Diesel

Toxicological overview

Key Points

Kinetics and metabolism

- As diesel is a mixture of chemicals, there is no definitive ADME (absorption, distribution, metabolism and excretion) data

Health effects of acute exposure

- Diesel may be irritating to the eyes, respiratory system and skin
- The main hazard associated with diesel is chemical pneumonitis that may arise following aspiration of vomitus (secondary to ingestion) or inhalation of aerosol (or aspiration of liquid) during manual siphoning

Health effects of chronic exposure

- Prolonged skin exposure to diesel may cause a variety of dermatitic conditions and is generally a result of inadequate or inappropriate use of personal protective equipment
- Diesel does not have a measurable effect on human reproduction or development
- There is currently no unequivocal evidence to link diesel with the incidence of cancer in humans but there is limited evidence for carcinogenicity in animals following prolonged exposure

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Toxicological Overview

Diesel is a complex mixture of hydrocarbons produced by blending several fractions of crude oil distillates with brand-specific chemical additives[a] (Annex I) [1]. The actual chemical composition of diesel varies widely according to the geographical source of crude oil, but generally comprises C_8 – C_{21} aliphatic hydrocarbons (boiling range 160 – 360 ºC) with up to 25% aromatic compounds.

The (UK) technical terms for diesel are “Class A1 Fuel Oil” and “Class A2 Fuel Oil” and refer to use in domestic and agricultural vehicles, respectively (Annex II). For the purpose of this document, “diesel” will be used as a synonym for A1 fuel oil.

Given its complex and highly variable composition, diesel is defined by physical characteristics rather than by chemical constituents (Annex III) [2].

This note does not consider diesel fumes arising from use in vehicle engines or from uncontrolled combustion.

[a] Diesel may also contain dyes or markers and up to 5% fatty acid methyl esters (FAME) in compliance with EN 14214:2003. Examples of additives are given at Annex I.

Summary of health effects

The principal adverse effect arising from the ingestion of diesel is chemical pneumonitis (secondary to aspiration of vomitus) [3, 4].

There is limited evidence to suggest that diesel may be nephrotoxic [5, 6].

Ingestion of diesel or acute exposure to vapour may lead to general signs of intoxication such as mild CNS symptoms (dizziness, headache, nausea) and vomiting [7, 8].

Skin exposure to diesel may result in dermatitis [3, 7].

Certain types of diesel are non-genotoxic animal carcinogens and are classified as Category 3 carcinogens under Chemicals (Hazard Information and Packaging for Supply) Regulations 2002. (CHIP) [8, 9].

Kinetics and metabolism

As diesel is a mixture of chemicals, there is no definitive absorption, distribution, metabolism and excretion (ADME) data available for either animals or humans [9]. The onset of local or systemic effects following dermal, oral or pulmonary exposure indicates that these are all potential routes of absorption for diesel.

Sources and route of human exposure

Occupational exposure may potentially occur during manual filling or discharge operations within the petrochemical industry [10], repair or service of diesel engines or from practices where diesel is used as a cleaning agent or solvent [9].

Domestic exposure to diesel is uncommon, although limited skin exposure may occur whilst refuelling domestic vehicles and pulmonary exposure may result from aspiration of liquid during manual siphoning. Leakage of diesel onto hot engine manifolds may liberate a respirable aerosol of micrometer-sized diesel particles [11].

Large-scale environmental contamination has occurred following the release of diesel from storage tanks and sea tankers [9] and some concern has been expressed over health effects of vapour arising from contaminated soil [12].

Diesel accounted for all spillages resulting from road traffic incidents in the UK during 2003 and 42% of all significant[2] (Environment Agency Category 1 or 2) pollution incidents for the same period [13].

[2] Significant refers to a Category 1 or 2 incident as defined by the Environment Agency's National Incident Recording System (Common Incident Classification, or CIC).

Health Effects of Acute / Single Exposure

Human Data

General toxicity

Under normal conditions of storage, handling or use as fuel, diesel should not present a hazard to health providing excessive skin contact is avoided [14]. The main hazard associated with diesel is chemical pneumonitis that may arise following aspiration of vomitus (secondary to ingestion) or inhalation of aerosol (or aspiration of liquid) during manual siphoning [4, 8].

There are few studies investigating the toxicity of diesel *per se*. Therefore, toxicological evaluations of diesel tend to be derived by considering the toxicity of similar (middle distillate) products such as kerosene and petrol [4, 8, 9, 11]. However, such comparisons do not take into account the toxicity of brand-specific additives, the effects of which cannot be predicted from complex hydrocarbon mixtures. Therefore, this note will mainly consider studies that are specific to diesel.

