THE TOXICITY OF COMMERCIAL JET OILS

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Abstract

Jet oils are specialised synthetic oils used in high performance jet engines. The have an appreciable hazard based on toxic ingredients, but are safe in use provided that maintenance personnel follow appropriate safety precautions, and the oil stays in the engine. Aircraft engines that leak oil may expose others to the oils through uncontrolled exposure. Airplanes that use engines as a source of bleed air for cabin pressurisation may have this source contaminated by the oil if an engine leaks. Examination of the ingredients of the oil indicates that at least two ingredients are hazardous: N-phenyl-1-naphthylamine (a skin sensitiser) and Tricresyl phosphate (a neurotoxicant, if ortho-cresyl isomers are present). Publicly available information such as labels and MSDS understates the hazards of such ingredients, and in the case of ortho-cresyl phosphates, by several orders of magnitude.

Introduction

Some commercial jet oils have been in use as engine oils in aviation for decades. For example, Mobil USA note that one of their products "Mobil Jet Oil II has been essentially unchanged since its development in the early 1960s" and "most changes have involved slight revisions of the ester base stock due to changes in raw material availability".[1]

A complex approval process exists for ensuring that materials used in aviation are manufactured to relevant standards, and the jet engine oil specification of the US Navy MIL-PRF-23699 is used for jet oils. This process of approval and re-approval for new product formulations has meant that there is some resistance to modifying formulations (for example, for health and safety reasons).

Consequently, changing approved formulations is not conducted without significant justification. In the case of the additive tricresyl phosphate (TCP), manufacturers have been reluctant to modify product formulations by substituting toxic TCP additives that perform well in critical applications. This has meant that potentially toxic products have continued to be available long after their toxicity was recognised.[2]

It is not known if an approved formulation containing, for example 3% tricresyl phosphate, is considered a change in formulation if the proportion of individual isomers in the TCP mixture is altered, but the 3% remains unchanged. However, as Mobil indicate, only the base stock esters have been modified over the past thirty or so years, suggesting that the mixture of isomers in TCP stock has not been changed.[3]

Mobil USA notes that one of their jet oil products (Mobil Jet Oil II) has a market share of 49%. With such a large market share, and the potential for significant exposure, it would be appropriate to investigate this material in some detail.

Mobil Jet Oil II

Mobil Jet Oil II is a synthetic oil product imported into Australia. All product worldwide is manufactured by one manufacturing facility in the USA. The product is not labeled in accordance with Australian requirements under the Hazardous Substances Regulation, but is assumed to comply by default.[4]

This product is normally marketed in 0.946 L (1 US Quart) cans.

Ingredients

Various sources, such as the supplier's label on the cardboard box the cans are shipped in, the product Material Safety Data Bulletin (MSDB), and information from Mobil USA, lists the following ingredients:

❍   synthetic esters based in a mixture of 95% C_5-C_{10} fatty acid esters of pentaerythritol and dipentaerythritol;

❍   3% tricresyl phosphate (Phosphoric acid, tris(methylphenyl) ester, CAS No 1330-78-5);

❏ 1% phenyl-alpha-naphthylamine (PAN) (1-Naphthalenamine, N-phenyl, CAS No 90-30-2);

❏ Benzamine, 4-Octyl-*N*-(4-Octylphenyl), (CAS No 101-67-7);

❏ a last entry "ingredients partially unknown" is also noted on some documentation.

In Australia, classification of materials as being hazardous substances under the Hazardous Substances Regulation use a list of hazardous substances[5] and approved criteria,[6] with reference to the list being the primary step. Of the ingredients in Mobil Jet Oil II, the most toxicologically significant ingredients are:

❏ N-phenyl-alpha-naphthylamine, which can contains a number of contaminants in trace amounts, including N-phenyl-beta–naphthylamine (135-88-6), 1-Naphthylamine (CAS No 134-32-7) and 2-Naphthylamine (CAS No 91-59-8); and

❏ Tricresyl phosphate, a blend of ten tricresyl phosphate isomer molecules (including tri-ortho-cresyl phosphate), plus other structurally similar compounds, including phenolic and xylenolic compounds.

There are a number of issues relevant to these ingredients, outlined below.

N-Phenyl-1-naphthalenamine

Chemistry

N-Phenyl-1-naphthylamine, (CAS No 90-30-2), also known as Phenyl-alpha-naphthylamine (PAN), is a lipophilic solid used as an antioxidant used in lubrication oils and as a protective agent in rubber products. In these products, the chemical acts as a radical scavenger in the auto-oxidation of polymers or lubricants. It is usually used in these products at a concentration of about 1%.

The commercial product has a typical purity of about 99%. Named impurities are: N-Phenyl-2-naphthylamine (CAS No 135-88-6, 500 to below 5000 ppm), 1-Naphthylamine (below 100-500 ppm) and 2-Naphthylamine (below 3 to 50 ppm), aniline (below 100 to 2500 ppm), 1-naphthol (below 5000 ppm), 1,1-dinaphthylamine (below 1000 ppm) (see Figure below).[7]

Figure -1: Possible Contaminants in N-Phenyl-1-naphthylamine
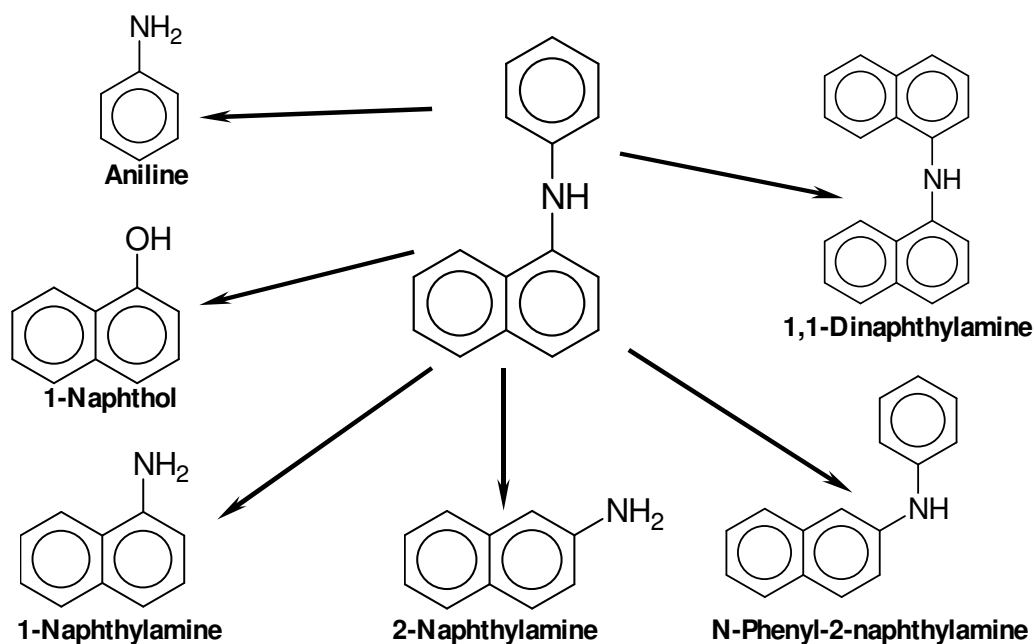
2-Naphthylamine (CAS No 91-59-8) is also known as the established carcinogen β-Naphthylamine.[8] Similarly 1-Naphthylamine is also known as α-Naphthylamine.

The formulation concentration of N-Phenyl-1-naphthalenamine in Mobil Jet Oil II is about 1%. As ingredients such as the naphthylamines have been deleted from product documentation such as the MSDB, the level of contamination of naphthylamines is presumed to be below the concentration cut off values for disclosure of Category 1 carcinogens specified in the Approved Criteria for Classifying a Hazardous Substance of 0.1% (1000 ppm).[6]

Indeed, information from Mobil Australia notes that the level of contamination of some of the contaminants in this material is partially known (50 ppm for N-Phenyl-2-naphthylamine; 0.5 ppm for 2-Naphthylamine), and that they stopped listing such ingredients in about 1992 "solely to a reassessment of what was considered meaningful information from a hazard communication perspective".[9]

2-Naphthlyamine is not listed on the 1992 Australian inventory of Chemical Substances (AICS),[10] and dependent on the amount present in the formulated product (0.2%), could technically breach the requirements of the Commonwealth Industrial Chemicals (Notification and Assessment) Act 1989. However, the probable concentration of this contaminant in Mobil Jet Oil II is too low to exceed requirements of this legislation. Further, this chemical is listed as a prohibited substance under the Australian Hazardous Substances Regulation.

