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# The Chemicals which show toxicological and carcinogenicity effect

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## The Chemicals which show toxicological and carcinogenicity effect

### Acetaldehyde

Acetaldehyde is a metabolic intermediate in humans and higher plants and product of alcohol fermentation. It is used as a intermediate in the production of acetic acid, ethyl acetate and other organic chemicals. The compound is also used as a flavouring agent in beverages, ice cream and ices, candy, baked goods, gelatine desserts and chewing gum.

Although acetaldehyde formed during the metabolism of ethanol provides the greatest source of human exposure. The general population may be exposed via cigarette smoke, air and high levels detected in some fruit juices, alcoholic beverages and vinegar, Very little to the exposure to drinking water, its effect on the aquatic and terrestrial environment is low. Toxic effects are observed in animals including degenerative changes in the olfactory epithelium and trachea and higher concentration, degenerative changes in the respiratory epithelium and larynx.

**Reference:** Environmental Health Criteria No. 167, 1995, 129p, ISBN 9241571675.

### Acetonitrile

A by-product of acetonitrile manufacture, which is widely used as an extractive distillation solvent in the petrochemical industry and as a solvent of polymer spinning and casting in laboratories. It is used in high performance liquid chromatography, analysis and as a solvent for DNA synthesis and peptide sequencing. These practical uses are identified as the major source of human exposure.

This chemical has low toxicity due to rapid volatilisation and biodegradation. Studies of kinetic and metabolism indicate that acetonitrile is readily absorbed by all routes and rapidly distributed throughout the body, where it is converted to cyanide. A review of studies conducted in laboratory mammals concludes that acetonitrile induces toxic effects similar to those observed in acute cyanide poisoning with prostration followed by seizures identified as the main symptoms. No animal studies on chronic or carcinogenic effects have been reported. In human, studies of accidental poisoning in occupationally exposed workers have identified the symptoms and sign of acute acetonitrile intoxication as chest pain, tightness in the chest, nausea, emesis, tachycardia, hypotension, short and shallow respiration, headache, restlessness, semi-consciousness, and seizures. This shows that the chemical should be clearly labelled with a warning about the danger of poisoning.

**Reference:** Environmental Health Criteria No.154, 1993,110p, ISBN 9241571543.

### Acrolein

The chemical produced in large quantities and used as an intermediate in the synthesis of several chemical most notably acrylic acid and its esters and DL-methionine, an essential amino acid used as a feed supplement for poultry and cattle. Acrolein also has direct application as an aquatic biocide used against algae, molluscs and herbs in re-circulating process water systems, irrigation channels, cooling water towers and water treatment ponds. Acrolein accounts for about 3 to 10% of total wood-smoke aldehydes and up to 7% of aldehydes in cigarette smoke.

Its exposure to the general population occurs mainly via air, with mainstream and side stream tobacco smoke representing the most important source, Other sources of exposure include inhalation of air polluted by vehicle exhausts, direct contact with acrolein-treated eater, and consumption of alcoholic beverages and certain food items. Concerning effects on the environment, it show adverse effects on crops grown on soil irrigated by acrolein treated eater, and a very high toxicity for bacterial, algae, crustacean and fish, with bacterial being the most sensitive species. Acrolein is noted to threaten aquatic life at or near sites of industrial discharge or spills and in areas where acrolein is used as biocide. They have also listed the toxicological effect conducted in laboratory mammals and in vitro test systems. Studies support the conclusion that acrolein is acutely cytotoxic, produces tetratogenic and embryotoxic effects, and is weakly mutagenic. Data on carcinogenicity were judged inadequate. In humans, case reports of accidental exposures and suicidal intoxication confirms the high toxicity of the chemical.

**Reference:** Environmental Health Criteria. No. 127, 1992, 119p, ISBN 9241571276.

## Acrylic Acid

Acrylic acid is used primarily in the production of acrylic esters, as a monomer for polyacrylic acid and salts, and as a co-monomer with acrylamide for polymers used as flocculent, with ethylene for ion-exchange resin polymers with methyl ester for polymers, and with it aconic acid or other co-polymers. Inhalation and dermal exposures occurring in occupational settings were judged to be the most important exposures affecting human health. Exposure via food was determined to be unlikely. Studies show that Acrylic acid show low to moderate acute toxicity by the oral route and moderate acute toxicity by the inhalation and dermal routes, Studies also confirm that acrylic acid is corrosive or irritant to the skin and eyes and strongly irritant to the respiratory tract. Studies indicate that the chemicals is not tetratogenic and has no adverse effects on reproduction. On the basis of animals studies and knowledge about the chemical and biological behaviour of the chemical and biological behaviour of the chemical, The report shows that it does not pose any obvious risks to the health of general population. Proposed guidance values for the general population are 9.9mg/litre for drinking water and 54 mg/m<sup>3</sup> for ambient air.

**Reference:** Environmental Health Criteria No. 191, 1997, Xviii, 106p, ISBN 9241571918.

## Aldicarb

Aldicarb, a carbamate insecticide applied, exclusively in granular form and below the soil surface, to control certain insects, mites and nematodes. Aldicarb has been approved for use on wide range of crops, ingestion of contaminated food is the main route of exposure for the general population, it is applied to subsoil, the evaluation of environmental fate concentrates on mobility and persistence in soil and on the circumstances under which aldicarb may contaminate shallow wells. The rapid uptake of aldicarb and its residues by food crops is another consistently reported finding. Studies in experimental animal show efficient absorption of aldicarb from the gastrointestinal tract and its wide distribution to all tissues including the developing foetus. Concerning risks to human health, the book draws on reports of several widespread outbreaks of aldicarb poisoning following the ingestion of contaminated cucumber, melons, watermelons and drinking water in each of these cases, poisoning resulted from the use of aldicarb on non-approved crop. It is concluded that aldecarb is one of the most potent and accurately toxic pesticides in use, its toxicity occur due to the use on non-approved crops or the failure to follow recommended safety precautions that the symptoms of poisoning are transient and really fatal and aldicarb poses no risk to the general population when applied at recommended rates and using current techniques. It is suggested that use of protective equipment during manufacturing, formulation and application of it.

**Reference:** Environmental Health Criteria No. 121, 1991, 130p, ISBN 9241571217.

## Aluminium

In view of recent evidence suggesting a role of aluminium exposure in the development or progression of Alzheimer's diseases, the report gives particular attention to the methodological strength and weaknesses of epidemiological studies and the relevance to humans of animal species. Over 700 studies were assessed in an effort to resolve current uncertainties about risk to the general population, exposed workers the elderly and several other susceptible sub-populations. The aluminium is released to the environment both by natural processes and from anthropogenic sources. As aluminium is a major constituent of the earth's crust and the third most common element, natural processes for outweigh the contribution of anthropogenic sources. Much higher exposure are occur in certain occupations and in people taking antiacids and buffered analgesics. The drinking water is a minor source of human exposure.

In review of human and animal data on kinetics and metabolism concludes that aluminium and its compounds are poorly absorbed in human the highest levels have been detected in the lungs. In animals, aluminium is distributed in most organs within the body with accumulation occurring mainly in bone at high dose levels. An evaluation of the large body of data from toxicity studies in experimental animals found no evidence that aluminum is carcinogenic and no evidence of fetotoxicity or adverse effects on reproduction. Considerable evidence indicates that aluminium is neurotoxic, with adverse effects on neurological development and brain function, studies have also, demonstrated toxic effects on bone and osteomalacia, as it presents in man, has been consistently observed. The report found no evidence that exposure induces a neurological pathology with the morphological and biochemical characteristic of Alzheimer's disease. The evaluation of effects on human health gives particular attention to several

Epidemiological studies carried out to test the hypothesis that aluminium in drinking water is a risk factor for the development of acceleration of Alzheimer's disease and possible cause of impaired cognitive function in the elderly and in occupationally exposed workers. Currently available evidence does not support a causal relationship between Alzheimer's disease and exposure to aluminum in exposures, either occupational or via drinking water, may be associated with non-specific impaired cognitive function ways likewise judged to be inadequately supported by available data. The study demonstrate that patients with renal failure are at risk of neurotoxicity and other disorders from aluminium present in haemodialysis fluid and pharmaceutical products. As iatrogenic aluminium exposure has been shown to pose a hazard to patients with chronic renal failure and to premature infants the report concludes that every effort should be made to limit exposure in these groups Concerning risks to environment, the report concludes that concentrations of aluminium can increase to level resulting in adverse effects on both aquatic organism and terrestrial plant in some areas subject to strong acidifying inputs.

**Reference:** Environmental Health Criteria No.194, 1997, XX, 282p, ISBN 9241571942.

## Amitrole

Amitrole is a herbicide with a very wide spectrum of activity against annual and perennial broad leaf and grass type weeds. Amitrole, which appears to act by inhibiting the formation of chlorophyll is widely used around orchard trees, on fallow land prior to Sowing, along roadsides and railway lines, and for weed control in ponds. The herbicide is not approved for direct application to food crops.

Amitrole is rapidly degraded in the environment with no evidence of either bioaccumulation or entry into the food chain. Exposure of the general public is expected to be minimal. Studies in both humans and animals show that amitrole is rapidly absorbed and rapidly excreted in urine in an unchanged form. It shows toxic effects on the thyroid. These findings support the conclusion that amitrole is goitrogenic, causing thyroid hypertrophy and hyperplasia, depletion of colloid, and increased vascularity. Experiment indicate that these changes precede the development of thyroid neoplasia, the precise mechanism triggering the change from hyperplasia to neoplasia remains to be elucidated. Although studies of occupationally exposed workers are largely reassuring, the book recommends annual monitoring of thyroid function in workers regularly handling amitrole at either the formulation or application stage. It is

concluded that amitrole poses no significant threat to the environment, the levels in food and drinking water should be extremely low and that the herbicide poses no threat to the health of workers of the general population when manufactured and used as recommended

**Reference:** Environmental Health Criteria No. 158, 1994, 123p, ISBN 9241571586.

## Anticoagulant Rodenticides

This was use to anticoagulants for rodent control in urban agricultural setting Warfarin, it was introduce in 1940'sis considered together with the more potent second generation anticoagulants including the single dose "Superwarfarins " because warfarin is widely used in the clinical management of thromboembolic disease, its effects on human health are well documented. Abundant information is also provided on the mechanism by which these anticoagulants act as Vitamin K antagonists.

An evaluation of effect on laboratory animals in vitro test systems demonstrates high acute toxicity by oral, percutaneous and inhalation routes. Anticoagulant rodenticides are noted to disrupt the normal blood clotting mechanisms, resulting in increased tendency to bleed and at higher exposures in profuse haemorrhage. The second generation anticoagulant rodenticides differ from warfarin in the greater toxicity, their longer retention time in the liver, and their corresponding tendency to induce bleeding for weeks instead of days.

An evaluation of effects on human health draws on the large number of case reports of accidental and intentional poisoning, a few case reports of accidental and intentional poisoning, a few case reports of intoxication following occupational exposure and extensive experience in the clinical use of warfarin. Following exposure to second generation anticoagulants, symptoms of human poisoning included haematomas, haematomesis effects have been demonstrated following the administration of wartarin during pregnancy. The report found no evidence that anticoagulant rodencides are mutagenic or carcinogenic, but did cite evidence that long term exposure to low levels may have an adverse effect on bone metabolism.

**Reference:** Environmental Health Criteria No. 175, 1995, 121p, ISBN 9241571756.

## Barium

Evaluates the risks to human health and the environment posed by the mining, processing and industrial use of barium. The opening sections review both natural and man made sources of release into the environment. Including nuclear fallout following the testing of weapons. A section on environmental behaviour notes the contribution of industrial emissions, especially from the combustion of coal and diesel oil, to the presence of barium in air particular concern centres on concentrations found in water where barium may have a residence time of several hundred years. Water supplies and food are identified as the most important routes of exposure for the general population.

Other section review what is known about the kinetics and metabolism of barium, discuss its capacity to mimic the role of calcium in many physiological processes and consider effects on organisms in the environment, including effects on the infectivity of several viruses.

The most extensive section evaluates experimental studies of barium toxicity, with particular attention given to report effects on cardiovascular functions. The final section devoted to effects on human health, evaluates finding from large scales outbreaks of barium poison and from epidemiological studies designed to determine whether high barium concentration in drinking water are linked to disturbances in cardiovascular function. On the basis of these evaluation, the book concludes that barium poses no special risk for the general population, potassium deficient individuals the elderly, exposed workers and

populations consuming high concentrations of barium in drinking water may experience adverse effects on health.

**Reference:** Environmental Health Criteria No. 107, 1990, 148p, ISBN 9241571071.

## Benomyl

Evaluates the risks to human health and the environment posed by benomyl, a fungicide registered for use in 50 countries on over 70 crops, including cereals, cotton, soybean, tobacco, mushrooms, grapes, bananas and other fruits. One of the most widely used members of benomyl is effective at low usage rates against more than 190 different fungal diseases. Because benomyl is rapidly converted to carbendazim in the environment and extensively metabolized to carbendazim by experimental animals data from studies of carbendazim, which is a fungicide in its own right are also considered when evaluating the hazards of benomyl.

Concerning hazards to environmental organisms, the report cites data from laboratory and field studies indicating that benomyl applied at recommended rates has little effect on soil microbial activity, but some adverse effect on groups of fungi. Benomyl is toxic to earthworm in laboratory experiments at realistic exposure concentration and as a result of recommended usage in the field. Earthworm populations may take more than two years to recover. Although high toxicity to aquatic organisms has been demonstrated in laboratory tests, the report concludes that this effect is unlikely to be seen in the field due to the low bioavailability of sediment bound residues. For the general population, the main source of potential exposure is noted to be through the ingestion of food crops, containing residues of benomyl and carbendazim. Though benomyl has been shown to cause contact dermatitis and dermal sensitisation in some farm workers, the report found no evidence that either of these compounds can cause systemic toxic effects in occupationally exposed subjects or the general population. The report cites findings suggesting that both compounds pose a very low risk for acute poisoning in humans.

