1980s to enhance octane ratings. In city areas where there are concerns over pollutants like carbon monoxide, EPA may require the use of MTBE or ethanol as an oxygenating agent to make the fuel burn more cleanly during the winter months. Fuels containing these additives are called reformulated gasolines. Most MTBE is mixed with gasoline, so most people would come in contact with it while exposed to automobile fuel vapours or exhausts. MTBE has other special uses as a laboratory chemical and in medicine to dissolve gallstones. Some people who were exposed to MTBE while pumping gasoline, driving their cars, or working as attendants or mechanics at service stations complained of headaches, nausea, dizziness, irritation of the nose or throat, and feelings of spaciness or confusion. These symptoms were reported when high levels of MTBE were added to gasoline in order to lower the amount of carbon monoxide, a known poison, released from cars. Some people might feel irritation of the nose or throat before noticing the smell. MTBE caused side effects in some patients who were given MTBE to dissolve gallstones. If MTBE leaks from the gallbladder into other areas of the body, the patient can have minor liver damage, a lowering of the amount of white blood cells, nausea, vomiting, sleepiness, dizziness, and confusion. These effects are not long-lasting. In animal studies, some rats and mice died after they breathed high amounts of MTBE. MTBE also caused irritation to the noses and throats of animals that breathed MTBE. The most common effect of MTBE in animals is on their nervous systems. Breathing MTBE at high levels can cause animals to act as if they are drunk. For example, some became less active, staggered, fell down, were unable to get up, and had partially closed eyelids. These effects lasted only for about an hour, and then the animals seemed normal again. Some of the male rats developed cancer in the kidney, but whether this has meaning for humans is not known. When mice breathed high levels of MTBE for several hours every day for a year and a half, some had larger livers than normal, and some mice developed tumours in the liver. When rats were given high levels of MTBE by mouth for 2 years, some male rats developed cancer in the testes and some female rats developed leukemia and lymphoma. The Department of Health and Human Services (DHSS), and the EPA have not classified MTBE for its ability to cause cancer.

Chemical Name	Comments
	Some rats and mice died after being given very large amounts of MTBE by mouth. **OSHA:** Methyl-tert-butylether (MTBE) is listed as a carcinogen. **IARC:** There is inadequate evidence in humans for the carcinogenicity of methyl-tert-butyl ether. There is limited evidence in experimental animals for the carcinogenicity of methyl-tert-butyl ether. Overall evaluation: Methyl-tert-butyl ether is not classifiable as to its carcinogenicity to humans (Group 3).
Trichloronate **O-P** Very toxic by inhalation, ingestion and skin absorption due to cholinesterase inhibition. Not classified by IARC.	**PubChem:** Trichloronate is a highly toxic organophosphate and organochlorine insecticide. It was used against vegetable fly larvae and soil pests. It is an amber liquid but not sold in the U.S or Canada. Not registered as a pesticide in the U.S. Trichloronate, being an organophosphate, the toxic effects are due to action on the nervous system. It has high oral toxicity and death can occur in acute poisonings. Delayed neurotoxicity has been reported. The symptoms of poisoning are due to the toxicity common to all organophosphate chemicals, and are associated with cholinesterase inhibition: excessive salivation, sweating, rhinorrhoea and tearing; muscle twitching, weakness, tremor, incoordination; headache, dizziness, nausea, vomiting, abdominal cramps, diarrhoea; respiratory depression, tightness in chest, wheezing, productive cough, fluid in lungs; and pin-point pupils, sometimes with blurred or dark vision. In severe cases: seizures, incontinence, respiratory depression, loss of consciousness, and death. **OSHA:** Not listed as a carcinogen. **IARC:** Not classified.