Toxicology

PAN is readily absorbed by mammalian systems and rapidly converted to metabolites.[11] Both urine and feces appear to be the main routes of excretion.[12]

By single dosing, PAN does not seem particularly toxic, with LD_{50}s above 1 g/kg. The chemical has a similar mechanism of toxicity of many aromatic amines, of methaemoglobin production. PAN is not irritating in primary skin and eye irritation studies. However, in a guinea pig maximisation test, PAN was shown to be a strong skin sensitiser.[13] This result is supported by case studies in exposed workers.[14,15] At the concentration used (1%), Mobil Jet Oil II is classified as a hazardous substance in Australia for its sensitisation properties.[6]

Most genotoxicity studies report negative results, suggested little genotoxicity potential.[12]

Most repeated dose toxicological studies focus on its potential carcinogenicity. An experimental study, using both PAN and the related compound N-phenyl-2-naphthalenamine administered subcutaneously to mice found a heightened incidence of lung and kidney cancers.[16] While the methodology used in this study makes evaluation of the results problematic (use of one gender, small sample sizes, limited number of dose groups, subcutaneous administration as an inappropriate route of exposure, and so on). A high incidence of various forms of cancer was also found among workers exposed to antirust oil containing 0.5% PAN.[17] While these animal and human results offer only limited information, they are at least supportive of a mild carcinogenic effect.

This must be contrasted with the results of long term carcinogenicity bioassays in rats and mice conducted by the US National Toxicology Program with the structurally related N-phenyl-2-naphthylamine (studies were not carried out on PAN), which have not reported any carcinogenic potential for this chemical.[18]

Regulatory Classification

PAN is not listed on the NOHSC Designated List of Hazardous Substances.

However, the NOHSC Approved Criteria for Classifying Hazardous Substances[6] note that mixtures containing sensitisers should be classified as an "Irritant" hazardous substance if included in the product at a concentration at or greater than 1%. Further, a product containing a skin sensitiser at or above this value should carry risk statement R43 – *May cause skin sensitisation by skin contact.*

The data on carcinogenicity of PAN is too limited to make a determination sufficient to allow classification for regulatory purposes.

Nevertheless, based on established sensitisation properties and possible carcinogenic properties, exposure to materials containing N-phenyl-1-naphthylamine should be avoided.
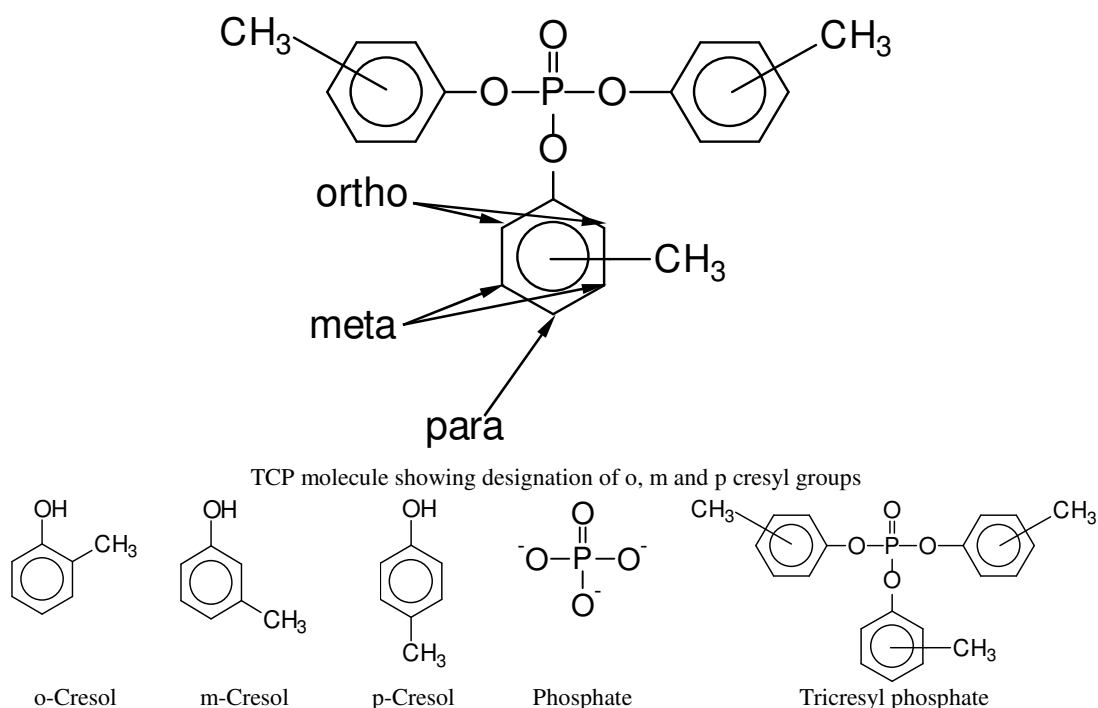
Tricresyl phosphate

Phosphoric acid, tris(methylphenyl) ester (CAS No 1330-78-5) is better known as Tricresyl phosphate (TCP) or Tri-tolyl phosphate.

Chemistry of the Cresols and Tricresyl phosphate

Industrial manufacture

TCP is a molecule comprised of three cresyl (methylphenyl) groups linked to a phosphate group. Cresol is an aryl structure comprising a hydroxyl (-OH) and methyl (CH_3) group attached to a benzene molecule. Industrial cresol is a mixture of three isomers, ortho- para- and meta-cresol molecules in varying concentrations. The ortho-, meta- or para- prefixes denote how far apart the hydroxyl and methyl groups are on the cresol molecule (see Figure below).

Figure-2: Structure of Tricresyl Phosphate

TCP molecule showing designation of o, m and p cresyl groups

| o-Cresol | m-Cresol | p-Cresol | Phosphate | Tricresyl phosphate |

Industrially, the chemical is made by reaction of phosphorus oxychloride ($POCl_3$) with industrial cresol.

Commercial grade TCP is a complex mixture of structurally related compounds, some of which are known to have neurotoxic properties. These are produced from the ortho-alkyl substituted phenols or xylenol present in the manufacturing process. ortho-methyl phenols (cresol) or ortho-ethyl phenols lead to toxic components, whereas ortho-substituted xylenols do not.[19]

Initially, TCP contained high levels of all isomers. The neurotoxic potential of the ortho-cresyl isomers, most notably tri-ortho-cresyl phosphate (TOCP), was recognised quite early.[20] Indeed much research has been carried out on the toxicity of TOCP, presumably on the basis that as it had three cresyl groups, it must be more toxic than molecules with less.

There have been substantial modifications of TCP containing materials. Earlier TCP products, such as "torpedo oil" used in World War II, were highly toxic, containing perhaps 25-40% ortho-cresol. Notably, this product was more toxic than TOCP

itself.[21] This is a critical finding, because it meant that the conventional view that the toxicity of TCPs was correlated to their tri-ortho-cresyl content was incorrect. The presence of other ortho-cresyl containing molecules (not just TOCP) needs consideration in evaluating the overall toxicity of TCP.

Manufacturers reduced the levels of ortho-cresyl and ortho-ethylphenyl isomers to reduce the potential for neurotoxicity. Changes to the phenolic mixture used to manufacture TCP, introduction of processing alternatives and improved purification methods all assisted in reducing ortho-cresol content. By the 1950s, commercially available TCP contained about 3% ortho-cresol isomers. Further refinements in the 1980s to 1990s have decreased the ortho-cresol content further. How much these refinements had removed the toxic impurities outlined above is not known. Indeed, toxicity was still being detected in commercially available products in 1988.[2]

It is difficult to obtain data on the amount of TOCP contamination in commercially available materials now being marketed world-wide containing TCP. However, conservative estimates of about 0.1-1% (1,000-10,000 ppm) seem realistic. This suggests that a product containing 3% TCP would contain about 0.003-0.03% TOCP (30-300 ppm). The "new generation" materials are claimed to have an even lower TOCP content, although data on content is sparse.[2] Importantly however, is that the focus of attention on the toxicity of TOCP has masked the study of the toxic potential of other orthocresyl isomers. Further, work by Henschler and colleagues in the 1950s (published, but published in German) was not reconsidered until the 1990s.

Typically, jet turbine engine oils are formulated with about 3% TCP. This includes Mobil Jet Oil - 3% TCP is stated on MSDB, and is supported by data published in elemental analyses,[22] where a Mobil Jet Oil was shown to contain 0.29% Phosphorus, which extrapolates to about 3.5% organophosphate.

Uses of TCP

TCP has been a commercially useful material, and has been used as a plasticiser, lubricant, hydraulic fluid, paint additive, oil additive, dust suppressant and so on.[23,24] Most commercial uses have now ceased.

In jet oil, TCP is used in the formulation of lubricants as an anti-wear additive to enhance load bearing properties and improve tolerance to increasing speed of rotating or sliding motion. It also has flame retardant properties. While some other triaryl phosphates have similar properties and may also be used as oil additives, the anti-wear properties of TCP are considered unique. For example, pure tri-para-cresyl phosphate is considered to have poorer lubricating properties than commercial TCP.[2]

Isomers of TCP

Generally, the chemical known as TCP comprises a mixture of unspecified ortho- para- and meta-cresol molecules (as cresyl groups, see above), which can be formed into a number of separate structures with similar chemical formulas (isomers).

Technically, there are ten possible tri-cresyl phosphate structures (see below).