**Reference:** Environmental Health Criteria No. 148, 1993, 135p, ISBN 9241571489.

## Benzene

Evaluates the risks to human health and the environment posed by exposure to benzene, a naturally occurring chemical found in crude petroleum and manufactured in extremely large quantities world-wide. The presence of benzene in gasoline and in cigarette smoke, combined with widespread use as an industrial solvent and resulting in the presence of this chemical in the environment. Because benzene is a well-established human carcinogen, its effect on the general population and exposure of workers depend upon the duration of exposure. Its emission from motor vehicles is the largest source of its exposure. Indoor exposure caused by cigarette smoke results in the exposure of non-smokers to benzene. Its exposure to side stream smokes residents in areas of heavy automobile traffic and those workers handling the use of benzene and its derivatives.

The most extensive section reviews the large number of toxicity studies of benzene. Particular attention is given to the numerous animal studies demonstrating carcinogenicity and exploring the mechanism by which benzene damages bone marrow and exerts its other toxic effects. The epidemiological studies show that benzene is a human leukaemogen because the health risk of low level benzene exposure is not yet clearly established, so that its exposure should be avoided as much as possible.

**Reference:** Environmental Health Criteria No. 150, 1993, 156p, ISBN 9241571500

## Beryllium

Evaluate risks to human health and the environment posed by the use of beryllium, a brittle metal having major applications in the electronics and micro-electronics industries, in nuclear energy and in the

production of military devices including satellites, missiles, atomic bomb and other weapons. Beryllium has also proved its superiority as a structural material for aircraft and spacecraft.

An evaluation of sources of exposure cites the combustion of fossil fuels as the most important source of atmospheric beryllium, with coal singled out the main pollutant source. For humans the report notes that toxicologically relevant exposure is almost exclusively confined to the workplace. Only two applications pose a risk to the general population, mantle type camping lanterns and the use of beryllium in dental prostheses and cements.

It evaluates data from large number of toxicological studies documenting the development of acute chemical pneumonitis and highly species-specific induction of pulmonary cancer. An evaluation of effects on humans which concentrates on occupational exposures summaries findings on the occurrence of both acute and chronic beryllium disease. The review and yields clinically useful information on exposure levels, characteristic signs and symptoms and the most reliable diagnostic test. In view of the controversy concerning the carcinogenicity of beryllium particularly are full attention was given to several studies, reporting a significantly elevated risk of lung cancer in exposed workers, evidence was judged sufficient to confirm the role of beryllium in the development of human lung cancer. The report further concludes that the potential of beryllium to provoke contact allergic contact stomatitis in dental patients, calls for a reconsideration of the use of this metal in dentistry.

**Reference:** Environmental Health Criteria No. 106, 1990, 210p, ISBN 9241571063.

### **Beryllium, Cadmium, Mercury and exposures in the glass manufacturing industry.**

Evaluates the carcinogenic risk to human posed by exposure to selected metals and their compounds. Separate monographs are presented for beryllium and beryllium compounds. Cadmium and Cadmium compounds and mercury and inorganic and methyl mercury compounds, because several metallic salts and pigments are used in the manufacture and colouring of certain glass products. More than 1200 references to the recent literature are included. The first monograph evaluates biological and epidemiological data on metallic beryllium, beryllium-aluminium and copper alloys and some beryllium compounds. Data from studies in humans and several well designed animal investigations support the conclusion that beryllium and beryllium compounds are carcinogenic to humans. The monograph on cadmium and cadmium compounds gives particular attention to new analyses of epidemiological cohorts and new studies in experimental animals. These data support the conclusion that cadmium and cadmium compounds are carcinogenic to humans. The monograph on mercury and mercury compounds classifies methylmercury compound as possibly carcinogenic to human. Metallic mercury and inorganic mercury compounds could not be classified.

Citing evidence from recent cohort studies the monograph on exposures in the glass manufacturing industry concludes that the manufacture of art glass, glass containers and pressed ware entails exposures that are probably carcinogenic to humans. Occupational exposures in flat-glass and special glass manufacture could not be classified as to their carcinogenic to human.

**Reference:** IARC Monographs on the Evaluation of Carcinogenic Risk to Humans, Volume 58, 1993, 444 p, ISBN 9283212584.

### **Brominated Diphenyl Ethers**

Evaluate the risks to human health and the environment poses by exposure to ten brominated diphenyl ethers. Of these three (decabromodiphenyl ethers, octabromodiphenyl ether and pentabromodiphenyl ether widely manufacture and used as additive flame compounds retardant or impurities in commercial brominated flame retardant. The remaining seven compounds occur as contaminants or impurities in commercial brominated flame retardant. Brominated biphenyl ethers are used in increasing quantities in a wide range of products. Concern about potential risks to human health and the environment has centred on the persistence of these chemicals in the environment, their tendency to bioaccumulate, their

detection in several food items and in human adipose tissue and milk, their tendency to leach or escape from finished products during normal operation, and the release of polybrominated dibenzofurans and polybrominated dibenzodioxins as breakdown products under certain conditions.

For decabromodiphenyl ether, which is the most important of these products, the report cites evidence of persistence in the environment accumulation in sediment and soil occupational exposure during manufacturing and formulation and an insignificant exposure of the general population. Similar risks to the environment were found for octabromodiphenyl ether. For pentabromodiphenyl ether, evidence of environmental hazards and potential human exposure via the food chain supports the conclusion that this product should not be used. In its conclusions, the report stresses the need to minimise environmental contamination with these persistent compounds and their breakdown products. Introduction of such chemicals into widely used products may create a considerable long term diffuse source of emissions into the environment.

**Reference:** Environmental Health Criteria No.162, 1994, 347p. ISBN 9241571624.

## Cadmium

Evaluates the large body of experimental and epidemiological evidence linking cadmium exposures to adverse effects on the health of workers and the general population. In view of the global importance of cadmium as a potentially dangerous environmental pollutant. The book makes a special effort to establish a dose response relationship for the widely documented adverse effects on the kidney and other organs observed in chronically exposed populations. Findings from over 700 investigations were critically appraised.

The report notes that most human uptake of cadmium occurs via the inhalation of air and the ingestion of contaminated food and drinking water, with other sources contributing only small amounts to the total uptake. A review of data on the kinetics and metabolism of cadmium in laboratory mammals and human concludes that exposure via inhalation is more important than exposure via the gastrointestinal route that the highest cadmium concentrations are generally found in the renal cortex and that as exposure levels increase, a greater proportion of the absorbed cadmium is stored in the liver.

The second half of the report evaluates the manifestation of cadmium toxicity. Data from experimental studies support the conclusion that long term exposure to cadmium leads to renal dysfunction with proteinuria, glucosuria, aminoaciduria. The histopathological changes in the kidney. The evaluation of effects on humans draws upon epidemiological and clinical studies conducted in occupationally exposed workers and in populations from environments polluted with cadmium. The report concludes that exposure to cadmium produces a wide variety of effects involving many organs and systems. From the point of view of preventive medicine, the detection of early effects on the kidney is regarded as crucial to the prevention of more severe effects on the kidney, lungs and bone.

**Reference:** Environmental Health Criteria No. 134, 1992, 280p, ISBN 9241571349.

## Cadmium-Environmental Aspects

Evaluates the threat to ecosystems posed by contamination of the environment with cadmium from natural and industrial sources. More than 350 investigations were critically assessed. The opening sections outline the most important natural and industrial sources of environmental contamination, describe mechanisms of environmental transport and summarise data on concentration of cadmium found in various biota. Natural sources identified include zinc, lead and copper ore and volcanic activity. Nothing a major shift in industrial applications over the past few decades, the report cites a decline in the use of cadmium for electroplating and significant increase in the use in batteries. Other important sources of environmental contamination include steel production and the use of phosphate fertiliser.



Kinetics and metabolism are reviewed in the third section, which concentrates on the many environmental variables, such as temperature, salinity, pH and the chemical composition of water and soil, that influences cadmium uptake in different aquatic and terrestrial systems and determine the toxic impact on organism and micro-organisms. The remaining sections evaluate data on toxicity to microorganisms, aquatic organism and terrestrial organism and review the results of field investigations. Documented consequence of environmental contamination with cadmium from either natural or man made sources include the development of cadmium tolerance in some species, reduced breakdown of leaf litter and recycling of nutrients, physiological abnormalities in fish and kidney damage in sea-birds. Because of flaws in the design of many investigations, the book concludes that the impact of cadmium on ecosystem may have been underestimated.

**Reference:** Environmental Health Criteria No. 135, 1992, 156p, ISBN 9241571357.

## Carbaryl

Evaluates the design and finding of over 700 studies in an effort to determine the risk to human health and environment posed by carbaryl. This broad spectrum contact and ingestion insecticides has been widely used for over 30 years to control various insect pests on food and fibre crops, trees, and ornamental. In veterinary practice carbaryl is used to control flies, mosquitoes, ticks and lice in cattle, poultry and pests. The compound is also used to treat body louse infection in human. Carbaryl is currently processed by more than 290 formulation into over 1500 register product. The general population may be exposed through food or following pest control operations in the home and in camping, picnic and other recreational areas. Worker can be exposed during manufacturing, formulation, packing, transportation, storage and during and after application.

The most extensive section reviews the large number of experiments designed to assess the toxic effect of carbaryl and elucidate its mechanisms of action. These studies, supported by limited data on humans, confirm that carbaryl poses no risk of including genetic changes in either the somatic or the germinal tissue of humans that toxic effects are consistent with the sign and symptoms of cholinesterase inhibition, and that signs of intoxication develop quickly appear well before dangerous dose is absorbed and disappear rapidly when exposure end.

The book concludes that under normal condition of use carbaryl poses a low risk to the environment and to the health of the general population. Levels detected in food and drinking water are unlikely to endanger health, when reasonable safety precautions and measure for personal protection are enforced, Occupational exposure to carbaryl during manufacture formulation and application will not create health hazards for workers.

**Reference:** Environmental Health Criteria, No.153, 1994, 358p. ISBN 9241571535.

## Carbendazim

Evaluates the risks to human health and the environment posed by exposure to carbendazim a systemic fungicide, which is the most widely used compound in the benzimidazole family of fungicide. Carbendazim is used to control a wide range of fungi responsible for several important plant diseases. Plant protected by this fungicide include cereals, cotton, sugar beet, soybean, vegetables, fruits and many other food crops. Because carbendazim is the main metabolite of benomyl in mammals and the degradation product of benomyl in mammals and the degradation product of benomyl in the environment, data from studies of both compound are considered in the report.

The most extensive section reviews the large number of experiment studies designed to investigate the toxicity of carbendazim. Although data on human exposure are limited to two studies, the report draws on the large body of experimental work, supported by knowledge of how carbendzim exerts its toxic

effects in both target and non-target species, to conclude that the likelihood of systemic toxicity following exposure in either the general population or workers is remote. Given current occupational exposures and the low rate of dermal absorption, the report further concludes that when proper protective clothing is worn, health risks of agricultural exposure are low.

Concerning effects on organisms in the environment the report cites evidence that both benomyl and carbendazim are highly toxic to certain aquatic organisms in laboratory tests, but concludes that the toxicity is not likely to occur under field conditions due to the compounds' low bioavailability in surface waters, the report also cites evidence, from both laboratory and field investigations that benomyl and carbendazim, applied at recommended rates, cause deaths and sub-lethal reproductive effects on earthworms. The compound has shown low toxicity for birds and is classified as relatively non-toxic to honey bee.

**Reference:** Environmental Health Criteria. No. 149, 1993, 132p, ISBN 9241571497.

## Chlordimeform

Evaluates the risks to human health and the environment posed by chlordimeform, a broad spectrum acaricide activity against motile forms of mites and ticks and against the eggs and early instars of some Lepidoptera insects. Introduced in the late 1960's the compound was initially used in numerous countries to protect a wide variety of food crops. Application was later restricted to cotton and in one country, to rice. Although world-wide production and use ceased a decade ago, concern continues to centre on evidence that exposure is linked to an increased risk of urinary bladder cancer in humans.

Concerning risks for the general population the main sources of previous exposure are identified as the consumption of residues in food. Of greater importance is the large number of workers exposed to higher levels during the compound's manufacturing or application, particularly in view of the long latency period of urinary bladder cancer.

The most extensive section evaluates the results of toxicity studies in laboratory mammals and in vitro test systems. Following short and long-term exposure, treatment-related changes observed include haematological abnormalities and at high doses, hyperplasia of the epithelium of the bile duct and urinary bladder. Studies in mice, but not in rats, produce evidence of a dose-related increase in haemorrhage malignant tumours of vascular origin. The report found no evidence of teratogenic potential or adverse effects on reproduction. The evaluation of effects on human health draws on epidemiological studies of exposed workers as well as close to 1,000 case reports of accidental or intentional poisoning. These studies support the conclusion that chlordimeform has significant potential to cause both immediate and long term toxicity in exposed humans. Current evidence also supports the conclusion that exposure to the metabolite, 4-chloro-o-toluidine and to lesser extent chlordimethorn is associated with an increased risk of urinary bladder cancer in humans in view of the long latency period for the cancer, the report calls for the continued screening of previously exposed workers in programmes that include urinary cytology and test for haematuria.

**Reference:** Environmental Health Criteria. No. 199, 1998, XIX, 159p. ISBN 9241571993.

## Chlorendic Acid and Anhydride

Evaluates the risks to human health and the environment posed by chlorendic acid and anhydride. These closely related compounds are important reactive flame retardants used in polyester resins and plasticizers for electrical systems and paints, and in fibreglass-reinforced resins for process equipment in the chemical industry. As all flame retardants are eventually released to the environment, either directly or as breakdown products, the review gives particular attention to studies of the environmental behaviour and ultimate fate of these chemicals. Firm conclusions were limited by the paucity of data and inadequate design of several studies.

The report concludes that exposure of the general population to chlorendic acid, chlorendic anhydride and products derived from them. Should be minimised. The report further recommends caution in the disposal of these chemicals and their waste products to prevent exposure of the general population and minimise environmental risks.