Inhalation

One study has examined the effects of a combined exposure to diesel (5 ppm) and acetaldehyde (0.5 ppm) in Gulf War veterans but did not report any adverse effects in healthy volunteers [15].

It has been stated that inhalation of diesel vapour may lead to central nervous system (CNS) / respiratory depression and cardiac arrhythmias [7]. There do not, however, appear to be any specific case studies to confirm these effects; it is assumed that the (limited) presence of low molecular weight hydrocarbons in diesel is sufficient to contribute to such signs of toxicity [16]. Most clinical instances of myocardial sensitisation occur following exposure to volatile solvents such as those found in adhesives, lighter fluid, nail polish remover and aerosol propellants [17]. Diesel vapour (at 37°C) predominantly contains C_{10+} hydrocarbons [18].

Direct aspiration of diesel [19] or aspiration of contaminated vomit is a secondary source of pulmonary exposure that may lead to chemical (lipoidal) pneumonitis [20], a delayed onset and potentially fatal lung disorder characterised by cyanosis, dyspnoea and chest x-ray opacities [21].

Ingestion

The signs of toxicity following oral intake are generally stated to include nausea, vomiting, diarrhoea, irritation of the aero-digestive and GI tracts [7]. In one reported case of intentional self-poisoning, chemical pneumonitis was observed (which may have been due to aspiration of vomitus) [22].

Dermal / ocular exposure

Eye exposure to diesel may cause transient pain and/or hyperaemia [7]. Diesel is generally considered to be less irritating to the eyes than other middle distillate fuels such as kerosene or petrol [8].

Acute dermal exposure may result in local irritation (erythema, pruritis) which is generally more severe than that seen with other middle distillate products [23]. The incorporation of additives (such as biocides) may augment dermal sensitivity to diesel [24]. It has been suggested that the inclusion of visible markers (dyes) may increase the self-perceived dermal irritancy of diesel [25].

Neurotoxicity

No reports on the neurological effects of human diesel exposure were available in the literature. However, diesel is known to contain a number of potentially neurotoxic substances [11] and exposure to other mid-distillate fuels has resulted in neurological disorders including drowsiness, neurasthenia and decreased sensorimotor speed [4].

Nephrotoxicity

Several case studies have cited acute renal failure (secondary to acute renal tubular necrosis) as a potential complication following acute exposure to diesel [6, 8, 9, 26]. Signs included oliguria (progressing to anuria), nausea, abdominal cramps and diarrhoea.

Delayed effects following an acute exposure

There is limited evidence to suggest that long-term pulmonary residual effects may occur following chemical pneumonitis (as a result of aspiration-induced pneumonitis) [20, 27]: these chronic effects are of unknown clinical relevance [28].

Animal and In-Vitro Data

General toxicity

The oral toxicity of diesel is relatively low, with two studies reporting LD_{50} values of 7.5 g kg^{-1} [29] and 16 ml kg^{-1} in the rat[3] [30]. Diesel was reported as being non-irritating to the eyes but severely irritating to skin of rabbits [29]. No deaths were reported following acute dermal exposure to 5 g kg^{-1} in rats [9].

In a study using rats, a Ct of 1440 mg min m^{-3} was not lethal if given as a 4 hour exposure, but the same Ct was lethal for a 6 hour exposure [4].

[3] Conversion from ml kg^{-1} to g kg^{-1} was not possible, as the density of the material used in the study was not stated.

Delayed effects following an acute exposure

The available literature pertaining to the long-term effects of diesel following acute exposure is mainly concerned with jet fuels [11, 31] and thus its relevance is uncertain due to the presence of chemical additives and different hydrocarbon profile. In general, single (acute) oral, dermal and ocular exposures do not appear to result in persistent effects.

Health Effects of Chronic / Repeated Exposure

Human Data

General toxicity

Under normal industrial or domestic use, dermal contamination is the most likely exposure scenario. Chronic or repeat exposure to diesel may result in dermatitis although there is some evidence to suggest that hyperkeratosis may be a common feature of regular contact with diesel [8].