Figure-3: Possible Isomers of Tricresyl phosphate
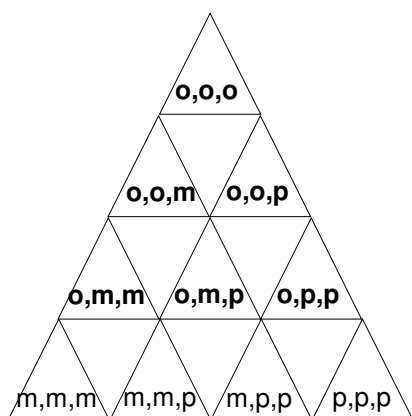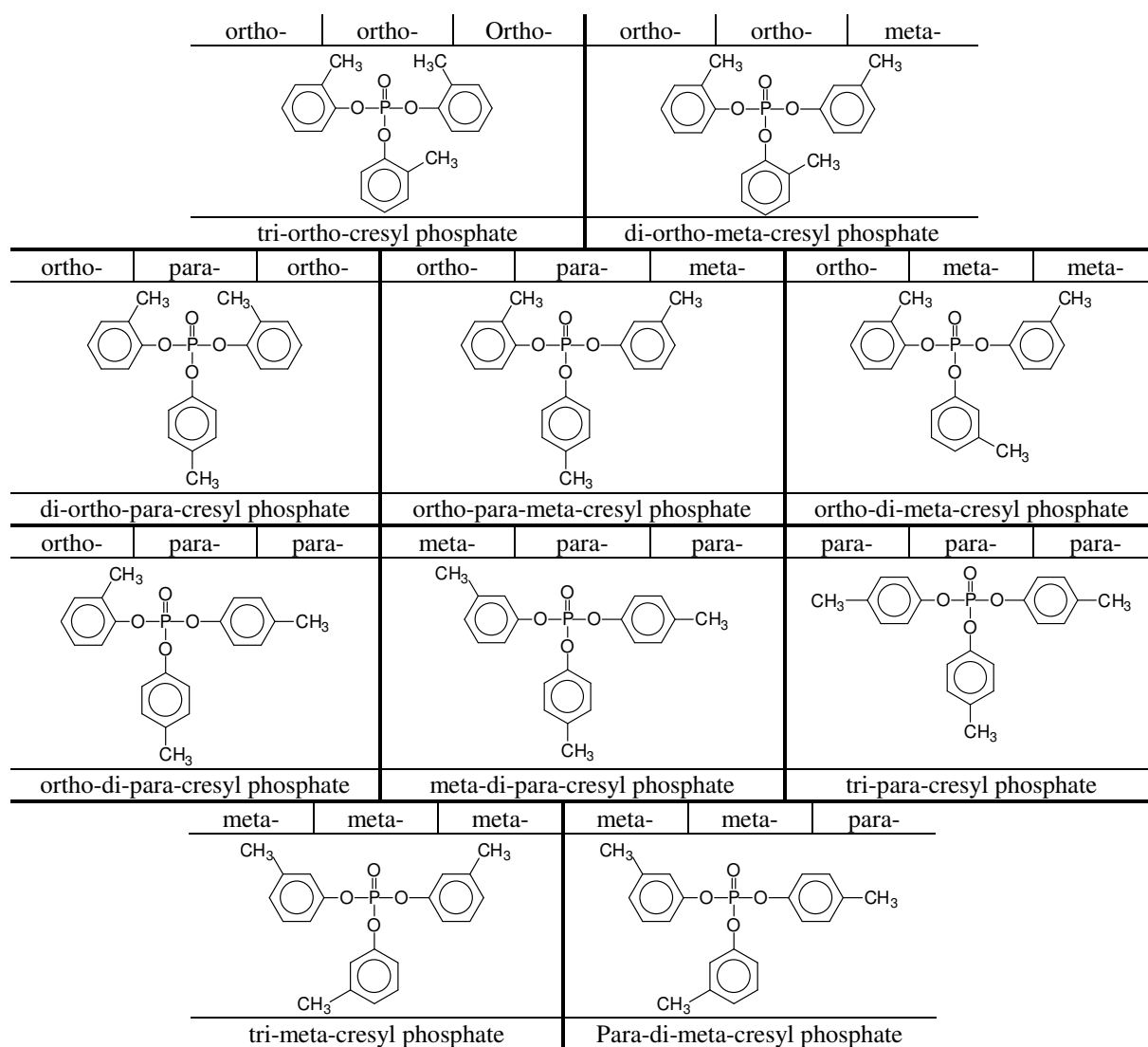

o   ortho-cresyl group

m   meta-cresyl group

p   para-cresyl group

ortho-cresyl group containing molecules are highlighted in **bold**

The structures of the ten different isomers are shown below.

Figure -4: Possible Tricresyl phosphate Structures

ortho-	ortho-	Ortho-	ortho-	ortho-	meta-
tri-ortho-cresyl phosphate			di-ortho-meta-cresyl phosphate		

ortho-	para-	ortho-	ortho-	para-	meta-	ortho-	meta-	meta-
di-ortho-para-cresyl phosphate			ortho-para-meta-cresyl phosphate			ortho-di-meta-cresyl phosphate		

ortho-	para-	para-	meta-	para-	para-	para-	para-	para-
ortho-di-para-cresyl phosphate			meta-di-para-cresyl phosphate			tri-para-cresyl phosphate		

meta-	meta-	meta-	meta-	meta-	para-
tri-meta-cresyl phosphate			Para-di-meta-cresyl phosphate		

The different isomers of TCP have different properties, and indeed, different toxicities. Most notably, tri-orthocresyl phosphate (TOCP) is a well established neurotoxicant (see below).

TCP Nomenclature

Describing Tricresyl phosphate isomers chemically can be a complicated task. However, the Chemical Abstracts Service (CAS) has simplified this process by allocating four unique identifying CAS registry numbers to Tricresyl phosphate mixtures. These are listed on the Australian Inventory of Chemical substances:[10]

❍   CAS No 1330-78-5 Phosphoric acid, tris(methylphenyl) ester ($C_{21}H_{21}O_4P$), which denotes Tricresyl phosphate (unspecified cresyl groups);

❍   CAS No 78-30-8 Phosphoric acid, tris(2-methylphenyl) ester ($C_{21}H_{21}O_4P$), which denotes Tricresyl phosphate (containing ortho-cresyl groups);

❍   CAS No 563-04-2 Phosphoric acid, tris(3-methylphenyl) ester ($C_{21}H_{21}O_4P$), which denotes Tricresyl phosphate (containing para-cresyl groups);

❍   CAS No 78-32-0 Phosphoric acid, tris(4-methylphenyl) ester ($C_{21}H_{21}O_4P$), which denotes Tricresyl phosphate (containing meta-cresyl groups).

In the past, disclosure of tricresyl phosphate ingredients in products containing this chemical invariably used the nonspecific 1330-78-5 CAS number. Unfortunately, this provides no information about the various isomers in the mixture.

In its classification systems for hazardous substances, the European Union (EU) has introduced modifications of two of the CAS descriptions for tricresyl phosphate chemicals, being:

❍   CAS No 78-30-8 Tricresyl phosphate (containing o-o-o, o-o-m, o-o-p, o-m-m, o-m-p, o-p-p isomers);

❍   CAS No 78-32-0 Tricresyl phosphate (containing m-m-m, m-m-p, m-p-p, p-p-p isomers).

The reason for this change was to discourage use of the general TCP mixture CAS Number 1330-78-5 (which is proposed to be deleted), and encourage better disclosure of ortho-cresyl containing mixtures. Newer documentation by jet oil manufacturers suggests this has not yet happened, with the older 1330-78-5 CAS Number still in use on product information. It can be argued that the continued use of the older 1330-78-5 number by industry indicates that they are ignorant of the changes at the EU level and the implications of these changes for disclosure on labels and material safety data sheets.

The new CAS numbers will assist in identifying those products that contain the toxic ortho-cresyl ingredients. At the moment, it may be presumed that from a marketing perspective, disclosure of the new CAS number that indicates the presence of ortho-cresyl containing TCP in commercial products is undesirable, and therefore companies are persisting with the older generic CAS number. From this, it may be assumed that the absence of the non-ortho-cresyl containing TCP CAS number indicates that ortho-cresyl groups are present in the mixture. This is further supported by the absence of positive statements about the absence of ortho-cresyl containing isomers in TCP products.

The EU chemical names and numbers are listed in the Australian List of Designated Hazardous Substances, which forms a major part of the classification of hazardous substances under the hazardous substances regulations.[5] Suppliers of tricresyl containing materials should be referring to the new CAS numbers and chemical descriptions as soon as practicable. Further, a requirement to "state on the label whether the substance is a specific isomer or a mixture of isomers" is included in the List.

Toxicity of Tricresyl phosphates

Toxicology of the Organophosphates

Human toxicity to organophosphorus compound has been known at least since 1899, when neurotoxicity to phosphocreosole (then used in the treatment of tuberculosis) was reported.[25]

The study of the toxicity is extensive, with two very well established mechanisms on esterases and on neurotoxic esterases (NTE).

Poisoning with Organophosphates

The organophosphorus compounds are generally characterised by a toxicity of inhibition of the esterase enzymes, most particularly cholinesterases[26] and neurotoxic esterases.[27] The mechanism of effect is phosphorylation.[28] The effect is a specific mechanism of organophosphate toxicity.