**Reference:** Environmental Health Criteria, No. 185, 1996, 74p, ISBN 9241571853.

## **Chlorinated drinking water chlorination by-products, some other Halogenated compounds, cobalt and cobalt compounds**

Evaluates the carcinogenic risk to humans posed by the consumption of chlorinated drinking water by two chemicals used in the chlorinating of drinking water by a number of halogenated by-products formed when chlorine interacts with organic matter in water and by selection of other halogenated compounds found in drinking water, Chlorination was selected for evolution because of its widespread use and because potentially carcinogenic by-products have been measured in chlorinated water. The book also includes a separate monograph on cobalt and cobalt compounds.

The volume opens with a discussion of the many methodological problems that complicate efforts to assess the carcinogenicity of chlorinated water, the book evaluates the design and findings of all studies relevant to the carcinogenicity assessment of chlorinated drinking water two chemicals (sodium chloride and hydrochlorite salts) used the chlorination water either of the by-products, most frequently measured in drinking water and three additional halogenated chemicals detected in drinking water. Because of the formidable methodological obstacles faced by all investigations, only one of these substances could be classified, bromodichloromethane was classified as possibly carcinogenic to humans.

The final monograph consider data on metallic cobalt, cobalt alloys, including cobalt-containing surgical implants and dental devices and cobalt compounds. In view of the strength of evidence linking cobalt metal powder and cobalt and cobalt compounds are classified as possibly carcinogenic to human.

**Reference:** IARC Monographs on the Evaluation of Carcinogenic Risk to Human, Vol. 52, IARC, 1991, 544p, ISBN 9283212525.

## **Chlorinated Paraffins**

Evaluates the risks to human health and the environment posed by exposure to chlorinated paraffins. These complex mixtures are widely used throughout the world as a secondary plasticizer in polyvinyl chloride, as extreme pressure lubricant additives in the metal working industry, and in fire retardant and water repellent fabric treatment. Chlorinated paraffin's are also added to paints, coating and sealant to improve resistance to water and chemicals.

The most extensive section assesses finding from toxicity studies in experimental mammals and in vitro test systems. Studies demonstrate low acute oral toxicity and suggest that acute toxicity by the inhalation and dermal routes is also low. Repeated dose toxicity studies by the oral route concisely show that the liver, kidney and thyroid are the primary targets of toxic action. Long-term carcinogenicity studies in rodents have demonstrated increases in the incidence of hepatic renal and thyroid tumours following exposure to a short chain compound. Following exposure to a short chain compound. Following exposure to a long chain compound an increased incidence of malignant lymphomas and tumours of the adrenal gland has been observed.

In reviewing the limited data on human health effects the report notes that despite widespread use of these compounds, no case reports of skin irritation or sensitisation have been recorded. This observation is supported by studies of dermal exposure in human volunteers. The report concludes that

when proper personal hygienic and safety procedures are followed, risks to the health of exposed workers should be minimal. Since chlorinated paraffin's bioaccumulate are toxic to environmental organisms, the report recommends that use and disposal of these compounds should be controlled to avoid release to the environment.

**Reference:** Environmental Health Criteria No.181,1996, 181 p, ISBN 9241571810.

### **Chlorobenzenes other than Hexachlorobenzene.**

Evaluates the risks to human health and the environment posed by exposure to monochlorobenzene, dichlorobenzenes, trichlorobenzenes, tetrachlorobenzenes, and produced in huge quantities for use as intermediates in the synthesis of pesticides and in the production of a wide range of consumer and commercial products.

A reviews of data on sources of environmental exposure notes that release to the environment occurs primarily during manufacture and that incineration of chlorobenzenes may lead to the emission of polychlorinated dibenzo-p-dioxins and dibenzofurants. Sections concerned with sources and levels of human exposure conclude that the general population is exposed to the lower chlorinated congeners mainly through inhalation, whereas a greater proportion of the total daily intake of the higher chlorinated compounds is ingested in food, breast-fed babies may receive a higher dose than adult. Particular concern centres on risks of human exposure arising from the ingestion of contaminated fish and from contaminated indoor air linked to use of these compounds as moth repellents and air fresheners. The report was unable to predict the environmental impact of low level contamination but noted the need to avoid discharge of chlorobenzenes in to the aquatic environment as this can result in the build up of persistent residues.

Concerning risks to human health, findings from case reports to occupationally exposed populations point to transient effect on the central nervous system, and irritation of the eyes and upper respiratory tract as the principle health effects of exposure.

**References.** Environmental Health Criteria No. 128, 1991, 252p. ISBN 9241571284.

### **Chloroform**

Evaluates the risks to human health and the environment posed by exposure to chloroform, a volatile liquid used in pesticide formulations and as solvent and chemical intermediate. Its use as an anaesthetic and in proprietary medicines has been discontinued in many countries, following well-documented reports of adverse effects on respiratory, cardiac and liver function. Exposure of the general public occurs via food, drinking water and indoor air, with water use in homes making a substantial contribution to levels in indoor air. Studies have demonstrated significant dermal absorption while showering.

The most extensive chapter reviews the results of toxicity studies in laboratory animals and in vitro test systems. While both the liver and the kidneys are target organs the most universally observed toxic effect is damage to the liver. Studies indicate that cytotoxicity followed by cell proliferation is the most important cause for the development of liver and kidney tumours. Following experimental exposure to chloroform. The severity of toxic effects was observed to vary according to species, vehicle and route of administration.

A chapter on health effects in humans notes disturbances in respiratory and cardiovascular functions observed following short term exposures in animals, liver and kidney damage was the most frequently reported adverse effect of long-term exposure. Data were judged inadequate to implicate chloroform exposure via drinking water as a cause of human cancer. Concerning effects on the environment, the report concludes that the low levels of chloroform in surface water should not pose a hazard to aquatic organisms.

**Reference:** Environmental Health Criteria No. 163, 1994, 174p, ISBN 9241571632.

## Chlorothalonil

Evaluates the risks to human health and the environment posed by exposure to chloroethalonil, a fungicide widely used in agriculture to protect pome and stone fruits, citrus, currants, berries, bananas, tomatoes, green vegetables, peanuts, potatoes, onions and cereals chlorothalonil, which has a broad spectrum of activity, it also used on turf, lawns and ornamental plants and in wood preservatives and anti-fouling paints. Particular attention is given to crop residue studies.

The most extensive section evaluates the results of toxicity studies conducted in laboratory mammals and in vitro test systems. Studies show that chlorothionil has low acute oral and dermal toxicity, the main effects of repeated oral dosing are on the stomach and kidney. The evaluation gives particular attention to several feeding studies which demonstrated a rapid onset of toxic effects on therefore stomach and renal tumours in rodents, but not in other species, including the dog. Most studies failed to demonstrate mutagenicity, the limited data available indicate that the compound is not teratogenic and shows no reproductive toxicity.

Data on effects on human health are confides to case reports of contact dermatitis following occupational or accidental exposure. In interpreting the relevance of experimental bindings to human health, particularly the evidence of carcinogenic potential in rodent models, the report notes important species difference in metabolic pathways and postulates the chlorothalonil probably exerts its carcinogenic effects in rodents via a non-genotoxic mechanism. Concerning effects on other organisms in the laboratory and field, the report cites evidence that chlorothalonil is highly toxic to fish and aquatic invertebrates in laboratory studies, but is not phytotoxic and should not pose a risk to wild mammals.

**Reference:** Environmental Health Criteria No. 183, 1996, 145p, ISBN 9241571837.

## Chromium, Nickel and Welding

Evaluate the carcinogenic risk to humans posed by industrial exposure to chromium and its compounds, nickel and its compounds and welding fumes and gases. Occupational exposure principally by inhalation is noted to affect about three million workers world-wide. The first and most extensive monograph evaluate the carcinogenicity of chromium and its compounds. The monograph is divided in to subsections based on the oxidation state and solubility of the compounds, with separate evaluation made for metallic chromium, chromium (III) compounds, chromium (IV) compounds and from a fourth group of tested agents that were extensive sections evaluate the design and findings of over 500 investigations of carcinogenicity in animals and experimental systems studies of metabolic fate in animals and humans, and case reports and epidemiological studies in human populations. On the basis of this evaluation, the monograph concludes that chromium (IV) is carcinogenic to humans. The carcinogenicity of chromium (III) and of metallic chromium could not be determined on the basis of available evidence.

The second monograph presents similar information for metallic nickel and nickel alloys nickel oxides and hydroxides, nickel sulphides, nickel salts, and other nickel compounds. Nickel carbonyl is identified as the most acutely toxic nickel compound, causing sever damage to the respiratory system in experimental animals and in humans. The evaluation concludes that nickel compounds are carcinogenic to human and that metallic nickel is possibly carcinogenic to human.

The final monograph evaluates the carcinogenic risk posed by exposure to welding gars and fumes. On the basis of evidence from human and animal studies, welding fumes are classified as possibly carcinogenic to humans.

**Reference:** IARC Monographs on the evaluation of carcinogen Risk to humans. Vol. 49. IARC, 1990, 677p, ISBN 9283212495.

## Coffee, Tea, Mate, Methylxanthines and Methylglyoxal

Reports the deliberations of a working group convened to evaluate the strength of evidence linking the drinking of coffee, tea, and mate to the development of human cancer. Separate evaluations are also provided for caffeine, theophylline, theobromine and methylglyoxal, which are chemical constituents of coffee, tea and several other popular beverages.

First and most extensive monograph evaluates the large number of studies designed to assess the carcinogen potential of coffee. On the basis of available data the working group concluded that coffee is possibly carcinogenic to the human urinary bladder. Evidence further suggests that coffee may actually protect human against cancer of the colon and rectum. The risk for breast cancer was shown with remarkable consistency, to have no association with coffee drinking.

The second monograph evaluates the carcinogenicity of black and green teas. Although available data were judged inadequate to classify tea according to its carcinogenic risk, the analysis uncovered evidence suggesting that the temperature at which tea is drunk may be a more important determinant of risk than the chemical composition of the beverage.

This observation is further supported in the monograph on mate, a South American beverage which is usually drunk very hot following repeated addition of almost boiling water to the infusion. While mate could not be classified on the basis of available data, not made drinking was judged to have a probable association with the development of oesophageal and oral cancers. Evidence was inadequate to assess the carcinogenicity of caffeine, theophylline, theobromine and methylglyoxal

**Reference:** IARC Monographs on the Evaluation of carcinogenic risks to human, Vol. 51, IARC 1991, 513p, ISBN 9283212517.

## Cresols

Evaluate the risk to human health and the environment posed to the exposure to cresols. Commercial cresols have a wide variety of uses as solvent and disinfectant.

And chemical intermediate for pharmaceuticals, fragrances, antioxidants, dyes, pesticides and resins. Cresols are also used in the production of lubricating oils, motor fuels, and rubber polymers and in the manufacture of explosive. The general population may be exposed to cresols present in air, drinking water food and beverages, and consumer products, such as soap and disinfectant.

The most extensive sections evaluate data on toxic effects linked to different routes and levels of exposure. In the laboratory animals, toxic effects including damage to the respiratory and gastrointestinal tracts are associated with the strong irritant and corrosive activity of cresols. Although acute poisoning via inhalation is judged unlikely due to the low vapour pressure of cresols, dermal exposure causes irreversible tissue damage in experimental animals and can be fatal at high concentrations.

In humans, toxic effects and clinical sign following accidental or intentional ingestion are identified as burning of the mouth and throat, abdominal pain and vomiting. Studies of acute poisoning in workers indicate that occupational exposure is usually the result of dermal contact which can result in severe burns and scarring of the skin, haematological changes, kidney failure, coma and death. Data were judged inadequate to evaluate potential reproductive effects and carcinogenic risk. The report concludes

that at concentrations normally detected in the environment, cresols do not pose a significant risk to the general population.

**Reference:** Environmental Health Criteria No. 168, 1995, 144p, ISBN 9241571683.

## Cyhalothrin

Evaluate the risks to human health and the environment posed by the use of cyhalothrin a synthetic pyrethroid insecticide having high level of activity against a wide range of agricultural pests. Cyhalothrin is also used in public health and animal health, where it effectively controls a board spectrum of insects, including cockroaches, flies, mosquitoes, and ticks

Residues in food are identifies as the most important potential hazard for the general population though a review of available studies indicates that residues in excess of the established acceptable daily intake are very unlikely to occur. Concerning effects on organisms in the environment, the report cites laboratory evidence of high toxicity to fish, aquatic arthropods, and honey bees, but concludes that this high toxicity in the laboratory is not translated in to significant field hazard for these species.

The most extensive section reviews data from experimental toxicity studies. The review uncovered no evidence of carcinogenicity, mutagenicity, or disturbed reproductive functions, and no evidence of adverse effects on any aspect of foetal development at any of the experimental doses used. The final section devoted to effects on human, considers the clinical significance of subjective facial sensation reported in laboratory workers, workers in manufacturing plants and field operators handling cyhalthrin. While nothing the documented occurrence of the syndrome, the report concludes that it a transient phenomenon, that symptoms are not associated with objective physical sign and that recovery is complete. On the basis of these evaluations the report concludes that when recommended safety precautions and rates of application are followed, cyhalothrin is highly unlikely to pose a risk to the health of the environment, the general public or occupationally exposed workers.

**Reference:** Environmental Health Criteria No. 99, 1990, 106p, ISBN 9241542993.

## Alpha-cypermethrin

Evaluates risks to human health and the environment posed by the use of alpha-cypermethrin. A potent and versatile pyrethroid insecticide used against a wide range of pests encountered in agriculture. Main agricultural applications include the protection of oilseeds, pome fruits, peaches fruiting vegetables, berries, leafy vegetables, maize, hops and tobacco. Marketed since late 1983, alpha cypermethrin is also used against disease carrying insects and in the control of parasites of veterinary importance.