Inhalation

There are currently no unequivocal studies to relate chronic or repeated diesel exposures to long-term pulmonary dysfunction (other than that associated with aspiration of contaminated water or vomit). There is limited evidence to suggest that chronic exposure to long-chain hydrocarbon mixtures may be associated with a tightness of chest and breathing difficulties, although a review of the duration and extent of exposure in such circumstances was not reported [31]. In one case, a lorry driver was exposed to (an unknown concentration of) diesel vapour over a ten day period. Signs and symptoms included abdominal cramps, nausea, vomiting, acute renal failure, anaemia and thrombocytopenia [32].

Ingestion

Chronic, oral exposure to diesel is unlikely to arise under normal circumstances and there is currently no data available on the chronic effects of diesel ingestion in humans.

Dermal / ocular exposure

There are no reports on the effects of chronic ocular exposure to diesel in humans.

Acne and folliculitis have been reported in one subject who may have received chronic (occupational) exposure to diesel ([33] as reviewed in [8]). An investigation of Azerbaijan oil field workers identified hyperkeratosis as being associated with diesel exposure ([34] as reviewed in [8]).

Genotoxicity

There was evidence of increased chromosomal aberrations in a small cohort of drivers exposed to diesel ([35] as reviewed in [9]). However, the group size was small (6 smokers and 6 non-smokers) and the effects of exposure to other substances (such as diesel exhaust fumes) could not be discounted.

Carcinogenicity

In a multi-site, case-control study, there was evidence for an increased risk of prostate cancer and squamous cell carcinoma of the lung [36] but this effect could not be attributed to any particular chemical. The International Agency for Research on Cancer (IARC) have evaluated diesel fuels as being "not classifiable as to their carcinogenicity to humans (Group 3)" [9]: there is "inadequate evidence" to classify diesel as a human carcinogen and "limited evidence" for the carcinogenicity of diesel to experimental animals.

Reproductive and developmental toxicity

There is currently no information concerning the effects of diesel exposure on human reproduction and development. Exposure to diesel is not an indication for invasive prenatal diagnostic tests or termination of pregnancy [37].

Animal and In-Vitro Data

General toxicity

A number of studies have reported hyaline droplet nephropathy syndrome in rats; this pathological response is not considered to be relevant to humans [8].

Inhalation

In one study, mice were exposed to diesel vapour at concentrations of 65, 135 and 204 mg m^{-3}, 8 hours a day for 5 days (equating to a daily Ct of 31, 65 and 98 g min m^{-3}, respectively) [18]. Three of ten animals died in the highest dose group. There were no general effects noted in the lowest dose group.

Following exposure to diesel vapour (≤ 6 mg L^{-1}; ≤ 6h duration; ≤ 3 $week^{-1}$; ≤ 9 exposures), the primary signs of toxicity in rabbits were observed in the lung. Such effects included an increase in leukocytes in bronchial lavage (BAL) fluid and (non-dose dependent) changes in lung function parameters ([38] as reviewed by [8]).

No substantial signs of toxicity were observed in rats exposed to diesel aerosol (≤ 1.5 mg L^{-1}; 4h per day; 2 $week^{-1}$; 13 weeks): other signs deemed to be indicative of slight toxicity (including decreased weight and increase in BAL macrophages) were described as "generally reversible" following an eight week recovery period ([39] as reviewed by [8]).

Ingestion

There were no available reports on the chronic oral toxicity of diesel in animals.

Dermal / ocular exposure

Exposure of rabbits to diesel (4 or 8 ml kg^{-1}; 24h day^{-1}; 5 days $week^{-1}$) for 14 days resulted in dose-dependent dermal irritation and anorexia, leading to cachexia and death in the highest-dose group [29].

Genotoxicity

Diesel was reported as being negative in the Ames *Salmonella* assay [40]. (This was interpreted as diesel being "weakly mutagenic" by the IARC [9]). In the same study, diesel was determined to be non-mutagenic in the L5178Y (TK +/- and TK -/- strains) mouse lymphoma assay. Dimethyl sulphoxide extracts of diesel (containing aromatic or aliphatic fractions) did not induce mutations in *S. typhimurium* TA100 ([41] as reviewed by [9]). No effect was observed on the frequency of dominant lethal mutations in mice (CD-1) exposed to diesel (≤ 400 ppm; 6 h day^{-1}; 5 days $week^{-1}$) for a total of 8 weeks ([8, 42] as reviewed by [8]).

In-vivo bone marrow clastogenicity studies showed a clear increase in chromosome aberrations only at very high dose levels (6 ml kg^{-1} body weight) [41]. No details of the type of aberration were provided and no definitive conclusions can be drawn.

The available data indicate that diesel does not have any mutagenic potential.