An organophosphorus molecule can be represented by the general structure:

$$R_3 - \overset{\overset{\textstyle O}{\|}}{\underset{\underset{\textstyle R_2}{|}}{P}} - R_1$$
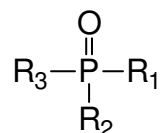
Where P is the Phosphorus atom, O is an oxygen atom and R_1-R_3 represents organic structures that can give the molecule a wide range of properties.

Because cholinesterases break down endogenous choline esters, inhibition of these enzymes produces an accumulation of levels of choline esters. Most critical of these esters is acetylcholine, a neurotransmitter molecule released throughout the cholinergic nervous system. Any organ or tissue that receives a cholinergic input will become more active or excited if cholinesterases are not available to catalyse the breakdown of acetylcholine. Indeed, cholinergic overstimulation produces most, if not all, of the symptoms of poisoning from single and short term exposure to organophosphates.

Signs of low level intoxication include headache, vertigo, general weakness, drowsiness, lethargy, difficulty in concentration, slurred speech, confusion, emotional lability and hypothermia.[29] The reversibility of such effects has been questioned.[30]
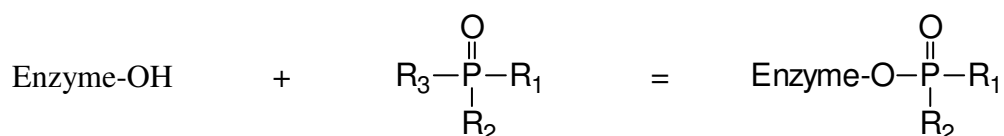
Signs of poisoning are usually foreshadowed by the development of early symptoms related to acetylcholine overflow and include salivation, lacrimation, conjunctivitis, visual impairment, nausea and vomiting, abdominal pains and cramps, diarrhoea, parasympathomimetic effects on heart and circulation, fasciculations and muscle twitches.[31]

This is the basic site of inhibition for all OP molecules.[32,33]

Organophosphate Induced Delayed Neuropathy (OPDIN)

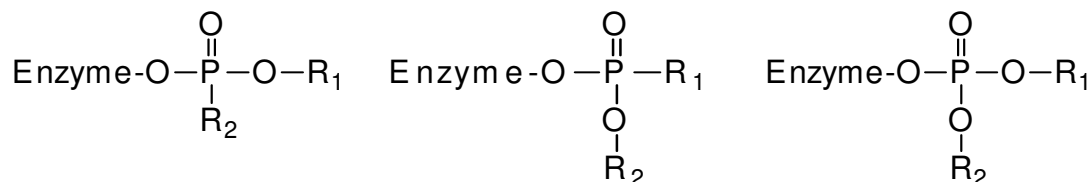There is a second reaction that leads to further neurotoxic and neuropathological changes.

Inhibition of neurotoxic esterases (NTE) can lead to a neuropathological condition of progressive neuronal damage, called organophosphorus induced delayed neuropathy (OPIDN).[34,33] The mechanism of toxicity is now fairly well understood, as indeed are the organophosphorus structures which are predicted to cause OPIDN.[35] Basically, all OP molecules react with any -OH groups on the active site of the enzyme:

$$\text{Enzyme-OH} \quad + \quad R_3{-}\overset{\displaystyle \overset{O}{\|}}{\underset{\displaystyle R_2}{P}}{-}R_1 \quad = \quad \text{Enzyme-O}{-}\overset{\displaystyle \overset{O}{\|}}{\underset{\displaystyle R_2}{P}}{-}R_1$$

The basic process is the initial phosphorylation of a group of esterases called the neurotoxic esterases (NTE). This is followed by a second reaction of enzyme "aging", where the enzyme structure (or its microenvironment) was modified so that it can no longer function properly. The basic mechanism is a break in the P-O-R bond, resulting in a negatively charged P–O⁻ group, and a free -R group. A determinant of toxicity is the extent of inhibition of these enzymes, in that marked toxicity occurs after inhibition of over 50%.[36]

Several theories about the significance of these events in the development of OPIDN,[37] and a pathway of events have been proposed.[38]

The likelihood of this reaction occurring is dependent on the molecular structure of the OP molecule. Where either or both of the R_1 or R_2 groups are linked to the phosphorus with a P-O-R bond (instead of a P-R bond), OPIDN can develop. These OP structures are:

$$\text{Enzyme-O}{-}\overset{\displaystyle \overset{O}{\|}}{\underset{\displaystyle R_2}{P}}{-}\text{O}{-}R_1 \qquad \text{Enzyme-O}{-}\overset{\displaystyle \overset{O}{\|}}{\underset{\displaystyle \overset{O}{|}}{\underset{\displaystyle R_2}{}}}{-}R_1 \qquad \text{Enzyme-O}{-}\overset{\displaystyle \overset{O}{\|}}{\underset{\displaystyle \overset{O}{|}}{\underset{\displaystyle R_2}{}}}{-}\text{O}{-}R_1$$

The main classes of organophosphorus molecules that have the potential to cause OPIDN are phosphates (two P-O-R bonds) and phosphonates (one P-O-R bond). A further group known to cause OPIDN are the phosphoroamidates, where the oxygen in the P-O-R bond is replaced by nitrogen (R-N-R).

Where the OP molecule only contains P-R bonds, aging (and therefore delayed neuropathy) will not occur. The main classes of organophosphorus molecules that have these structures are the phosphinates.[39]

Not all animal species are susceptible to developing OPIDN: for example, rodents are not particularly sensitive[40] (although neurological damage can be produced in the rat[41]). However, along with the cat[42] and chicken,[43,44] humans are considered to be among the most sensitive species.[45]

OPIDN is caused when the organophosphate molecule binds with NTE in the long processes of the nerves (the axons). The enzymes have functions related to transport of nutrients and energy molecules from the cell body to the end of the nerves. Phosphorylation of such proteins results in localised disruption of axoplasmic transport. If prolonged, these effects are followed by swelling of the axon, followed by degeneration from the site of the damage to the end of the axon. If exposure continues, this process can continue up the axon by the phosphorylation of more proteins. Lesions are characterised by degeneration of axons followed by degeneration of the cells that surround (and contribute to the insulation of the fibres) the myelin containing support cells.[45] This effect can occur in sensory or motor nerves in either the central or peripheral nervous systems.[46] Initially, the condition arises as a distal symmetrical sensori-motor mixed peripheral neuropathy mainly affecting the lower limbs with tingling sensations, burning sensations, numbness and weakness. In severe cases paralysis may develop.[47] Longer nerves are affected more, probably because or their requirements for active nutrient supply (shorter nerves may continue to get supplied through passive mechanisms, such as diffusion). Regeneration is possible if exposure ceases and damage is not too extensive.[48,37]

The Intermediate Syndrome

OPIDN is severe. It is quite likely that such a severe condition would be presaged with a range of clinical and pre-clinical signs and symptoms. These have been reported extensively, and an "intermediate syndrome" was defined in 1987.[49] Symptoms of the intermediate syndrome include: proximal limb paralysis, weakness of neck muscles, inhibition of respiratory muscles and cranial nerve involvement. The mechanism of effect is different from poisoning or OPIDN effects, and is considered to be due to the effect of the organophosphate at the level of the neuromuscular synapses.[50]

Chronic Organophosphate Neuropsychological Disorder (COPIND)

More recently, chronic exposure to organophosphates has been associated with a range of neurological and neuropsychological effects.[51,52,53,54,55] Such symptoms (mainly neurological and neurobehavioural symptoms) may also be seen in exposed individuals who have been sufficiently fortunate in not having exposures that were excessive enough in intensity or duration to lead to clinical disease.

A distinct condition - chronic organophosphate neuropsychological disorder (COPIND) has been described, of neurological and neuropsychological symptoms.[56] These include:

- diffuse neuropsychological symptoms (headaches, mental fatigue, depression, anxiety, irritability);

- reduced concentration and impaired vigilance;

- reduced information processing and psychomotor speed;

- memory deficit and linguistic disturbances;

COPIND may be seen in exposed individuals either following single or short term exposures leading to signs of toxicity,[52] or long term low level repeated exposure with (often) no apparent signs of exposure.[54] The basic mechanism of effect is not known, although it is not believed to be related to the esterase inhibition properties of organophosphorus compounds. It is also not known if these symptoms are permanent.

Toxicology of TCP and TOCP

Much of the early study of OPIDN was investigated not just with organophosphorus compounds, but with the tricresyl phosphates[57,58] following outbreaks of poisoning after accidental or criminal adulteration of food or beverages with TCP containing products. A large literature is now available on the toxicity of the tricresyl phosphates (most particularly, TOCP) and the basic mechanisms are well established.[59] TCP produces acute poisoning based on cholinesterase inhibition, and a well defined syndrome of neurological degeneration (either from short term or long term repeated dose exposure). As well as affecting the nervous system, TCP also has toxic effects in the adrenal glands, ovaries and testes.[60] TCP is also known to be a skin irritant and to cause allergic dermatitis.[59]

Neurotoxicity has been reported in TCP manufacture.[61] The toxic effects of oils containing TCP have also been long recognised.[62]

The toxic properties of tri-ortho-cresyl phosphate have been recognised for decades, and the presence of this isomer in products containing TCP presents a significant occupational health problem. Further, as noted above, there are five other orthocresyl phosphate isomers:

- two di-ortho-cresyl phosphates (di-ortho-mono-meta-cresyl phosphate or o-o-m and di-ortho-mono-para-cresyl phosphate or o-o-p); and

- three mono-ortho-cresyl phosphates that contain only one ortho-cresyl group but various combinations of meta-cresyl and para-cresyl groups (o-p-p, o-p-m, o-m-m).