In view of the uses of this pesticide, an evaluation of sources of human exposure draws upon crop residue data obtained from a large number of supervised trails conducted throughout the world. The report concludes that exposure of the general population is negligible when the pesticide is used in keeping with good agricultural practice. Toxicity studies conducted in laboratory mammals and in vitro least systems indicate that alpha-cypermethrin had moderate to high acute oral toxicity and is 3-4times more toxic than cypermethrin. Short term exposures have not been shown to cause toxic effects. Several studies provide evidence that alpha-cypermethrin is non-mutagenic. No data on long term toxicity, teratogenicity, carcinogenicity, or immunotoxicity were available for evaluation.

The report concludes that, when good work practices, hygienic measures, and safety precautions are followed use of alpha-cypermethrin is unlikely to pose a hazard to occupationally exposed workers. Though laboratory studies have documented high toxicity for fish. Studies show that this toxicity is not realised indoor field conditions, where the rapid loss of alpha-cypermethrin from water facilities the complete recovery of affected population.

**Reference:** Environmental Health Criteria No. 142, 1992, 112p, ISBN 924157142X.

## Deltamethrin

Evaluates the risks to human health and the environment posed by the use of deltamethrin a synthetic pyrethroid insecticide mainly used against agricultural pests. Marketed since 1977. Deltamethrin is most common used on cotton, fruit and vegetable crops, and on cereals, corn, and soybean. Deltamethrin is also used for the post harvest protection of stored cereals, grains, coffee beans and dry beans. Major public health applications include use in the control of dengue disease and malaria.

Dietary residues, particularly following post harvest treatment, are identified as the most important source of exposure for the general population. While deltamethrin has been shown to be highly toxic to fish, aquatic arthropods and honey bees in laboratory investigations field studies and observations following wide spread use indicate that this insecticide, when used according to good agricultural practice is unlikely to have lasting effects on these species.

The main part of the book examines investigations of the toxic effects of deltamethrin on experimental animals and in vitro test systems. The review found no evidence of mutagenicity, teratogenic or reproductive effects, though it did cite evidence that the combined use of deltamethrin with some organophosphorus compounds can potentiate toxicity. The final section evaluates effects on humans and observed for lowering poisoning, occupational accidents and both short and long term occupational exposure. The book concludes that exposure of the general population to deltamethrin is very low and that provided recommended rates of application are followed use of this insecticide is unlikely to present a hazard to either occupationally exposed workers or the environment

**Reference:** Environmental Health Criteria No. 97, 1990, 133p, ISBN 9241542977.

## Demeton-s-methyl

Evaluate the risk to human health and the environment posed by exposure to demeton-s-methyl, a systemic and contact organophosphorus insecticide and acaricide having high acute toxicity. The compound has been used for over 30 years to protect cereals, fruits, vegetables and ornamental plants.

Studies of the environmental behaviour of demeton-s-methyl indicate that the compound is rapidly metabolised in soil, plants and mammals does not persist and is not accumulated by organisms. Workers may be exposed during manufacturing or application via the dermal or inhalation routes. Residues in food crops are identified as the principal source of exposure for the general population. Although data on dietary levels are limited the report concludes that exposure of the general population to residues in foods is unlikely to cause adverse effect on health.

Concerning effects on experimental animals and in vitro test systems, the report cites abundant evidence that demeton-s-methyl causes cholinergic toxicity. The report found no evidence of embryotoxic or teratogenic potential adverse effects on reproduction or development or carcinogenic action.

The evaluation of effects on human health draws on several reports of accidental and suicidal poisoning in the general population and episodes of poisoning in inadequately protected workers. These findings confirm the high acute toxicity demonstrated in experimental studies. The report concludes that demeton-s-methyl should be handled and applied only by well trained and closely supervised operators, when good work practices, hygienic measures and recommended safety precautions are followed exposure to the compound during manufacturing or application was judged unlikely to cause adverse effects on health.



**Reference:** Environmental Health Criteria. No. 197, 1997, xviii, 83p, ISBN 9241571977.

## Diazinon

Evaluate the risks to human health and the environment posed by diazinon a contact organophosphorus insecticide with a wide range on insecticide activity, Diazinon has been used since the early 1950's to control adult and juvenile forms of flying insects, crawling insects, ticks, mites and spiders. Application include the protection of food crops, the control of indoor pests and the control of ectoparasites in veterinary medicine. Although diet is identified as the principal route of exposure for the general population, levels detected in edible crops and food animals have been far below the acceptable daily intake.

Concerning effects on experimental animals and in vitro test systems, the report notes that manufacturing practices during the past two decades have significantly reduced the content of highly toxic impurities, resulting in low acute toxicity for currently marketed formulations. The report found no evidence of embryotoxic or teratogenic potential, adverse effects on reproduction function or carcinogenic action. The Principle; adverse effect of concern was judged to be dose related inhibition of acetyl cholinesterase activity.

The evaluation of effects on human health draws on several reports of accidental and international poisoning. Acute poisoning was noted to cause signs and symptoms consistent with inhibition of plasma cholinesterase activity. Acute pancreatitis has also been observed in cases of sever poisoning. Although fatalities in occupationally exposed workers have occurred most have been linked to the former presence of highly toxic impurities or associated with poor hygienic practices. The report concludes that when good work practices safety precaution and hygienic measures are followed. Diazinon is unlikely to present a hazard to occupationally exposed workers. The report further concludes that diazinon does not pose a significant health hazard for the general population.

**Reference:** Environmental Health Criteria No. 198, 1998, xx, 140p, ISBN 9241571985.

## 1,2-Dibromoethane

Evaluates the risks to human health and the environment posed by 1,2-dibromoethane. This highly volatile chemical is used as lead scavenger in antiknock gasoline, as a fumigant for soil, grains, and fruits as an intermediate in the synthesis of dyes and pharmaceuticals and a solvent for resins, gums, and waxes. Although world demand has been reduced substantially following bans on the use of lead gasoline and on agricultural applications, 1,2-dibromoethane is still used in large amount for many industrial purposes in industrialised countries.

Studies in laboratory mammals and in vitro test systems demonstrate acute toxicity to animals systems demonstrate acute toxicity to animals with the main effects observed in the liver and kidneys. Exposure via inhalation has been shown to cause nasal irritation and depression of the central nervous system is several studies adverse effects on reproductive function have also been observed. Concerning carcinogenicity, studies have shown that long term exposure causes tumours in rat and mice, in a variety of organs.

An evaluation of effects on human health draws on case studies of accidental and intentional poisoning as well as epidemiological studies of occupationally exposed workers in human. 1,2-dibromoethane is strongly irritant to the eyes, skin and respiratory tract. Symptoms of poisoning are identified as headache, sever vomiting, diarrhoea, respiratory tract irritation and death, usually caused by pneumonia following damage to the lungs. Other targets of toxic action include the liver and kidneys, function in occupationally exposure workers were judged inconsistent. Although carcinogenicity studies in humans

are extremely limited, strong and consistent evidence from animal studies supports the conclusion that 1,2-dibromoethane is a potential human carcinogen.

**Reference:** Environmental Health Criteria. No.177, 1996, 148p, ISBN 9241571772.

### Di-n-butyl Phthalate

Evaluates the risks to human health and the environment posed by exposure to di-n-butyl Phthalate (DBP). DBP is used as a specially plasticizer for nitrocellulose, polyvinyl acetate and polyvinyl chloride, in adhesives, in coatings, and in miscellaneous applications, including paper coating. The compound is also used as a lubricant for aerosol valves, an antifoaming agent, a skin emollient, and numerous other spray, fingernail polish and numerous other cosmetic products. Although DBP has low volatility its widespread use in many thin polymeric sheets and coating provides large surface areas for volatilisation during the manufacture use and disposal of those products.

An evaluation of studies on environmental presence and behaviour notes that DBP is rapidly and completely eliminated by aerobic degradation. Concerning sources of exposure for the general population, food is identified as the principal source, followed by much lower exposures from indoor air and drinking water. Ingestion was identified as by far the most important route of exposure for the general population.

The most extensive section examines the results of toxicity studies conducted in laboratory mammals and in vitro test systems. Concentrating on the numerous studies of oral exposure in rodent models. Toxic effects observed include hepatomegaly, increased number of hepatic, peroxisomes, fetotoxicity, teratogenicity and testicular damage. Alterations in the liver were judged to be indicative of metabolic stress. On the basis of these findings, the report concludes that DBP is teratogenic in certain species at high doses and that susceptibility to teratogenesis varies with developmental stage and period of administration. The report further noted that toxic effects on development and reproduction occurred at concentrations well above those to which people are normally exposed in the general environment. The report found no evidence that DBP is genotoxic.

Concerning effect on humans, the report considered findings from isolated case reports of skin sensitization, a single case of accidental poisoning and epidemiological studies of workers exposed to mixture of phthalates. Although limited these data combined with findings from extensive animal studies, support the conclusion that exposure to DBP a level at currently found in the general environment, is unlikely to cause adverse effects on human health. Carcinogenic effect was also judged unlikely. The report further urges the continuation of current measures to limit the release of DBP also the environment and to control the use in food packaging material.

**Reference:** Environmental Health Criteria No. 189, 1997, 205p. ISBN 9241571896.

### 3,3-Dichlorobenzidine

A concise assessment of the risks to human health and the environment posed by 3,3-dichlorobenzidine a chemical used primarily as an intermediate in the manufacture of pigments for printing inks textiles, paints and plastics. The document is part of new series of brief report aimed at the characterisation of hazard and dose response for exposure to selected industrial chemical with this goal in mind, documents in the series focus on studies and findings considered critical for risk characterisation.

Several properties of 3,3 dichlorobenzidine including its relatively low volatility, very short persistence and low concentration in the atmosphere, support the conclusion that the chemical will not contribute to the greenhouse effect, depletion of the ozone layer or the formation of ground level ozone. The assessment of toxic effects in experimental animals found sufficient evidence of carcinogenicity in found sufficient evidence of carcinogenicity in several species and substantial evidence of genotoxicity. The

very limited epidemiological studies were considered inadequate to assess the chemical's carcinogenicity to human.

**Reference:** Concise International Chemical Assessment Document No.2, 1998, iv, 21p, ISBN 924153002.2.

## 1,2-Dichloroethane

A concise assessment of the risks to human health and the environment posed by exposure to 1,2-Dichloroethane and industrial chemical mainly used in the synthesis of vinyl chloride. The compound is also used in the manufacture of various chlorinated solvents as a fumigant and in the manufacture of antiknock additives for gasoline. The document is the first in a new series aimed at the characterisation of hazard and dose response for exposures to selected industrial chemicals. With this goal in mind documents in the series focus on studies and findings considered critical for risk characterisation.

A review of findings from studies in laboratory animals and limited epidemiological studies in humans supports the conclusion that 1,2-Dichloroethane is a probable human carcinogen and that exposure should be reduced as much as possible. Using the results of gavage studies in experimental animals the carcinogenic potency, expressed as the dose associated with a 5% increase in tumour incidence was calculated to be 6.2-34 mg/kg body weight per day. As humans are exposed primarily via the inhalation route, guidance values for air of 3.6-20 µg/m<sup>3</sup> or 0.36-2.0 µg/m<sup>3</sup> were derived. Calculated on the basis of a margin of 5,000 fold or 50,000 fold less than the estimated carcinogenic potential. This margin of 5,000 to 50,000 affords protection similar to that associated with the range of low dose risk estimates generally considered to be essentially negligible. The report notes however, that the calculation based on the results of average studies, probably overestimates the risks of human exposure as 1,2-Dichloroethane when inhaled.

**Reference:** Concise international chemical assessment document No.1, 1998, iv, 28p, ISBN 9241530014.

## 1,2-Dichloroethane

Second edition.

Evaluate the risks to human health and the environment posed by exposure to 1,2-Dichloroethane and industrial chemical mainly used in the synthesis of vinyl chloride the compound also used in the manufacture of various chlorinated solvents as a fumigant and in the manufacture of anti-knock additives of gasoline.

Most emissions during production are to air with the stratosphere providing the predominate environmental sink. Though photolysis may produce chlorine radical which may in turn react with ozone, 1,2-Dichloroethane present in indoor and outdoor air is the main source of human exposure. Levels detected in drinking water are low and food is judged to be an unlikely source of exposure.

The most extensive section evaluates studies of toxicity in laboratory mammals and in vitro test systems. Particular concern centred on several animal studies that produced convincing evidence of increases in both common and rare tumours at several sites. 1,2-Dichloroethane has also been shown to be genotoxic in vitro and in vivo assays.

An evaluation of effects on humans draws on case reports of poisoning as well as epidemiological studies of occupationally exposed workers. The report cites findings from limited epidemiological studies indicating an increased risk of pancreatic cancer and leukaemia. On the basis of these and other findings, the report concludes that 1,2-dichloroethane is a probable human carcinogen. Since a safe

level for human exposure by any route could not be established, the report further concludes that all appropriate measures should be taken to eliminate or minimise human exposure to 1,2-Dichloroethane.

**Reference:** Environmental Health Criteria No.176, 1995, 148p, ISBN 9241571764.

### **1,3-Dichloropropene, 1,2-Dichloropropane and mixtures.**

Evaluates the risk to human health and the environment posed by 1,3-Dichloropropene, 1,2-Dichloropropane and mixtures of these chemicals. Since the two compounds and mixture have been widely used in agriculture as pre-plant fumigants applied by soil injection the report gives particular attention to studies investigating behaviour in soil, risks of leaching and ground water contamination, uptake by food crops, residues detected in drinking water and food and risks to agricultural workers and the general population. Over 300 studies including proprietary toxicological data from the manufacturers were critically assessed.

The report concludes that, when used at the recommended rate, 1,3-dichloropropene is unlikely to attain levels of environmental significance. Risks to the general population were judged negligible. Concerning occupational hazards, the report cites deviance, largely from case reports of poisoning, underscoring the need to follow appropriate safety precautions.

The report concludes that 1,2-dichloropropane poses a negligible risk to the general population. When used at the recommended rate, the compound is unlikely to attain levels of environmental significance. For workers, the compound is judged unlikely to pose a hazard, provided good work practice, hygienic measures, and safety precautions are followed.