Carcinogenicity

It is generally considered that most middle-distillate fuels (e.g. kerosene, petrol and diesel) are non-genotoxic carcinogens [43-46].

In the most recent study of tumorigenic potential, rats were administered diesel by oral gavage (in olive oil) four times per week for 104 weeks [47]. The authors surmised that there was a non-dose dependent increase in the incidence of total malignant tumours (which may be of limited relevance) and an increase in uterus-vaginal malignant tumours (which was described as dose related). No further details are available.

Reproductive and developmental toxicity

No teratogenic (developmental) effects were observed in rats subject to inhalation of diesel vapour between gestational days 6 and 15 (6h day^{-1}; 100 & 400 ppm) ([48] as reviewed in [9]).

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Annex I: Categories of Diesel Additives.

Category	Concentration Range	Example(s)	Notes
Antioxidants	9 – 25 ppm	Hindered phenols (e.g. 2,4-dimethyl-6-tert-butylphenol).	Prevent “gum-forming” reactions
Stabilisers	25 - 200 ppm	Polymethacrylate, polyisobutane	Prevent sediment formation if diesel product is prepared from craked components.
Metal deactivators	~10 ppm	N,N’-disalicylidene-1,2-propanediamine	Chelate metal ions
Cetane improvers	200 – 800 ppm	2-ethyl hexyl nitrate	Decrease time between injection of ignition in combustion chamber.
Combustion improvers	0.2% v/v	Historically include barium, manganese and copper.	Catalytic effect on combustion. No longer in common use.
Flow improvers	500 ppm	Ethylene acetate / vinyl acetate polymers	
Detergents	100 - 200	Amines, amides, imidazolines	Prevent “gummy deposits”.
Corrosion inhibitors	5 ppm	Surfactants based on esters or amine salts of alkenyl succinic acids, alkyl orthophosphoric acids and aryl sulphonic acids.	Primarily to protect pipelines during transport.
Antistatic additives (Static Displacement Additives)	1 – 5 ppm	Toluene, alkyl benzene sulphonate, mono and di-alkyl salicylic and dodecyl sulphosuccinic acid (Cr and Ca salts).	Added to prevent build-up of charge during bulk transfer under fast pumping rates.
Dehazers and demulsifiers	5 – 20 ppm	Quaternary ammonium salts.	Added to storage tanks on an ad hoc basis to remove water contamination.
Lubricity additives	0.03 w/w%	Phosphate ester amides.	Improve lubricity caused by hydrotreatment (to remove sulphur).
Anti-icers	Up to 30 ppm	Alcohols / glycols.	Added to delivery tanks.
Biocides	200 ppm	Thiazine derivatives.	Prevent bacterial spoilage on storage in fuel tanks.
Antifoamants	10 – 20 ppm	Silicone additives.	Prevent foaming, allowing more more complete filling of engine.
Odour masks and odorants	10 – 20 ppm		Neutralise or mask smell.
Drag reducers	50 ppm	High molecular weight, oil-soluble polymers.	Reduce drag through pipelines to increase throughput.

Table A1: summary of common additives used to improve burn, storage or transport characteristics of diesel [1].

Annex II: UK Classification of Fuel Oils.

Category	Crude Fraction	Primary Application
A1	Middle distillate	Automotive diesel fuel.
A2		Agricultural engine fuel.
C1	Paraffin	Flue-less heating appliances.
C2	Kerosene	Vaporising or atomising domestic heating appliances.
D	Middle distillate	Atomising burners for domestic, commercial or industrial applications.
E - H	Residual distillate	Atomising burners for boilers or certain industrial engines which may require pre-treatment or additives.

Table A2: Classification of various grades of fuel oil according to crude distillate fraction ("crude fraction") and application. Source: Annex A to BS 2869:1998.

Annex III: UK Physicochemical Standards for Diesel

Property	Minimum	Maximum
Cetane №.	51	-
Density at 15 °C (kg m^{-3})	820	845
Viscosity at 40 °C (mm^2 s^{-1})	2.0	4.5
Flash point (°C)	> 55	-
Polycyclic aromatic hydrocarbons (% w/w)	-	11
Sulphur content (mg kg^{-1})	-	50
Water content (mg kg^{-1})	-	200
Ash content (% w/w)	-	0.01
Fatty acid methyl ester content (% v/v)	-	5

Table A3: Summary of standard physicochemical properties of diesel (BS EN 560:2004).

This document will be reviewed not later than 3 years or sooner if substantive evidence becomes available.