These mono- and di- ortho-tricresyl phosphates are reported to have measurable toxicities similar to the neurotoxicity produced by TOCP.

Other ortho-cresyl containing ingredients

Tricresyl phosphate will also contain mixed esters of orthophosphoric acid with different cresyl radicals, of the mono- and di-cresyl types.

Other contaminants, such as ortho containing di-cresyl phosphates may also be toxic. Further, mono-ortho-cresyl-diphenyl phosphate (that is, an organophosphate molecule with one cresyl group only (see below) appears to be the most toxic molecule of all.[21]
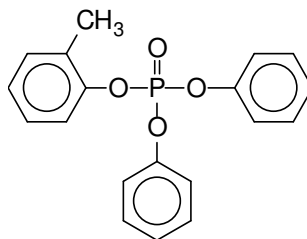
Mono-ortho-di-phenyl phosphate

Further, other ortho-containing molecules, such as 2,3-Tri-xylenyl phosphate and 2,4-Tri-xylenyl phosphate, are weakly neurotoxic (this is a cresyl molecule with an extra methyl group, the 2- indicates the ortho- position, see below).[19]

Possible Tri-xylenyl phosphate Structures

| 2,3-Tri-xylenyl phosphate | 2,4-Tri-xylenyl phosphate |
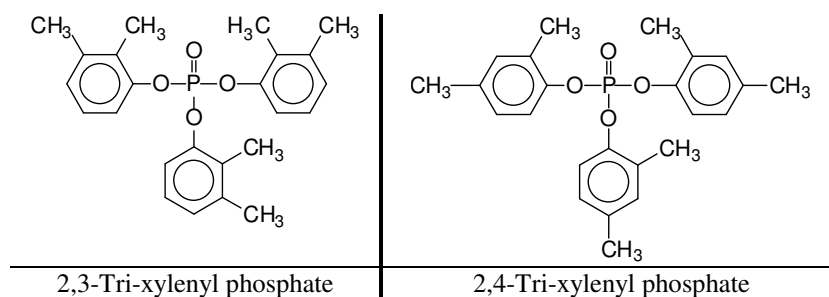
Other trixylenyl phosphates, such as 2,5, 2,6, 3,4 and 3,5 were not neurotoxic.

Still other impurities, such as triphenyl phosphate, di-phenyl-mono-cresyl- phosphate, di-phenyl-mono-xylenyl phosphate and tri-xylenyl phosphate may also be neurotoxic. The presence of structures with methyl groups adjacent to the ester –O-P bond, needs consideration in evaluating the overall toxicity of TCP.

Recent research has focused on identifying a dose response relationship for TOCP. Results of a short term repeated dose study in hens of aviation engine oil containing various amounts of commercial TCP suggest that oil containing 1% TCP (a TCP equivalent of 20 mg/kg/day) was considered a no observable effect level.[63] Similar findings were reported in a later study.[64]

Finally, it is generally assumed that most exposure to TOCP is by the inhalational route (ingestion is unlikely for persons not directly handling this material). However, absorption through skin exposure should not be discarded, as significant exposure (maximally estimated at a transdermal flux rate of 0.01 mg/cm^2/hr) through this route is possible.[65]

Relative Toxicity of the ortho-Cresyl Containing Tricresyl phosphate Isomers

The ten isomers that make up TCP are toxicologically different, and it is well established that the ortho containing isomers are the most toxic. Much research in the past has concentrated on the tri-orthocresyl phosphate isomer (TOCP), which has

shown to be associated with organophosphate induced delayed neuropathy (OPIDN). TCP manufacturers have expended considerable energy in reducing levels of TOCP in commercial grades of TCP.

However, what is less well known is that there are other ortho containing isomers in TCP, three mono-ortho (MOCP) isomers and two di-ortho (DOCP) isomers. These are not specified in mandated lists of hazardous chemicals, and this may be one reason why they are not disclosed on labels and MSDS.

All these compounds are neurotoxic in the same way as TOCP - however they are known to be more neurotoxic. For instance the DOCPs are five times more toxic, and the MOCPs ten time more toxic, than TOCP.[19,21] The total toxicity of a particular mixture is therefore dependent on consideration of the proportion of each ingredient, their relative toxicities, and the effect of any interaction between mixtures of chemicals.

In evidence to the Australian Senate Aviation Inquiry, Mobil USA noted that Mobil Jet Oil II contains less than 5 ppb (0.005 ppm) TOCP.[3] This is an impressively low amount, and suggests that the neurotoxic potential from a chemical containing such a low level of tri-ortho-cresyl isomer be vanishingly small.

Concentrations of other neurotoxic ingredients were not so readily available. In evidence to the Australian Senate Aviation Inquiry, it became apparent that DOCPs were present in TCP at a concentration of 6 ppm, and MOCPs were present at a concentration of 3070 ppm.[3] As these ingredients are present in higher concentrations than TOCP, and have a significantly higher toxicity than TOCP, it is suggested that a statement of low TOCP content is misleading as it underestimates the toxicity of the – OCP ingredients by a factor of 30,730 (see the Table below).

Table 1: Tricresyl Phosphate: Toxicity of Isomers

Isomer	Concentration (ppm)	Relative Toxicity	Equivalent Toxicity
TOCP	0.005	1	1 $\times$
DOCP	6	5	30 $\times$
MOCP	3070	10	30700 $\times$
		Total	**30731 $\times$**

Further, the chemically similar organophosphates such as xylenols and phenolics are also present in as contaminants in tricresyl phosphate. These also have a similar neurotoxicity to the cresyl isomers, which would add to the relative toxicity listed above.

New products are being introduced into the market. Claims that they are organophosphate clear are untrue. Mobil 291, one such replacement oil contains less than 1 ppb TOCP, 1.1 ppm DOCP and 1760 ppm MOCP.[3] This gives an equivalent toxicity of 17606, which is about half that of the previously used product, Mobil Jet Oil II. While this is a significant decrease in -OCP containing monomers, it is not phosphate free.

Regulatory Classification

Tricresyl phosphate is listed on the NOHSC Designated List of Hazardous Substances.

The first edition of the Designated List was current from 1994 to 1999.[66] This edition contains three entries for Tricresyl phosphate.

The first entry for Tricresyl phosphate (as Tri-tolyl phosphate) uses the CAS No 1330-78-5. This entry notes that mixtures this ingredient should be classified as "Harmful" hazardous substances if included in the product at a concentration at or greater than 0.2% and "Toxic" hazardous substances if included in the product at a concentration at or greater than 1%. Further, a product containing a this ingredient at or above 0.2% should carry risk statement R23/24/25 – *Toxic by inhalation, in contact with skin and if swallowed* and R39 – *Danger of very serious irreversible effects.*

There are two other entries in the 1994 edition of the Designated List, based on two other chemical descriptions. Tricresyl phosphates (<1% o-cresol) and Tricresyl phosphates (>1% o-cresol). Regulatory requirements for the former are classified as Harmful if present in a mixture above 5% with risk phrases R21/22 – *Harmful in contact with skin and if swallowed.* Regulatory requirements for the latter are the same for Tri-tolyl phosphate (CAS No 1330-78-5).

A final entry also is listed for Triorthocresyl phosphate under the CAS No 78-30-8, but no classification cut-off values are listed or risk phrases suggested.

Entries on product documentation have invariably used the 1330-78-5 description, perhaps because of the problem of obtaining a true estimate of all the various structures containing the "o-cresol" groups.

The second edition of the designated list has been current since 1999.[5] All entries for TCP have been deleted, with two new entries:

- ❍ CAS No 78-30-8 Tricresyl phosphate (o-o-o, o-o-m, o-o-p, o-m-m, o-m-p, o-p-p);[†]
    - ▪ Classified as "Harmful" at concentrations above 0.2%, with the risk phrases R21/22 – *Harmful in contact with skin and if swallowed.*
    - ▪ Classified as "Toxic" at concentrations above 1%, with the risk statements R23/24/25 – *Toxic by inhalation, in contact with skin and if swallowed* and R39 – *Danger of very serious irreversible effects.*
- ❍ CAS No 78-32-0 Tricresyl phosphate (m-m-m, m-m-p, m-p-p, p-p-p)
    - ▪ Classified as "Harmful" at concentrations above 5% with the risk phrases R21/22 – *Harmful in contact with skin and if swallowed.*

[†]   This CAS No is also used to describe the entry for Tri-ortho-cresyl phosphate (TOCP), suggesting that any Tricresyl phosphate containing ortho-cresyl containing isomers, can now be loosely called TOCP.

While these two new entries have attempted to clear up the confusion apparent in the earlier entries, it is not known at which point that contamination of a non-ortho-cresyl-TCP with ortho-cresyl containing monomers converts a low hazard "non-o-TCP" to an o-TCP.