Data on mixtures of dichloropropenes and dichloropropane are evaluated in the final monograph. The technical mixture previously enjoyed wide use as a soil nematode before planting. Citing evidence of a significant potential for 1,2-dichloropropane derived from the mixture to leach from soil and contaminate well water and groundwater, the report recommends that mixtures of dichloropropenes and dichloropropane should not be used as a soil fumigant.

**Reference:** Environmental Health Criteria No.146, 1993, 261p, ISBN 9241571462.

### **Diesel fuel and exhaust emissions**

Draws on findings from over 600 studies to evaluate the risks to human health and the environment posed by exposure to diesel fuel and diesel exhaust emissions. The two categories of exposure are evaluated in separate parts.

The evaluation of diesel fuel opens with a discussion of the complexity of these mixtures and may variables that affect their quality and composition. An evaluation of toxicity studies in laboratory animals and in vitro test systems concludes that diesel fuel has low acute toxicity when administered via oral, dermal and inhalation routes. Findings on embryotoxicity, teratogenicity, mutagenicity and genotoxicity were judged to be either negative or equivocal. In view of inadequacies in the few studies of carcinogenic risks the report concludes that the main effect of exposure on human health is dermatitis following skin contact.

The second and largest part evaluates diesel exhaust emissions. A review of the abundant data demonstrating adverse effects on the environment concludes that the major components of diesel exhaust contribute to acid deposition, troposphere ozone formation and global warming. The most extensive sections discuss the epidemiological studies in human and studies in experimental animals considered useful for the assessment of risk to human health. Although a number of epidemiological studies have indicated an increased risk of lung cancer in bus and railroad workers all studies suffered from weaknesses. The report concludes that diesel exhaust is probably carcinogenic to humans and

that inhalation of diesel exhaust contributes to both neoplastic and non-neoplastic diseases, including asthma. The report further concludes that the particulate phase has the greatest effect on human health.

**Reference:** Environmental Health Criteria No.171, 1996, xxiii, 389p, ISBN 9241571713.

## Diethylhexyl Phthalate

Evaluates the risks to human health and the environment posed by the production, processing use, and disposal of diethylhexyl phthalate (DEHP). DEHP is produced in large quantities for use as a resin-softening plasticizer, with major application in the production of polyvinyl chloride used in the construction and packaging industries and in components of medical devices, including tubes used in transfusions and dialysis. Findings from over 300 recent studies were critically assessed.

The opening sections characterise the behaviour of DEHP in different environmental media and summarise. Data indicating concentrations decide in air, precipitin, water, sediment, soil, biota, food and workplace environment. These studies show that while DEHP is rapidly photodegraded in the atmosphere, aerobic biodegradation is slow and anaerobic degradation is even slower. The report concludes that adverse effects on environmental organisms are likely in areas where water and sediment are highly contaminated.

The most extensive section examines the results of numerous toxicological studies in laboratory animals and *in vitro* test systems, significant findings include testicular atrophy and neoplastic effects on the liver in rats and mice. An evaluation of numerous studies on the mechanisms of hepatotoxicity concludes that the livers of rats and mice are exquisitely sensitive to DEHP and other peroxisome proliferation's, while the livers of guinea pigs, monkeys and human show minimal or no response.

Determination of the effects of DEHP on human health was limited by paucity of available data. Case reports of adverse effects linked to haemodialysis and artificial ventilation under score the need to reduce exposure arising from the use of plastic tubes containing DEHP in such clinical procedures as transfusion, haemodialysis and artificial respiration.

**Reference:** Environmental Health Criteria No. 131, 1992, 141p, ISBN 9241571314.

## Diflubenzuron

Evaluates the risks to human health and the environment posed by exposure to diflubenzuron, a synthetic compound used in agriculture, forestry and public health programmes to control mosquitoes and other insect pests and vectors. As this insecticide is usually applied directly to plants and water particular attention is given to studies of its behaviour in the environment and its effects on ecosystems and aquatic organisms.

Numerous studies support the conclusion that diflubenzuron has minimal or reversible effects on most aquatic invertebrates. Studies of forest spraying found no adverse effects on bird and mammal populations. Concerning sources and levels of human exposure, the report cites evidence that exposure of the general population to diflubenzuron via water or food as a result of its use in agriculture, against forest insects or in mosquito control is negligible.

Concerning the toxicity of diflubenzuron in experimental animals and *in vitro* test systems, numerous studies consistently show that the primary manifestation of toxicity is methemoglobin induction attributable to the metabolite 4-chloroaniline. Which is known to induce methemoglobin formation in several animal species and in humans. A review of studies of long term dietary administration supports the conclusion that diflubenzuron is not mutagenic or carcinogenic. Although the main metabolite 4-chloroaniline. Which is known to induce methemoglobin formation in several animal species and in humans. A view of studies of long terms dietary administration supports the conclusion that

diflubenzuron is not mutagenic or carcinogenic. Although the main metabolite 4-chloraniline, has been reported to cause methaemoglobinemia in exposed workers and in adversely exposed neonates no data on the direct effects of diflubenzuron on human health were available for evaluation. The extensive toxicology studies in animals nonetheless support the conclusion that exposure to 0.02mg/kg body weight will probably not cause adverse effects in humans and any exposure route.

**Reference:** Environmental Health Criteria No.184, 1996, 163p, ISBN 9241571845.

## Dimethylformamide

Evaluates risks to human health and the environment posed by the production and use of dimethylformamide, an organic solvent produced in large quantities throughout the world. Dimethylformamide is widely used in the chemical industry as a solvent, an intermediate and an additive with the largest quantities used in the production of acrylic fibres and polyurethanes. Dimethylformamide is also used in the production of pharmaceutical products.

The opening sections outline the main sources of human and environmental exposure and review studies of the behaviour of dimethylformamide in the environment. Because of its complete solubility in water dimethylformamide is noted to move readily through soils, accumulation in the food chain is judged unlikely. Concerning effects on organisms in the environment, the limited data available suggest low toxicity for aquatic organisms.

The second half of the book reviews findings useful in determining the risks to health posed by exposure of workers and of the general population to dimethylformamide. An extensive review of findings from experimental studies reveals consistent evidence that dimethylformamide is a hepatotoxic agent. Both teratogenic and embryotoxic effects have been demonstrated in several species. The final section which evaluates data from human studies, notes that symptoms associated with cases of acute accidental occupational poisoning are transient and followed by complete recovery. Biochemical signs of liver dysfunction are observed to accompany long term repeated occupational exposure, but evidence suggesting an increased risk of certain cancers in exposed workers was judged inadequately.

**Reference:** Environmental Health Criteria No.114, 1991, 124p, ISBN 9241571144.

## Dry cleaning, some chlorinated solvents and other industrial chemicals

Evaluates the carcinogenic risks to humans posed by exposures in the dry cleaning industry by eight chlorinated solvents and related industrial chemicals. Dry cleaning is evaluated in the first and most extensive monograph concerning exposures to specific chemicals tetrachloroethylene is identified as the most commonly used solvent during the last two to three decades. The evaluation also considers exposure to the wide range of chemicals used in the treatment of spots. A review of epidemiological studies on dry cleaning indicated that the risks for cancer at two sites, urinary bladder and oesophagus may be increased by employment in dry cleaning. The monograph concludes that dry cleaning entails exposures that are possibly carcinogenic in humans.

A second group of monographs evaluates selected chlorinated solvents and related chemicals used in dry cleaning, metal cleaning and degreasing as chemical intermediates and in the production of insecticides and herbicides. Trichloroethylene, tetrachloroethylene and 1,2,3-trichloropropane were classified as probably carcinogenic to humans. 1-chloro-2-methyl propene was classified as possibly carcinogenic to humans. The remaining chemical chloral and chloral hydrate, dichloroacetic acid, trichloroacetic acid and 3-chloro-2-methylpropane could not be classified.

For the remaining seven chemicals used in a diversity of industrial applications. Vinyl fluoride was classified as probably carcinogenic to humans. Furan, benzofuran and vinyl acetate were classified as possibly carcinogenic to human. Acrolein, crotonaldehyde, and furfural could not be classified.

**Reference:** IARC Monographs on the evaluation of carcinogenic Risks to humans Vol. 63, 1995, iv, 551p, ISBN 9283212630.

## Endrin

Evaluates the risks to human health and the environment posed by endrin and organochlorine insecticide used since the 1950s to protect cotton, rice, sugarcane, maize, and other crops against a wide range of agricultural pests. Because of high toxicity and persistence in the environment, endrin has been banned in many countries and severely restricted in other ingestion of contaminated food is the most important route of human exposure.

A review of levels of endrin detected in the environment, in animals in food, and in exposed human's draws upon the large number of older studies conducted when endrin was much more widely used. Finding from these studies which document widespread contamination indicate the health and environmental consequences arising from the indiscriminate use the disposal of the highly toxic pesticide. Reports of fish kills linked to the use of endrin confirm its environmental hazards which have been documented for other species.

Other sections review findings from experimental investigations of toxicity, case reports of accidental and suicidal poisoning, and epidemiological studies of occupationally exposed workers. Findings consistently point to the neurotoxicity of this pesticide and rapid onset of convulsions following exposure. The report concludes that endrin is unlikely to present a hazard to exposed workers where good work practices and recommended safety precautions are enforced. The occasional presence of low levels of endrin in air, food and surface and drinking water is judged to be of little public health significance, because of high toxicity of the pesticide, the report recommends that endrin should be used only in cases where no less toxic alternative is available. The report closes with advice on the medical treatment of endrin poisoning and on the emergency management of major status epileptics.

**Reference:** Environmental Health Criteria No.130, 1992, 241p, ISBN 9241571306.

## Ethylbenzene

Evaluate the risks to human health and the environment posses by exposure to ethylbenzene a chemical widely used in the production of styrene and to much smaller extent, in technical xylene used as a solvent in paints and liqueurs and the rubber and chemical manufacturing industries.

Industrial releases and vehicle emissions are identified as the main sources of human and environmental exposure. A review of data on the environmental behaviour and fate of ethyle benzene concludes that phot-oxidation and biodegradation rapidly degrade the chemical. The principal environmental sinks in the atmosphere, where photo-oxidation may contribute to photochemical smog formation. The most extensive section assesses the result of toxicity studies in experimental animals and in vitro test systems. These studies support the conclusion that ethylenzene has low acute and chronic toxicity and demonstrates no significant mutagenic properties or tetragenicity in the species tested data were judged inadequate to assess carcinogenicity and reproduction toxicity.

An evaluation of the limited data on toxicity to human notes that inhalation is the major route of exposure, through exposure may also occurs via skin absorption or ingestion. Toxic effects observed include preanarcotic effects on the central nervous system and limited irritation of the mucous membranes and eyes. As occupational exposure to ethylbenzene alone is rate the report was unable to reach conclusions according the health risks to workers. On the basis of the limited data available a tentative guidance value for ethylbenzene in inhaled air thus established using and uncertainty factor. The report further concludes that ethylbenzene is unlikely to cause adverse effects in aquatic or terrestrial ecosystem except in cases of spills or point-source emissions.

**Reference:** Environmental Health Criteria No. 186, 1996, 101p, ISBN 9241571861.

## Fenitrothion

Evaluate the risks to human health and the environment posed by fenitrothion, a moderately toxic organophosphorus insecticide used since 1959 to control pests on crops, stored grains and cotton. Fenitrothion is also used in forest spraying and in public health campaigns.

Because residues in food decline very quickly, the report concludes that exposure of the general population via the ingestion of contaminated food does not constitute a health hazard. A review of studies on the kinetics and metabolism of this insecticide shows that fenitrothion is unlikely to remain in the body for a prolonged period.

The remaining sections evaluate investigations of toxicity, case reports of accidental and intentional poisoning in human, epidemiological studies of exposed workers, studies of spray me and inhabitants following indoor spraying in large public health campaigns and studies of effects on organisms in the environment.

The report found no evidence of carcinogenic, mutagenic, embryotoxic or teratogenic effects, of delayed neurotoxicity or of an association between exposure to fenitrothion and the development of Reye's syndrome. Evidence supports the conclusion that fenitrothion is unlikely to constitute a health hazard for occupationally exposed workers when good work practices, hygienic measures and safety precautions are followed. Concerning effects on environmental organisms particularly following standard forest spraying operations the report notes that few, if any adverse effects have been detected despite the widespread use of this insecticide for several decades. Because fenitrothion is highly toxic for non-target arthropods the report recommends that this insecticide should never be sprayed over water bodies or streams.

**Reference:** Environmental Health Criteria No.133, 1992, 184p, ISBN 9241571330.

## Fenvalerate

Evaluates the risks to human health and their environment posed by fenvalerate a synthetic pyrethroid insecticide widely used for crop protection. Marketed since 1976, fenvalerate is also used in homes and gardens and for the control of insect infestation in cattle.

A brief discussion of sources of human exposure concentrates on studies of dietary residues, concluding that residues in groups grown by good agricultural practice are generally low. A section devoted to environmental behaviour cites studies documenting the rapid degradation and decomposition of fenvalerate, the reduced toxicity of its degradation products and the absence of leaching in soil. Other sections summarised studies of effects on aquatic and terrestrial organisms. Although laboratory tests have demonstrated high toxicity for fish and honey bees, these effects are shown to be markedly reduced under field conditions, where toxicity is mitigated by the adsorption of the compound to sediments and its strong repellent effects.

The remaining sections evaluate effects on health as determined from the results of animal experimentation, in vitro tests, case studies of accidental exposure and clinical investigations. The book concludes that exposure of the general population is very low that the effects of occupational exposure are transitory and that risks to the environment and human health are unlikely when fenvalerate is applied as recommended.

**Reference:** Environmental Health Criteria No.95, 1990, 121p, ISBN 9241542950.



## Formaldehyde

Evaluate the risks to human health and the environment posed by formaldehyde, a gas produced industrially in large quantity, for a wide range of application, include the production of glue for particle boards and plywood and the manufacturing of sterilising and disinfecting agent, medicines, cosmetic and several consumer goods.