Use of these two new entries is not widespread, with the 1330-78-5 CAS number remaining in common use. Unless an accurate measure of the ortho-cresyl (and probably the "ortho"-xenyl isomers) can be made, it is prudent to continue to assume that the TCP mixture contains significant levels of ortho-containing isomers.

Non-Organic Contaminants

One additional point that should be made is that these materials do not just contain organic molecules. They also contain low levels of other contaminants. The elemental analysis conducted by van Netten[22] investigated elemental concentrations of a range of elements in three commercially available jet oils (see Figure below).

Figure -5: Toxic Metal Contaminants in Commercial Jet Oils
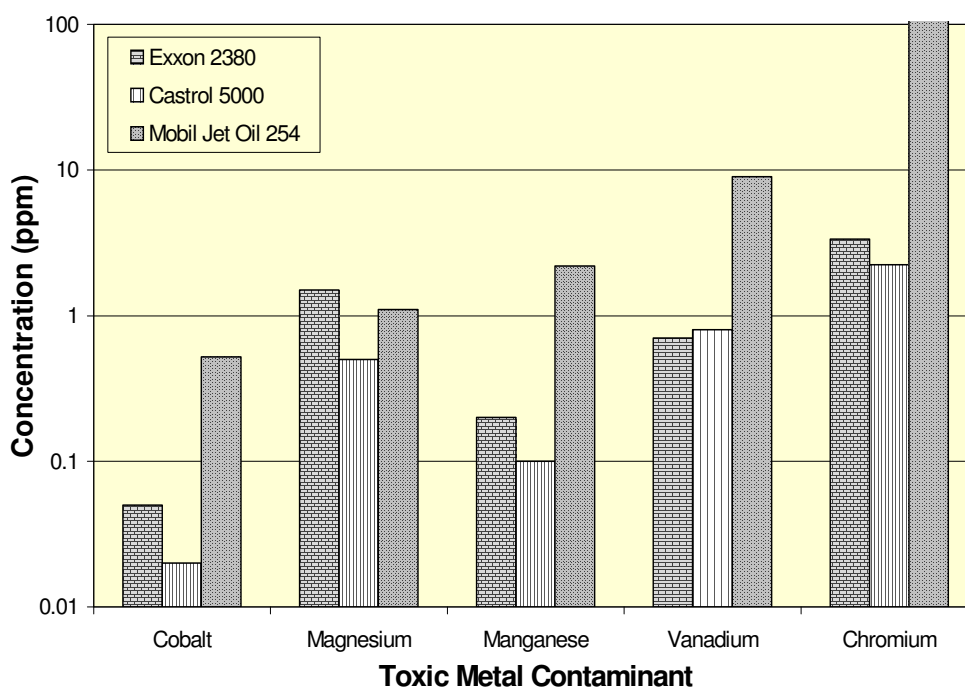
While concentrations of some metals are in ppm and even ppb concentrations, it is misleading to ignore the possible effects of these and other exposures either singly, or in combination.

Issues that can Impact on Exposure to Jet Oils

The Impact of Altitude

The concentration of oxygen at increasing altitude remains constant, at 20.9%. This suggests that oxygen levels are unchanged. This is not true. Basically, as altitude

increases, the atmospheric pressure declines. While the <u>proportion</u> of oxygen in air remains unchanged, the actual <u>amount</u> of oxygen in air decreases.

Atmospheric pressure at sea level is 760 mm Hg, with the corresponding partial pressure of oxygen in air is 159 mm Hg (20.9% or 760 mm Hg). The minimum O_2 concentration for work is considered to be about 136 mm Hg (18 kPa or 18%) O_2 in air at sea level.[67] A minimum oxygen partial pressure of 118 mm Hg (equivalent to an altitude of 2438 m/8000 ft) is required to prevent hypoxic cabin air in commercial aircraft during normal operations. This partial pressure is maintained by the cabin pressure system (a second requirement for release of oxygen dispensing units at 4572 m/15,000 ft is recommended).[68]

The altitude at which the partial pressure of 136 mm Hg is reached is also quite close to the pressure at which airplane cabins are pressurised (118 mm Hg). There is little margin of safety in people working at altitude, and in many cases, such workers may be beginning to become hypoxic.[69] This shown in the Figure below, where the area bounded by the dashed partial pressure of Oxygen in Air curve, and the dotted line representing the minimum physiological demand line represents the margin of safety at which workers can be considered to have sufficient oxygen to work safely). Further, the position of the cabin pressurisation line shows that in some cases, workers at altitude may not be obtaining enough oxygen for their physiological requirements.

Figure -6: Pressures and Oxygen Concentrations at Altitude
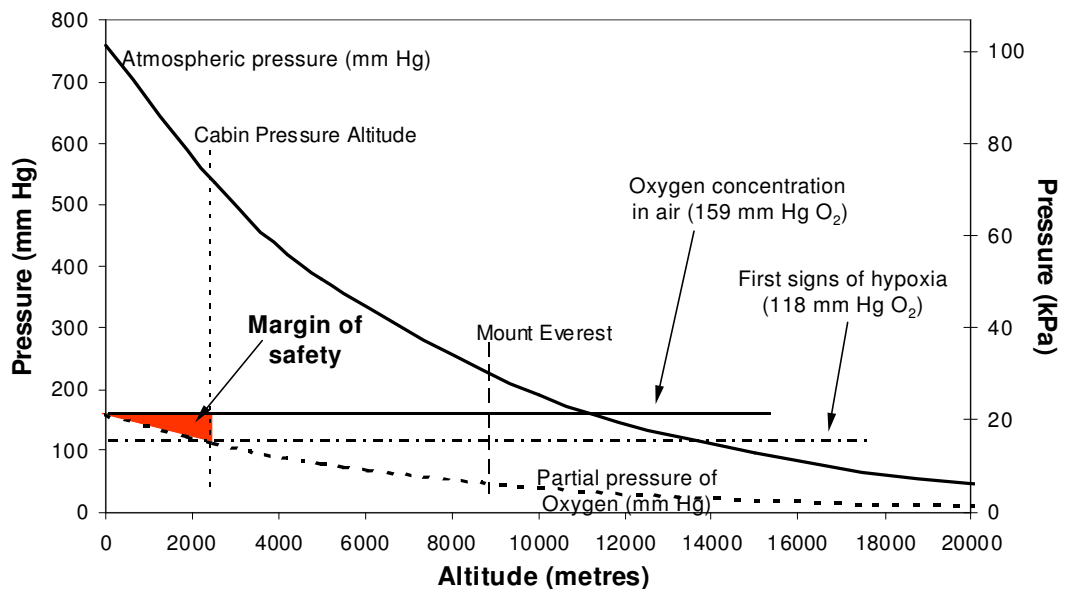
Assumptions:
Atmospheric pressure: 101 kPa (760 mm Hg) at sea level
Proportional concentration of O_2 in air: 20.9% (21 kPa or 159 mm Hg) at sea level)
Aircraft Pressurisation Pressure: Equivalent to an altitude of 2500 m (about 8000 ft).

Other problems with lowered oxygen concentrations include changes in sensitivity to toxic exposures (for example, the toxicity of carbon monoxide is 50% higher at 8000 ft than at sea level), and the possibility that incipient hypoxia may lead to higher respiratory rates and therefore increased exposure.

Other factors due to the manner in which air is circulated in planes, may also have an effect, such as humidity, temperature, or contaminants such as carbon dioxide, carbon monoxide, ozone and particulates.[70]

The effects of hypoxia/low humidity have not been studied adequately,[71] but are unlikely to be insignificant.

Issues Related to Vapours and Particulates

Airborne contaminants are generally divided into two types: gas/vapour and particulates.

Gases/Vapours: A gas is those molecules of a chemical that exist in a gaseous phase. Where all the molecules of a chemical are in the gaseous phase, the chemical is considered a gas. A vapour is the gas phase of a liquid at room temperature. Therefore, a vapour is that amount of liquid that evaporates into air (or dissolves into air). Gases and vapours form true solutions in air. The amount of evaporation is dependent on the individual vapour pressure of the contaminant. Where vapour pressure is low, only a small amount of the contaminant will evaporate. Generally, vapour pressure increases with temperature.

Where volatile organic chemicals (VOCs) have high vapour pressures, they will be present in air in high concentrations, are more likely to reach toxic concentrations and are amenable to sample collection and analysis using sorbent or gas collection methods. Where semi-volatile or poorly volatile chemicals have low vapour pressures, they are less likely to reach toxic concentrations unless they are highly toxic, and sorbent or gas collection methods are less useful for sample collection.

Particulates: These are materials that are suspended, not dissolved, in air, and include fumes, smoke, mists, aerosols, dusts, fibres and so on. Particulates may be in liquid phase (such as mists), solid phase (smokes, fumes and dusts) or mixed phases (aerosols). Precise criteria for these terms exist based on particle size and phase, but are unnecessary for the present discussion.[72]

Where a particulate is present in air and contains a volatile component, the volatile components will evaporate at a rate dependent on individual vapour pressures. However, depending on the amount of particulate present in air, it is possible to exceed the vapour pressure of an individual contaminant. Where a contaminant has a low vapour pressure, particulate exposure is more important than exposure to vapour.

Therefore, particulates containing a large proportion of volatile components will evaporate quickly (sometimes even before settling), indicating that the vapour phase of the contaminant is more important. Particulates containing poorly volatile components will stay in particulate form for a long time, until gravity or turbulence causes them to settle. Once settled, particles coalesce onto or adhere to surfaces, and any remaining volatile components become subject to evaporation through their vapour pressures. Where evaporative pressures are low, long term, low-level contamination leading to residual exposures will occur.

Further, because particulates can settle on exposed skin and be subject to absorption through skin, sometimes after airborne exposure has ceased, it is important to consider both the inhalational and skin routes when estimating exposure.

Particulates are not amenable to the same sampling and collection methods that are required for gases and vapours. They require specialised sampling, usually by filtration or gravimetric methods. Further, because particulates can exist in different sizes and diameters, an estimate of that fraction of the particulate that is taken into the respiratory system may be more critical than an estimation of the total concentration of particulate. Consideration of the type of airborne contaminants, whether in vapour, particulate or mixed phases is quite critical for the success and relevance of a monitoring program.

Issues Related to Combustion and Pyrolysis

Any chemical or chemical mixture is subject to degradation processes, such as oxidation or reduction. Over time, these can cause substantial loss of original chemical structures and properties. This process occurs more rapidly at higher temperatures and pressures, in accordance with the laws of thermodynamics. However, for most commercial purposes (except perhaps in the production of food), the processes of breakdown in chemical materials are slow, and can be disregarded.

However other breakdown processes are also possible, such as, a material subject to a source of heat energy can burn. This is called thermal degradation or thermolysis. The process of thermal degradation is a chemical process in which oxygen and energy are used to transform the original chemical into its oxidised form. For example, carbon containing materials will, in the presence of energy and oxygen, produce the two oxides of carbon: Carbon dioxide (CO_2) and Carbon monoxide (CO). The first of these (CO_2) is produced in the presence of an abundance of oxygen, the second (CO), where stoichiometric concentrations of oxygen are lacking (usually in conditions of incomplete combustion). Both of these oxides are gases, one (Carbon monoxide) is indeed toxic, even at low concentrations, causing toxic asphyxiation. Single or short term exposure to CO insufficient to cause asphyxiation produces headache, dizziness, and nausea; long term exposure can cause memory defects and central nervous system damage, among other effects.[73]

Where oxygen is completely lacking, the process of thermal degradation can still proceed, but this time, any carbon in a material, will be reduced from the chemical form it is located, to molecules containing proportionally more carbon (and proportionally less volatile components) and ultimately, carbon atoms. This process is called pyrolysis. Both oxides of carbon are gases, but elemental carbon is a solid (usually seen as smoke or soot). Further, the process of reducing carbon containing materials to carbon depends on the chemical nature of the source material, and will produce different pyrolysis products as the reaction process proceeds. Pyrolysis products may be fairly pure in carbon content, but are more usually found with other organic or inorganic breakdown products. The processes inherent in pyrolytic degradation are very complex, and vary depending on the source materials, the temperature and duration of combustion, and the progressive combustion of pyrolysis products that occur in the thermal degradation process.

Many combustion and pyrolysis products are toxic. The toxic asphyxiants, such as carbon monoxide or hydrogen cyanide were discussed above. Some thermal degradation products, such as acreolin and formaldehyde are highly irritating. Others, such as oxides of nitrogen and phosgene, can produce delayed effects. Still others, such as particulate matter (for example, soot) can carry adsorbed gases deep into the respiratory tract where they may provoke a local reaction or be absorbed to produce systemic effects.[74]

Of course, in a situation where a fire occurs, all three processes can occur. Where there is no oxygen, pyrolysis products (such as smoke) will be formed, where there is incomplete combustion carbon monoxide will form, and where there is complete combustion, carbon dioxide is formed. Further, these processes may proceed sequentially, as oxygen becomes available to the burning material.

Therefore, as well as particulate and gas/vapour phases, consideration of the type of airborne contaminants, whether in unchanged, degraded, combusted or pyrolised forms is also critical for the success and relevance of a monitoring program.

Exposure to Jet Oils in the Occupational Environment

Exposure standard

The only ingredient in Mobil Jet Oil II with an exposure standard is TOCP, with a 40 hr/week time weighted average concentration of 0.1 mg/m^3.[67] There is no exposure standard for other isomers, although at least some are known to be more toxic. Therefore estimating "acceptable" exposures based on monitoring for TOCP alone will severely underestimate exposure.

This is critical in the interpretation of the results of experimental and exposure studies. For example, chickens exposed to TCP mixtures containing about 1.5% TOCP (then the US Navy specification) developed OPIDN within five days of oral dosage, and sixty days of inhalational exposure at 23 mg/m^3 or more.[75] While this provides a measure of comparison of oral to inhalational exposure, it can not provide a true picture of the toxicity of TCP, as the concentrations of other orthocresyl containing TCP isomers in the mixture used were not known. If, as shown above, the proportion of such isomers is 30,000 times the concentration of TOCP, then using an exposure standard for one isomer as an estimate of exposure is virtually meaningless.

Exposure situations

On ground Engineering operations

Exposure to jet oil is possible during maintenance operations on airplane engines where the engine contains the oil. Personnel at risk in such operations are ground crew involved in engineering and maintenance. These operatives get relevant information (for example through engineering handbooks and maintenance), training, and are warned about the toxicity of Mobil Jet Oil II by warnings on the label. For example:

❍ Engine maintenance manuals note: *Do not keep the oil on the skin for a long time. If you do not clean the oil off, the oil can cause injury and Do not let the*

oil stay on your skin. You can absorb poisonous materials from the oil through your skin. This suggests that oil is not harmless. This information is obviously aimed at maintenance personnel, and presumably envisages that no one else will come into contact with the oil. Further, new notices warning against the inhalation of mists were added in 1997-8. Further, the exposure in maintenance operations is probably mainly by skin contact, as the oil does not have an appreciable vapour pressure in ambient conditions. Such operational conditions can be seen to keep the risk of exposure to the oil under control.

❍ The label for the pre-1998 container contained the following risk and safety phrases:

Caution: Avoid spilling on insulation, plastic, rubber or paint

> **Warning! Contains Tricresyl Phosphate.**
> **Produces paralysis if taken internally.**
> **Do not use as medicine or food product.**
> **Wash thoroughly after handling.**

❍ The label for the post-1998 container contained the following warnings, risks and safety phrases:

Avoid spilling on insulation, plastic, rubber or paint

> **WARNING!**
> **Contains Tricresyl Phosphate.**
> **Swallowing this product can cause nervous system disorders, including paralysis.**
> **Prolonged or repeated breathing of oil mist, or prolonged or repeated skin contact can cause nervous system defects.**
> **PRECAUTIONS:**
> **Never swallow. Wash hands after handling and before eating. Never use in or around food. Avoid prolonged or repeated overexposure to skin or lungs.**
> **FIRST AID:**
> **If swallowed, seek immediate medical attention. If medical attention is delayed, induce vomiting. In case of contact, wash skin with soap and water. Remove contaminated clothing.**
> **FOR INDUSTRIAL USE ONLY**
> **Not intended or suitable for use in or around a household or dwelling. Never use empty container to carry water or food. Do not cut or weld on empty container.**
> (In thirteen languages) **When using do not eat, drink or smoke. After contact with skin, was immediately with plenty of soap and water.**

The change in warning information in the two labels is quite significant (see Figure below).

Figure -7: Warnings: Mobil Jet Oil II

Warning (pre-1992)

Warning (post-1992)
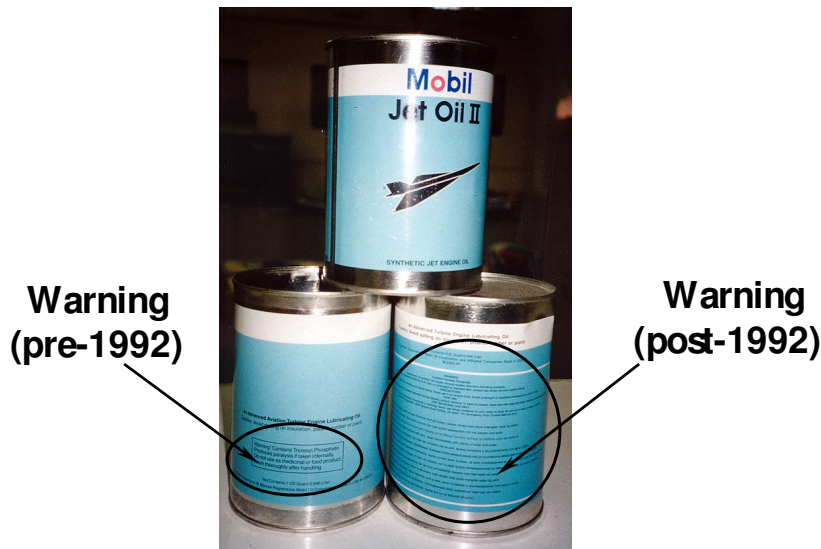
No reason was given to maintenance workers handling Mobil Jet II for the new label when it was introduced in 1998, although in evidence to the Senate Aviation Inquiry, Mobil note:

> Additional joint toxicology studies by Mobil and a major manufacturer of TCP confirmed that an oil with 3% TCP could produce toxic effects in animals administered very high doses. This led Mobil to adopt a very conservative labeling approach for its jet oils by including language recommending minimizing exposure by all routes and by emphasising the importance of good personal hygiene practices. The decision was made in 1997 and labeling was phased in during the year.[3]

In flight exposure

There is one other potential exposure to engine oils. This is when the engine leaks in flight, and leaking engine oils contaminate air flowing to the flight deck or passenger cabin. There are a number of possible exposure scenarios:

❍ exposure to the oil;

❍ exposure to a thermally degraded oil and its by-products;

❍ exposure to engine components, such as seals or bearings, that have worn down or have broken down into respirable particulates containing toxic elements such as nickel, beryllium and copper, entering the bleed air system.