In view of the wide range and diversity of exposure sources, the book makes a clear distinction between outdoor exposures, occupational exposure and exposures arising from the emission of formaldehyde into the indoor air environment. Particular attention is given to the case of hospitals and scientific facilities where formaldehyde is widely used as a sterilising and preserving agent and living spaces such as schools, kindergartens and mobile homes where uncontrolled emission of formaldehyde from building materials, furniture and tobacco smoking may pose a particular health hazard.

The book devotes most of its pages to the task of dealing with exposure levels and relating these to health hazards. The book cites evidence providing a relatively clear suggestion of a possible cancer risk for humans from exposure to formaldehyde. The book concludes that the carcinogenic potential is not high and that only nasal or nasopharyngeal tumours are likely to be causally related to formaldehyde. The book concludes that the carcinogenic potential is not high and that only nasal or nasopharyngeal tumours are likely to be causally related to formaldehyde exposure and that formaldehyde is not teratogenic. The final section presents a series of recommendations including proposed maximum allowable air concentrations in different settings and precautions to be followed in hospitals.

**Reference:** Environmental Health Criteria No.89, 1989, 219p, ISBN 9241542896.

## Fully Halogenated chlorofluorocarbons

Evaluates the risks to human health and the environment posed by the production and use of fully halogenated chlorofluorocarbons. Eight different commercial compounds, some of which are known to contribute to ozone depletion, are assessed. The opening section summarises the unique chemical and physical properties that account for the commercial importance of chlorofluorocarbons and explain why their degradation in the upper stratosphere destroys ozone. Subsequent sections summarise data on the global distribution of chlorofluorocarbons and evaluate the strength of evidence suggesting that increased ultraviolet-B radiation, resulting from ozone depletion, will endanger terrestrial and aquatic biota. The report concludes that even small increases in ambient ultraviolet-B exposure can result in significant ecosystem changes.

The second half of the book evaluates health risks associated with both direct exposure, mainly through inhalation during production and far more important indirect effects of ozone depletion. A review of extensive experimental data supports the conclusion that direct carcinogenic risk is concerning the consequences of increased exposure to ultraviolet-B radiation. The book notes documented and potential risks: the incidence of non-melanoma skin cancers, an increase in the incidence of cutaneous melanomas. Possible suppression of the immune system and an increase in the incidence of cataracts. The report concludes with an eight-point agenda for further research and calls for cuts of at least 80-90% in the emission of ozone-depleting chlorofluorocarbons.

**Reference:** Environmental Health Criteria No.113, 1990, 164p, ISBN 9241571136.

## Glyphosate

Evaluate the risks to human health and the environment posed by glyphosate, a post-emergent systemic and non-selective herbicide used primarily against deep-rooted perennial species in agriculture and forestry and for weed killing in water systems, parks, road verges and gardens. Roundup is the

major formulation of glyphosate. Because of the agricultural uses concern centres on the possible presence of residues in crops and animal tissues destined for human consumption.

Concerning possible presence of residues in crops and edible animal tissues, the report cites evidence that such residues are negligible. The report further concludes that the low toxicity, low volatility and low body absorption of glyphosate make its application by backpack sprayer safe when workers wear full protective clothing.

A review of studies in laboratory animals and in vitro test systems supports the conclusion that glyphosate has very low toxicity when administered by the oral and dermal routes, does not induce sensitisation, and shows no mutagenic, carcinogenic or teratogenic activity.

While the formulation Roundup is acutely toxic to human when ingested intentionally or accidentally, dermal absorption of low and no adverse effects are expected in properly protected workers. Studies of adverse effects on other organism in the laboratory and field demonstrate low toxicity for bees, earthworm and birds. The risk to most aquatic organism was judged to be small or negligible. While marked changes in populations of birds and small mammals have been documented following glyphosate application, these changes are attributed to alterations in habitat vegetation cover and food supply resulting from the herbicide intended effect.

**Reference:** Environmental Health Criteria No.159, 1994, 177p, ISBN 9241571594.

## Hexachlorobenzene

Evaluates the risks to human health and the environment posed by exposure to hexachlorobenzene (HCB). HCB has historically had many industrial and agricultural uses. Including extensive use as a seed dressing to prevent fungal disease on grains although concerns about effects on health and the environment prompted many countries to discontinue production in the 1970s, inadvertent production continues in the form of by-product and impurities generated during the manufacture of chlorinated solvents. Chlorinated aromatics and chlorinated pesticides. Other continuing sources of this highly persistent chemical include application of contaminated pesticides, incomplete incineration of chlorine containing waters and release from old dumpsites.

A discussion of the environmental behaviour of HCB cites properties, including its resistance to degradation, mobility and lipid solubility that help explain its detection in all environmental compartments and presence in the adipose tissues of virtually all members of the general population. Studies indicate that HCB undergoes significant bioaccumulation and biomagnification in the food chain. Concerning environmental levels and human exposure, food is determined to be the principal route of exposure for the general population. Although HCB is widely dispersed in ambient air, concentration is generally low. The contribution of levels in drinking water to total exposure is likewise estimated to be low. Limited data suggest that when poor industrial hygienic practices are followed, workers in certain occupations may be exposed to higher concentrations than the general population.

A review of data on the kinetics and metabolism of HCB in experimental animals concludes that the chemical is readily absorbed by the oral route and poorly via the skin. Studies demonstrate that HCB is slowly metabolised and eliminated, accumulates in lipid-rich tissues, crosses the placental barrier and is present in breast milk.

The most extensive section evaluates findings from the numerous studies of toxic effects in laboratory animals. Convincing studies demonstrate that HCB is carcinogenic in animals and has adverse non-neoplastic effects at relatively low doses on a wide range of organs and systems, including the liver, lungs, kidneys, thyroid, reproductive tissues and nervous and immune system.

The evaluation of effects on human health draws on numerous reviews of an accidental poisoning incident in Turkey that occurred in 1955-59 when HCB treated wheat grain was ground into flour and used to produce bread and resulted in more than 600 cases of porphyria cutanea tarda with high

mortality rate, In this included disturbances in porphyrin metabolism, dermatological lesions, hyperpigmentation, hyperichosis, enlarged liver, enlargement of thyroid gland and lymph nodes and osteoporosis or arthritis. Nursing infants of exposed mothers developed a disorder called pembyara, or pink or and most died within a year. Follow up of survivors at 20 and 30 years revealed persistent abnormalities. The report found no adequate epidemiological studies of cancer in exposed populations including workers.

On the basis of clinical evidence from the poisoning incident, supported by animal data demonstrating adverse effects at several sites in several species at relatively low doses, the report calls for measures to reduce the environmental burden of HCB and concludes that alternates should be found for any continuing present uses. The following health based guidance values for the total daily intake of HCB in humans were proposed for non-nepotistic effect 0.17 mg/kg body weight/day for nepotistic effect and 0.16 mg/kg body weight/day

**Reference:** Environmental Health Criteria No.195, 160p, 1997, xviii, ISBN 9241571950.

## Hexachlorobutadiene

Evacuates risks to human health and the environmental posed by exposure to hexachlorbutadene. This compound is essentially a waste product form during the manufacturing of various chlorinated hydrocarbons. Hexachlorobutadene has limited use as an agricultural fumigant in some parts of the world. The chemical contain also be used for the recovery of chlorinating gas in chlorine plants and as a wash liquor for removing certain volatile, organic compound s from gas streams.

Findings from field and laboratory studies support the conclusion that hexachlorbutadene has high potential to accumulate in sediment and persist in water. Hexachlorobutadiene is noted to be moderately to very toxic to aquatic organism, with fish species and crustaceans found to be the most sensitive.

A review of experimental studies concentrates on the large body of evidence demonstrating short and long-term effects on the kidney. These findings support the conclusion that the experimental animals, are the kidney and to a much lesser extent the liver. The report also cites evidence supporting the hypothesis that the nephrotoxicity, mutagenicity and carcinogenicity of hexachlorobutadiene are dependent on the biosynthesis of a reactive sulphur metabolite following conjugation with glutathione. In view of the shortage of human studies the evaluation of effects on health draws upon experimental data supported by evidence that the metabolism of hexachlorbutadiene is similar in human and animals. The report concludes that hexachlorbutadene should be regarded as a sensitising agent. Evidence for carcinogenicity is limited in animals and insufficient in human.

**Reference:** Environmental Health Criteria No.156, 1994, 136p, ISBN 924157156x.

## Alpha- and Beta-Hexachlorocyclohexanes.

Evaluates the risks to human health and the environment posed by exposure to alpha-and beta-hexachlorocyclohexanes (HCH).These two isomers are by-products in the manufacturing of lindane and may be present in the pesticide as impurities. Alpha- and beta –HCH which is used in agriculture and wood protection. Most environmental releases are linked to the use of technical grade HCH and to the inappropriate disposal of residues produced when lindane is purified.

Alph-and beta.HCH are evaluated in separate monographs. Both isomers are noted to be universal environmental contaminants, with concentrations detected in samples of air, rain, water, fresh water, sea water, soil, sediment, and numerous plant and animal species, as well as in several important food items.

A review of studies on environmental behaviour and metabolic fate concludes that alpha- and beta – HCH, when compared with lindane, are characterised by a higher bioconcentration in the environment, a slower rate of biodegradation by ultraviolet light and slower rate of elimination from organisms. Current exposures decreasing, supporting the conclusion that these isomers pose no serious health threat to the general public. A review of findings from toxicity studies in laboratory animals identifies growth retardation and effects on the liver and kidney as the major consequences of acute exposure

In its concluding section, the report expresses serious concern over the widespread pollution of the environment with these isomers. As neither has any insecticide action, the report concludes that use of technical-grade HCH products containing high concentrations of alpha- and beta –HCH is never justified.

**Reference:** Environmental Health Criteria No. 123, 1992, 170p, ISBN 9241571233.

## Hexachlorocyclopentadiene

Evaluates risks to human health and the environment posed by the production use and disposal of hexachlorocyclopentadiene (HEX). HEX is a chemical used in the production of several pesticides, including heptachlor, chloradane, aldrin, dieldrin, endrin, mirex, pentac and endosulfan. The compound is also used as an intermediate in the manufacturing of flame retardant and dyes.

A section devoted to sources of human and environmental exposure evaluates data on quantities released during production, processing and use, during the incineration of hazardous waste containing HEX. While exposure of the general population is judged to be very low, risk of exposure can be high in residential areas near HEX production, processing and disposal sites or hazardous waste incinerators. A discussion of environmental behaviour draws upon studies conducted following chemical accidents at manufacturing sites and waste treatment plants in the USA.

Findings from toxicity studies showed high toxicity for HEX vapour following oral, dermal and inhalation dosing in all species tested with dosing via inhalation causing the most acute toxicity. A review the limited data available on human health effects yield evidence of severe irritation to the eyes, nose, throat and lung. Major concern centres on the toxic effects on the human respiration system. A review of epidemiological studies found no evidence of the increase, attributed to HEX or its metabolites in the incidence of neoplasm's at any site.

**Reference:** Environmental Health Criteria No.120, 1991, 126p, ISBN 9241571209.

## n-Hexane

Evaluate the risks to human health and the environment posed by the n-Hexane, a chemical isolated from natural gas and crude oil and used in food processing to extract vegetable oil from beans, nuts, and seeds. n-Hexane is also used as a solvent, a cleaning agent, in the rubber industries, and in the manufacture of pharmaceuticals.

The opening sections review that is known about the behaviour of this highly volatile chemical in the environment and its metabolic fate in experimental animals and in the human body. A review of investigations in experimental animals and in vitro test systems concentrates on testicular lesions and neurotoxicity as the principal effects of repeated exposure to n-Hexane. Studies have also shown that neurotoxicity induced by n-Hexane is enhanced by co-exposure to methyl ethyl ketone, methyl isobutyl ketone and lead acetate, co-exposure to toluene decreases the neurotoxic effects of n-Hexane.

These findings are further supported by observation in humans, which draw upon several reports of peripheral neuropathy in workers, exposed to n-Hexane and in abusers of glues or solvents containing

this chemical. The report notes that the majority of occupational cases have occurred in poorly ventilated small industries.

While concluding that n-Hexane is not likely to present a hazard to either the general population or the environment, the report stresses the need for precautions in the occupational setting, including the use of suitably designed work processes and engineering controls for reducing atmospheric levels below the recommended occupational exposure limits. The book further recommends the use of protective clothing and ready availability of respiratory protection for use in enclosed spaces and in emergencies.

**Reference:** Environmental Health Criteria No. 122, 1991, 164p, ISBN 9241571225.

## Hydroquinone

Evaluates the risks to human health and the environment posed by exposure to hydroquinone, a chemical found in natural form, in a number of plants and animals. Hydroquinone is manufactured for a large variety of commercial applications, including use as a developer in black-and-white photography, in the production of medical and industrial X-ray films, in the manufacture of rubber antioxidants and antioxidants for food preservation and as a chemical intermediate for the production of agrochemical and performance polymers. Hydroquinone and products containing hydroquinone are used in cosmetics and medical skin preparation as a de-pigmentation agent to lighten small areas of hyper-pigmented skin and to treat various other disorders of pigmentation.

The most extensive section evaluates studies of toxic effects in experimental and in-vitro test systems. Particular attention is given to recent studies indicating that co-exposure to hydroquinone and various other phenolic compounds can greatly potentiate the toxic effects of the individual compound, causing cytotoxic, immunotoxic and genotoxic effects.

Although data from human studies were judged inadequate to evaluate carcinogenic potential, the report notes a well-documented association between exposure to hydroquinone and various skin disorders. Long term exposure to air borne hydroquinone has been over-served to cause a range of ocular disorders. Citing evidence that skin-lightening cream containing hydroquinone are frequently inadequately labelled and contain concentrations exceeding the permitted limit, the report recommends that over the counter sale of these products be restricted. The report also calls for the development of health education programmes to discourage the use of these creams for whole body skin lightening.

**Reference:** Environmental Health Criteria No. 157, 1994, 178p, ISBN 9241571578.

## Inorganic Lead

Evaluates the risks to human health posed by exposure to lead and inorganic lead compounds. Reflecting the focus of recent research, the report concentrates on mounting evidence that exposure to low levels of lead can have significant effects on health, particularly for infants and young children. Food, beverages and water constitute the major source of exposure for the adult general population. Infants and young children are exposed to an additional burden of lead present in soil and household dust.