In such circumstances, exposed crew and passengers are exposed to airborne contaminants that are leaking directly into air, and they are unaware of the toxicity of the contaminants they are inhaling. There is little control of exposure. Mobil "*do not believe that Mobil Jet turbine oils pose any significant toxicological risk to individuals accidentally exposed to aerosols or vapours in aircraft cabins. Such exposures are not what we would refer to as 'normal use' but the cabin levels that can be reached during such exposures … are considered safe*".[3] However, numerous leak incidents indicate that such exposures will produce symptoms of toxicity.

If exposure is to oil, it will be at least partially in a particulate (mist) form, where it can attain higher airborne concentrations than might be predicted from vapour pressures

(even at elevated, but rapidly cooling, temperatures). Further, the potential for skin exposure is greatly increased, as the mist can settle onto exposed skin, where it will then be available for dermal absorption. Further, the emission of oil vapours/smoke/mists into the passenger cabin would produce contamination of the cabin. Particulates would settle out onto surfaces (such as ducting, cabin walls, furniture and equipment), which would thereafter slowly vapourise, the rate of evaporation being dependent on individual contaminant vapour pressures. This residual contamination would continue until cleaned off or until it had evaporated.

While the toxicity of the oil has been established, little is known about the possible transformations that may have occurred in the oil while in operation. A leak of such an oil from an engine operating at altitude would see most of the oil pyrolise once it leaves the confined conditions of temperature and pressure operating in the engine. While it seems reasonable that any ingredients with suitable autoignition or degradation properties that allow such a transformation after release from the engine could be radically transformed, it is possible to speculate in only general terms about the cocktail of chemicals that could form.

Presumably this would include:

❍   combustion gases such as carbon dioxide and carbon monoxide;

❍   other irritating gases, such as oxides of nitrogen;

❍   partially burnt hydrocarbons (including irritating and toxic by-products, such as acreolein and other aldehydes); and

❍   TCP (which is fairly stable at high temperatures) or TCP thermal degradation products, such as highly toxic phosphorus oxides (TCP boils at 420ºC; TOCP boils at 410ºC); and

❍   Materials formed from worn or broken engine components that are present in the oil in particulate form.

These contaminants will be in gas, vapour, mist and particulate forms.

If the exposure is to a thermally degraded oil then as well any exposure to the oil mist (as outlined above), exposure can also include particulates such as soots; thermally degraded chemicals such as acreolin, and combustion gases such as carbon monoxide.

One final issue that should be given consideration on potential contaminants within a thermally decomposed jet oil. A number of papers discuss the possibility of formation of the strong neurotoxicant Trimethylolpropane phosphate (TMPP) in tricresyl phosphate containing aircraft lubricating oils.[76,77,78,79,80]   This chemical has an organophosphate structure (see below).

Figure -8: Structure of Trimethylolpropane phosphate
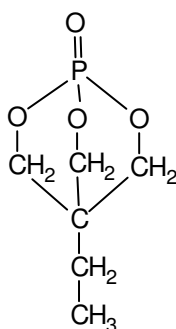
Operational temperature conditions for the maximal formation of TMPP (15%) is 550ºC.[80] Aircraft engines operate at such temperatures, although other conditions (presence of suitable reaction intermediates) may not be present. Investigation by the Naval Medical Research Institute Laboratory positively concluded that the thermal decomposition of aircraft lubricating oil produces TMPP,[81] although evidence for this synthesis is equivocal.[82] However, the toxic potency of TMPP is such that only a small amount formed in thermal degradation could provoke signs of toxicity, as "mechanistically, TMPP is thought to irreversibly inhibit the GABA-mediated inhibitory response and thereby produce epileptiform clonic/tonic seizures with convulsions followed by death".[81]

Conclusions

The jet oils are a commercially useful product. They are known to contain toxic ingredients. While the continued use of toxic materials is always a matter requiring caution and forethought, a full deliberation of risks and benefits may overcome such considerations.

This has occurred with the jet oils. Known to contain toxic ingredients, they have been used relatively unchanged for decades. The conservatism inherent in a complicated approval process, the reluctance to change toxic ingredients known to perform well in circumscribed situations, and the apparent lack of exposure scenarios where the toxicity could become apparent have all produced a conclusion that everything was within acceptable limits. Even the apparent toxicity of a jet oil reported from animal experiments in 1988 was not viewed as a significant problem.

However, an increasing number of oil leaks in the 1990's around the world and the increase in a number of flight attendants and flight crew reporting signs of toxicity after such events suggests the toxicity of the jet oils should be reconsidered:

❍ Publicly available information such as labels and MSDS appear to underplay the hazards of some toxic ingredients in Jet Oils. For PAN, no information is available regarding the presence of a skin sensitiser. For TCP, the almost complete reliance on expressing TCP toxicity in terms of how much TOCP is present is misleadingly deceptive and ignores the possible contribution of other ingredients, some present in higher amounts and with appreciably higher toxicities.

❍ The exposure scenario at altitude is utterly different from conventional exposures to the oils while using them in maintenance situations. Exposed individuals do not know to what they are being exposed, exposure by inhalational and dermal exposures can occur, the possibility of escape is absent, the possibility of cleaning or decontamination is absent).

❍ Options for the control of exposure are all but absent. Switching off an engine or bleed air system may offer some assistance, but is less useful if an entire ventilation system is contaminated.

❍ The exposure may be not only to gases and vapours, but also to particulates (such as oil mists or soots) that can be in proportionally greater concentrations than they would be for vapours.

❍ The exposure may to unchanged oil mists, or to combusted or pyrolised contaminants, or particulates arising from worn or broken engine components. The chemical make up of such a mixture would be difficult to deduce; the toxicity of exposure to such a mixture would be difficult to predict.

However, these contaminants could not be classified as being of low toxicity. The interactions of such effects with a specific toxic exposure is not known, but not presumed to be benign. The possible problems that might arise from exposure to such a cocktail cannot be dismissed without proper consideration.

Many of the signs and symptoms of exposure being reported by exposed flight crew[83] (and to a lesser extent, passengers). Symptoms arise from single, short term or long term exposures include:

❍ Symptoms from single or short term exposures include: blurred or tunnel vision, disorientation, memory impairment, shaking and tremors, nausea/vomiting, parasthesias, loss of balance and vertigo, seizures, loss of consciousness, headache, lightheadedness, dizziness, confusion and feeling intoxicated, breathing difficulties (shortness of breath, tightness in chest, respiratory failure), increased heart rate and palpitations, nystagmus, irritation (eyes, nose and upper airways).

❍ Symptoms from long term low level exposure or residual symptoms from short term exposures include: memory impairment, forgetfulness, lack of coordination, nausea/vomiting, diarrhoea, respiratory problems, chest pain, severe headaches, dizziness and feeling intoxicated, weakness and fatigue (leading to chronic fatigue), exhaustion, increased heart rate and palpitations, numbness (fingers, lips, limbs), hot flashes, joint pain, muscle weakness and pain, salivation, irritation (eyes, nose and upper airways), skin itching and rashes, skin blisters (on uncovered body parts), signs of immunosupression, hair loss, chemical sensitivity leading to multiple chemical sensitivity.

It is also apparent that some symptoms occur immediately or soon after exposure, for example, many of the irritant, gastric, nervous and respiratory effects. However, others, such as nervous system impairment, immunodepression and chemical sensitivity, develop later, perhaps months after exposures may have ceased. Further, while some of these symptoms are fully reversible, others appear to persist for longer. Debate is also continuing about the links between exposure and some of longer term

symptoms (such as chemical sensitivity).

Symptom severity depends on a number of factors, including the range of contaminants present, the intensity, duration and frequency of exposure, toxicity of compounds (expectedly influenced by cabin environment factors such as humidity, decreased oxygen concentration and contaminants such as carbon monoxide), and individual susceptibility.

These appear consistent with the toxicity of some of the ingredients of the oils. These include hydrocarbon neurotoxicity from exposure to organic chemicals, sensitivity from exposure to a sensitiser, COPIND from organophosphate exposure, or long term low level toxicity from exposure to carbon monoxide. These health problems need to be evaluated with more care than is apparent in the aviation industry at present.

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