A review of the kinetics and metabolism of lead draws upon studies using several biological markers of exposure and body burden. Particular attention is given to evidence that host factors, such as age, physiological status and nutritional condition, can influence lead absorption, metabolism and retention in tissues and bone, where lead is now known to accumulate throughout the life-span. Studies indicate that lead is readily transferred to the foetus throughout gestation, with lead metabolised from maternal bone serving as an important exposure source. Evidence also underscores the great vulnerability of infants and young children, who may absorb as much as 50% dietary lead, compared with only 10% of adults.

Additional evidence shows increased lead absorption when diets are deficient in calcium, phosphate, selenium or zinc.

An evaluation of effects on human health concentrates on the numerous epidemiological studies designed to investigate the possible neurotoxic effects of lead on the developing child. While nothing that several well designed studies have detected an association between exposure to lead and impaired intellectual performance the report concludes that existing studies can not provide definitive evidence of either a causal relationship or a threshold.

**Reference:** Environmental Health Criteria No.165, 1995, 300p, ISBN 9241571659.

## Inorganic Mercury

Assesses the risk to human health posed by the use of inorganic mercury in dental amalgam and in soap and creams used to lighten the skin. Although such skin lightening products are now banned throughout the European Economic Community, in north America and in many African states, the report reveals that mercury-containing soap continues to be manufactured in several European countries, is sold as germicidal soap to the third world and is illegally re-imported from Africa to European cities having a substantial black population.

Dental amalgam and food, most notably seafood are identified as the main sources of human exposure. Although exposure of the general population is judged to be low, toxic level may arise from the mishandling of liquid mercury, mercury dispensed from jars, broken thermometers, fluorescent lamps. The accidental ingestion mercury batteries. The use of skin lightening soap and creams results in substantial exposure.

The most extensive sections review findings from toxicology studies in the experimental animals and clinical reports and epidemiological studies in humans. Results from experimental studies show that inorganic mercury can induce autoimmune glomerulonephritis in all species tested, but not in all strains, indicating a genetic predisposition which is in good agreement with clinical findings. Experimental evidence of adverse effects on the menstrual cycle and on foetal development is also supported by observation in humans. Clinical manifestations of mercury poisoning are described in full detail. Concerning the health hazards posed by dental amalgam, no firm conclusions could be reached in the light of several weaknesses in the design of most epidemiological studies. The book also includes information on reported levels of mercury vapour in dental clinics and the corresponding risk to the dental profession.

**Reference:** Environmental Health Criteria No.118, 1991, 168p, ISBN 9241571187.

## Isobenzan

Evaluates the risks to human health and the environment posed by exposure to isobenzan. The cyclodiene insecticide as manufactured in the Netherlands from 1958-1965 and used from existing stocks for several years there after present sources of human and environmental exposure are restricted to the original waste disposal sites and to ponds which were built up using mud dredged from contaminant harbour area. Although recent research on this insecticide has been limited, the report draws heavily on a number of proprietary toxicological studies made available by the manufacturer.

The opening sections summarise the physical and chemical properties of isobenzan and review data on mechanisms of biodegradation in soil and water. A section devoted to environmental levels and human exposure assesses findings from the monitoring of water and soil samples, food crops, dairy products and terrestrial and aquatic organisms. Other studies reviewed show that isobenzan is readily absorbed through the gastrointestinal tract and accumulates in the tissues and organs of laboratory animals is very persistent in the environment and is highly toxic to fish, shrimp and birds.

Concerning the results of toxicological studies in laboratory animals, the report cites over stimulation of the central nervous system. Resulting in convulsions as the predominant effect of exposure. The observation is supported by 15 cases of clinical intoxication in exposed, workers including eight cases with convulsions. No studies of teratogenicity or mutagenicity were available for evaluation. Despite the limited number of studies, the report concludes that isobenzan poses a significant hazard to the environment and to exposed workers and that no human or environmental exposure to this substance. Whether used as an insecticide or for any other purpose, should be allowed

**Reference:** Environmental Health Criteria No. 129, 1992, 62p, ISBN 9241571292.

## Isophorone

Evaluate the risks to human health and the environment posed by the widespread use of isophorone as a solvent for synthetic resins, polymers and pesticide formulations. Since these uses create numerous opportunities for environment contamination, most study of isophorone have concentrated on its presence and behaviour in the environment. Because isophorone is rapidly volatilised and biodegraded the report concludes that environmental persistence is low and that significant bio-concentration is unlikely.

Studies of kinetics and metabolism in laboratory animals demonstrate rapid absorption via the oral, dermal and inhalation routes and rapid elimination via urine and expired air. Data from animal studies indicate a low acute toxicity. Signs of toxicity following inhalation are noted to be similar to the effects produced by solvents and narcotics, eye and respiratory irritation, lacrimation, ataxia, dyspnoea, diarrhoea, central nervous system depression and death at high doses. Although some investigations have detected adverse effects on the liver, kidney and lung no conclusion could be drawn. Studies in vitro test systems suggest that isophorone is not mutagenic. Results from carcinogenicity investigations were inconclusive.

The limited data on toxic effects in humans indicate symptoms of eye, nose and throat irritation at low concentrations and nausea, headache, dizziness, faintness and inebriation at high concentrations. To protect the health of exposed workers the report recommends the use of adequate engineering controls and appropriate industrial hygienic measures. In view of the low toxicity demonstrated in experimental animals and the low levels detected in environmental samples, the risk posed by isophorone to the general population was judged to be minimal.

**Reference:** Environmental Health Criteria No.174, 1995, 84p, ISBN 9241571748.

## Limonene

A concise assessment of the risks to human health posed by exposure to limonene, a chemical released to the atmosphere in large amount from certain trees and bushes as well as from anthropogenic sources. In industry, limonene is used as solvent in degreasing metals prior to industrial painting, for cleaning in the electronic and printing industries and as a solvent in paint. The compound is also used as a flavour and fragrance additive in food, household cleaning products and perfumes.

The document is part of a new series of brief reports aimed at the characterisation of hazards and dose response for exposures to selected industrial chemicals. With this goal in mind documents focus on studies and findings considered critical for risk characterisation.

In experimental animals exposed to limonene, the liver is the principal target organ, exposure affects the amount and activity of different liver enzymes, liver weight, cholesterol levels and bile flow. Studies indicate that limonene is not genotoxic and has no teratogenic or embryotoxic potential. No case reports or epidemiological studies were available for the evaluation of health effects in humans.

For the general population, food is identified the principal source of exposure. The report established a guidance value for the ingestion of limonene of 0.1 mg/kg body weight per day. The report further concluded that at current estimated levels of intake. Limonene in food does not represent a significant risk to human health.

**Reference:** Concise international chemical assessment document No. 5, 1998, iv, 32p, ISBN 9241530057.

## Lindane

Evaluates the risk to human health and the environment posed by lindane, an isomer of hexachlorocyclohexane used, for more than four decades as a broad-spectrum insecticide. Although most lindane is used in agriculture for the treatment of seeds and soils, other important applications include the protection of wood and timber, the treatment of veterinary ectoparasites and the treatment of scabies and body lice in humans.

Concerning sources and levels of human exposure, the report cites residues in food as responsible for more than 90% of human exposure, nothing that populations throughout the world are exposed to lindane on a daily basis from the large number of studies that have measured levels in food, the report is able to conclude that such exposures are already be low the acceptable daily intake and are gradually decreasing.

The assessment of effects on human health benefits from the large number of recent well designed studies conducted in both experimental test systems and a range of different laboratory species and strains. These studies support the conclusion that dietary intake of lindane at currently measured levels, will not impair the health of general population, nursing infants, or toddlers. Citing evidence from well designed studies of exposed workers the report further conclude that under normal conditions of use, lindane poses no short or long term threats to the health of workers. Reports of sever toxic symptoms following the use of lindane to treat scabies underscore the need for strict adherence to prescribed doses, especially when treating children. Concerning risk to organism in the environment, the report notes that lindane, even when applied at recommended rates, is highly toxic for bats and should this be regarded as a major environmental hazard wherever bats might roost on lindane treated wood.

**Reference:** Environmental Health Criteria No. 124, 1991, 208p, ISBN 9241571241.

## Linear Alkylbenzene Sulfonates and related compounds

Evaluate a risk to human health and the environment posed by the exposure to linear alkylbenzene sulfonates and their salts. Alpha-olefin sulfonates and alkyl sulfates. These surface active agents are used in large quantities in shampoos, dish-washing products, household clearness, laundry detergents and industrial cleaners. Linear alkylbenzene sulfonate (LAS) form the major component of these detergent compounds and as such have been the most extensively investigated.

The three group of surfactants are evaluated in separate monographs. The first and most extensive monograph reviews the large number of studies that have investigated the environmental and biological toxicity of LAS. Adverse effects observed in experimental animals were largely confined to minor histopathological and biochemical changes in the liver. An assessment of toxic effects in humans draws upon a studies of dermal exposures, supported by a large number of case reports of accidental or suicidal ingestion. Mild to moderate skin irritation following repeated or prolonged dermal contact was the main adverse effect. The report concluded that the average daily intake of LAS by the general population, from all sources is may times lower than the levels shown to induce minor effects in experimental animals. Concerning effects on the environment, a report made a number of observation about the use of laboratory findings to predict adverse effects. Under environmental conditions,



biodegradation and adsorption result in decreased environmental concentrations, decreased bioavailability and the production of compound that are less toxic than the parent compound. The numerous laboratory studies were judged inadequately to support a generally applicable assessment of environmental risks. The remaining monographs provide similar evaluation for alpha-olefin sulfonates and alkyl sulfates.

**Reference:** Environmental Health Criteria No.169, 1996, 328p, ISBN 9241571691.

## Methanol

Evaluate the risks to human health and the environment posed by exposure to methanol. Although methanol occurs naturally in human, animal and plants. Anthropogenic sources are far more significant. Methanol is produced in large amount in many countries and is extensively used as an industrial solvent a chemical intermediate mainly in the production of methyl tertiary butyl ether, formaldehyde, acetic acid and glycol ethers as a denaturant of ethanol and in a variety of consumer products. Products containing methanol include paints, shellacs, varnishes, mixed solvents in duplicating machines, antifreeze and gasoline dicers, wind shield washer fluids, cleansing solution, and, model and hobby glues and adhesives. The general population is routinely exposed to low levels from metabolic processes and from such dietary sources as fruits, vegetables, fruit juices and foods and soft drinks containing the synthetic sweetener aspartame. The most notorious use of methanol is an adulterant in alcoholic beverages, which has led to large scale episodes of poisoning and numerous fatalities.

A review of data on environmental levels and human exposure notes that most emissions to the environment arise from the production and use of methanol as a solvent in industrial processes and to lesser extent, from a variety of other industrial processes and consumer applications. Concerning the behaviour of methanol in the environment, the report cites abundant evidence that the compound is readily and rapidly degraded in a wide variety of environmental media and has low bioconcentration and low toxicity. Evidence supports the conclusion that methanol is unlikely to have adverse effects on the environment except in the case of accidental spill. The report also draws attention to the potential large increase in environmental level associated with the use of methanol as a replacement for gasoline and predicted laws major automotive fuel in the next century.

A section on kinetics and metabolism in laboratory animals and human concludes that inhalation and ingestion are the primary routes of methanol exposure, with dermal exposure currently of much less importance in terms of total daily intake for both the general population and exposed workers. Studies indicate that methanol is readily absorbed by all three routes and widely and rapidly distributed to tissues according to the distribution of body water.

A review of findings from animal studies and in vitro test systems notes the great variation in acute and short term toxicity observed in different species, with toxicity highest in species such as humans and non-human primates. Characterised by poor ability to metabolize formal. Studies show that exposure to methanol induces a wide range of concentration dependent teratogenic and embryolethal effects. Although no evidence from animal studies indicates that methanol is a carcinogen the report notes the absence of an appropriate animal model for carcinogenicity assessment.

The evaluation of effects on human health draws on numerous reports of acute exposure following deliberate or accidental ingestion of adulterated alcoholic beverages. The clinical features of acute methanol poisoning are identified as transient central nervous system depression, followed by an asymptomatic latent period culminating in metabolic acidosis, severe ocular toxicity, blindness, coma, and death. Although data on the health effects on chronic exposure are limited, the report cites evidence of visual disturbances observed in workers exposed to high concentrations of methanol vapours. The report found no evidence of carcinogenic, genotoxic, reproductive or developmental effects in human attributed to methanol exposure.

**Reference:** Environmental Health Criteria No. 196, 1997, xviii, 180p, ISBN 9241571969.

## Methomyl

Evaluates the risks to human health and the environment posed by exposure to methomyl a carbamate pesticide with a well-characterised mechanism of action a cholinesterase inhibitor. Methomyl is used on a wide range of crop throughout the world, including fruit, vines, hops, vegetables, grain, Soya bean, cotton and ornamentals. The pesticide also has indoor uses to control flies in animal houses and dairies. In view of these uses, many studies have investigated levels detected in food items, including dairy products and the toxic effects associated with prolonged dietary exposure.

The report concludes that levels in groundwater, food and other crops, and dairy products are either very low or undetectable, total diet studies found either no detectable residues or very low levels. Experimental toxicity studies are evaluated in the most extensive section, which found high toxicity, by the oral and inhalation routes, but low dermal toxicity. Signs of toxicity were observed to be consistent with those of cholinesterase inhibitors, including profuse salivation, lacrimation, tremor, and pupil constriction. Studies further show that recovery from these effects is rapid with no gross pathological effects observed. Repeated dietary administration over longer periods did not lead to accumulation or an increase in toxic effects. The evaluation found no evidence of carcinogenicity, mutagenicity, or neurotoxic effects.

A section on the effects of methomyl exposure on human health draws on findings from cases of accidental and internal poisoning, including several fatalities. Findings from these case reports confirm the high acute toxicity by the oral route seen in experimental animals and the quick recovery and reversal of cholinesterase inhibition in survivors.

**Reference:** Environmental Health Criteria No. 178, 1996, 150p, ISBN 9241571780.

## 2-Methoxyethanol, 2-ethoxyethanol and their acetates

Evaluates the risks to human health and the environment posed by exposure to 2-methoxyethanol, 2-ethoxyethanol, and their two acetates, 2-methoxyethyl acetate and 2-ethoxyethyl acetate. These glycol ethers have a wide range of uses as solvents with particular a wide range of uses as solvent with particular application in paints stains, inks, lacquers, and the production of food contract plastics

Section concerned with sources of exposure note that patterns of use as evaporative solvent result in significant, widespread emissions to the environment, with great potential for direct human exposure in industry, in small workshops and during home use of numerous consumer products. A review of data on environmental behaviour points to rapid degradation, supporting the conclusions that the risk of hazardous environmental concentrations is small and that human exposure through food eater or the ambient air is probably negligible. A review of experimental studies of toxicity reveals strong and consistent evidence across all species investigated of adverse effects on the male reproductive system, developmental toxicity, and humans are scarce results from case reports and workplace epidemiological studies confirm the finding from animal research pointing to a clear risk of disturbances in the male reproductive system and of embryotoxicity.

The book concludes with a series of recommendations to authorities, including the need to find less toxic solvents to alert users to the hazards of these chemicals and to be aware that air monitoring alone is not an adequate measure of safety condition at the workspace.

**Reference:** Environmental Health Criteria No. 115, 1990, 126p, ISBN 9241571152.

## Methyl Bromide

Evaluates the risks to human health and the environment posed by exposure to methyl bromide. This highly toxic gas is present in the environment both as a natural product of biological processes in the environment and as a commercial product widely used as fumigant for pest control. The compound's

ability to penetrate quickly and deeply in to sorptive materials makes it an effective and versatile fumigant. Methyl bromide is used to control nematodes and soil borne fungi in fields and green houses to treat fresh fruits and vegetables in competence with quarantine regulation, and control termites and other indoor pests in homes and buildings.

Data support the conclusion that occupations exposure, particularly during fumigation, posses the greatest potential threat to human health. Concerning risks to the environment, evidence points to the presence of methyl bromide in the troshphere and stratosphere, where it contributes substantially to ozone depletion.

The toxic effect of exposure are examined in the most extensive section, which reviews the large number of experimental studies, finding confirm the high toxicity of methyl bromide for all animal species by all routes of administration investigated. Data on carcinogenicity were judged inadequate.

A section on toxic effects in humans draws on hundreds of case histories of accidental and occupational poisoning, including numerous fatalities. Neurological manifestations are cited as the major clinical signs of toxicity. Exposure may also result in permanent injury commonly characterised by sensory disturbances, weakness, disturbances of gait, irritability and blurred vision, in view of the high toxicity of the substance, the report stresses the need to follow strict safety precautions, particularly when using methyl bromide to fumigate green houses buildings, and silos and other food storage facilities.

**Reference:** Environmental Health Criteria No. 166, 1995, 324p, ISBN 9241571667.

## Methyl Ethyl Ketone

Evaluates risks to human health and the environment posed by exposure to methyl ethyl ketone. Because of its excellent properties as a solvent, methyl ethyl ketone is widely used I the application of protective coatings and adhesives, in magnetic tape production in the dewaxing of lubricating oil, and in food processing. Methyl ethyl ketone is also a common ingredient in consumer products such a varnishes and glues. International abuse of solvent mixtures containing this chemical is of particular public health concern since injuries can be severe permanently disabling and even fatal.

Although methyl ethyl ketone is a natural component of many foods, the report notes that concentration are consistently low, other sources of population exposure include drinking water, tobacco smoke and volatilisation from building materials and consumer products. The report concludes that methyl ethyl ketone does not pose a significant threat to the environment except in cases of major spills or discharges.

The remaining sections concentrate on evidence, from animal studies, in vitro test systems, and observations in humans, of the toxic effects of this chemical. Evidence from several out-breaks of poisoning linked to solvent abuse is also considered. The report concludes that the principal toxic effects observed with methyl ethyl ketone exposure stem form its well –documented ability to potentate the toxicity of two classes of organic solvents, unbranded aliphatic hexacarbons and haloes, while methyl ethyl ketone on its own appears to be relatively safe organic solvent, chronic co-exposure with these other organic solvents represents a significant potential occupational hazard. A concluding section urges industries to take all precautions necessary to ensure that workers are not exposed to both methyl ethyl ketone and solvent wholes toxicity is potentate by this chemical.

**Reference:** Environmental Health Criteria No. 143, 1993, 161p, ISBN 9241571438.

## Methyl Isobutyl Ketone

Evaluates risks to human health and the environment posed by the widespread production and use of methyl isobutyl ketone as a solvent with major applications I the production of lacquers and paint

solvents, including car and industrial spray paints. Methyl isobutyl ketone also occurs naturally in food, is a permitted flavouring agent and is used in food contact packaging materials.

Sections concerned with the behaviour of methyl isobutyl ketone in the environment note its rapid evaporation into the atmosphere, rapid photo transformation, ready biodegradation and low potential for bioaccumulation. A review of data on metabolic pathways and toxicity to organisms concludes that production and use of this chemical pose no threat to wildlife or the environment, except in the case of accidental spills or inappropriate disposal of wastes.

The most extensive section reviews findings from a large number of studies, conducted in experimental animals and in vitro test systems, designed to test the toxicity of the chemical, including its actions as a skin and respiratory tract irritant, the effects on reproduction and its embryotoxicity, teratogenicity, carcinogenicity and mutagenicity. A review of studies conducted in human volunteers and in occupationally exposed workers concludes that exposure to methyl isobutyl ketone can cause eye and respiratory irritation as well as symptoms of headache, nausea and vertigo. The review found no evidence that exposure to this chemical causes permanent damage to the nervous system of workers or that its presence in the environment and in food poses any threat to the general population.

**Reference:** Environmental Health Criteria No. 117, 1990, 79p, ISBN 9241571179.

## Methylene chloride

Evaluates the risks to human health and the environment posed by exposure to methylene chloride. Due to its volatility, stability and properties as a solvent, methylene chloride is widely used in aerosols, paint remover, the chemical and pharmaceutical industries, polyurethane foam manufacturing, and metal cleaning. Virtually all atmospheric release of this chemical results from its use as an end product by various industries, combined with the use of paint removers and aerosol products at home. The general public is exposed to methylene chloride primarily through the use of consumer products, such as paint removers, which can result in relatively high indoor levels.

The most extensive sections evaluate the toxicity of methylene chloride in experimental animal and humans, giving particular attention to studies indicating carcinogenic potential in some species. Studies indicate that methylene chloride is rapidly absorbed through lung and gastrointestinal tract and is distributed throughout the body, and rapidly excreted via the lungs. The main toxic effect in exposed humans is reversible central nervous system depression and carboxyhaemoglobin formation. Studies have also reported liver and renal system functions, haematological effects and neurophysiological and neurobehavioural disturbances. Although several studies have investigated the link between human exposure to methylene chloride and cardiovascular disease and cancer, the report cites several inadequacies in these studies and concludes that no firm link with either cardiovascular disease or cancer can be made.

Concerning risks to the environment, the report concludes that with the exception of accidental spills, use of methylene chloride has no significant impact on the environment.

**Reference:** Environmental Health Criteria No. 164, 1996, 242p, ISBN 9241571640.

## Methylmercury

Evaluates the risks to adult and foetal health posed by exposure to compound of monomethylmercury. In view of the irreversible neurological damage produced in severe cases of poisoning, the book makes a special effort to clarify the ways in which this highly mobile metal enters the food chain and define the pathways that constitute a risk to human health, close to 400 recent investigations, including numerous clinical studies following outbreaks of poisoning are crucially assessed.

A section on sources of human exposure concentrates on environmental release from man made sources. Nothing that the general population primarily exposed through the dietary intake of contaminated fish and fish products, the book give particular attention to the mechanisms by which methylmercury enters the food chain and metabolised and transported to tissues in the human body.

A review of studies in animals and in vitro test systems conducted since 1976, documents the consistent neurotoxicity and fetotoxicity of methylmercury. Chapters devoted to effects in human draw upon what has been learned from poisoning outbreak in Minamata, Japan and in Iraq as well as from studies of population consuming high quantities of fish. An evaluation of effects on developing tissues draws upon the considerable amount of new data available on dose-response relationship, concluding that prenatal life is especially sensitive to methylmercury. The final chapter issues conclusions concerning levels of exposure and associated health risks in the general public in population consuming high quantities of fish and in pregnant women.

**Reference:** Environmental Health Criteria No. 101, 1990, 144p, ISBN 9241571012.

## Methyl Methacrylate

A concise assessment of the risks to human health posed by exposure to methyl methacrylate, a synthetic chemical used primarily in the production of cast acrylic sheet, acrylic emulsions, moulding and extrusion resins, and several consumer and medical products, including dental prostheses, surgical bone cement and orthopaedic shoe insets. The document is part of a new series of brief reports aimed at the characterisation of hazards and so response for exposures to selected industrial chemicals with this goal in mind, documents in the series focus on studies and findings considered critical for risk characterisation.

Studies of environmental behaviour indicate that methyl methacrylate is emitted mainly to air does not persist in the atmosphere and is not expected to contribute to depletion of the ozone layer, inhalation is identified as the principal route of human exposure. The general population may be exposed to methyl methacrylate through the use of paints, varnishes, lacquers and other consumer products.

In animal studies, methyl methacrylate shows low acute toxicity. The principal effect observed with low doses were associated with adverse effects on the kidney and liver. Well designed studies indicate that the chemical has no adverse effects on development and is not carcinogenic. In humans, methyl methacrylate is a mild skin irritant and has the potential to induce skin sensitisation in susceptible individuals. Although occupational asthma associated with exposure has been reported evidence that methyl methacrylate is a respiratory sensitizer was judged inadequate. Evidence from epidemiological studies of carcinogenic risk in humans was considered inconclusive. On the basis of toxic effects observed in inhalation basis of toxic effects observed in inhalation studies in animals, the report established a tolerable daily intake of 1.2mg/kg body weight.

**Reference:** Concise International Chemical Assessment, Document No.4, 1998, iv, ISBN 9241530049.

## Methyl Parathion

Evaluates the risks to human health and the environment posed by methyl parathion, a highly toxic organophosphorus ester insecticide, introduced as a commercial chemical in 1949. Methyl parathion is used as a contact insecticide and acaricide for the protection of cotton, soybeans, cereals, tobacco, peanuts, vegetables, citrus fruits and other crops. The compound is applied as a foliar spray by aircraft or ground equipment.

Because methyl parathion is a non-selective pesticide that kills beneficial species as well as pests, a section devoted to effects on environmental organism concentrates on several studies documenting

high toxicity for honeybees. These studies also show that incidents of bee kills were more severe with this insecticide than with other underscoring the need to time spraying operations with extreme care. The report concludes that methyl parathion should never be sprayed under windy conditions and that over spraying of water bodies must be avoided.

The most extensive section evaluates studies of toxic effects observed in experimental animals and in vitro test systems. The report found no evidence of carcinogenicity associated with long-term exposure and no evidence that this insecticide acts as a primary eye or skin irritant. The final section evaluates effects on human drawing on a number of case reports to accidental and sometimes fatal poisoning. The report concludes that the only confirmed effects on humans are the signs and symptoms characteristic of systemic poisoning by cholinesterase-inhibiting organophosphorous compounds. No cases of organophosphorus induced, delayed peripheral neuropathy have been reported.

**Reference:** Environmental Health Criteria No. 145, 1993, 244p, ISBN 9241571454.

## Morpholine

Evaluate the risks to human health and the environment posed by the widespread industrial use of morpholine. Morpholine is an extremely versatile chemical with major uses as an intermediate in the rubber industry, as a corrosion inhibitor, as a solvent for numerous organic materials and the synthesis of optical brightness crop protection agents, dyes and drugs. In some countries the compound continues to be used in toiletry and cosmetic products and in several direct and indirect food additive applications. The ready conversion of morpholine in to n-Nitrosomorphole(NMOR), a proven animal carcinogen, is of particular concern. The report concludes that consumption of food contaminated with this compound is the main source of exposure for the general population.

The most extensive section which assessed the results of experimental toxicity studies, concludes that morpholine is not highly toxic under conditions of acute exposure. While the review found no evidence of either mutagenicity or carcinogenicity, the importance of ready conversion to NMOR was underscored.

A review of the limited data on health effects in humans supports the conclusion that morpholine does not create any significant risk of systemic toxic effects as a result of occupational or environmental exposures. However view of the compound's conversion to NMOR the report prudent to consider morpholine as increasing the carcinogenic risk in exposed populations. The report further concludes that contamination of food through food packaging and food processing should be avoided, and that morpholine should not be used in rubber products intended for direct contact with humans or in tottery or cosmetic preparations. The report also underscores the need for rigorous treatment of industrial effluents to avoid contamination of drinking water.

**Reference:** Environmental Health Criteria No. 179, 1996, 63p, ISBN 9241571799.

## Nickel

Evaluates close to 900 studies in an effort to determine the role of various nickel compounds as environmental hazards and causes of human diseases, including cancer. A special effort is made to determine the specific exposure levels for nickel and nickel compound that pose a threat to the environment, the general public and workers exposed to nickel containing dusts and fumes.

A section on sources of exposure evaluates both natural and man-made releases in to the environment, offering especially detailed information o emissions associated with the nickel incineration of sewage sludge and waste. Exposure of the general population is noted to occur via inhaled air, ingestion of food and drinking water and dermal contact, particularly with jewellery and coins.

Because most health hazards associated with occupational exposure have resulted from inhalation, a section devoted to kinetics and metabolism concentrates on mechanisms of deposition, retention and clearance of nickel. Extensive section reviews the large body of data from experimental studies of an effects of short and long term exposures on the respiratory tract, endocrine system, cardiovascular or immune system, skin and eye. Tests for mutagenicity, embryotoxicity, teratogenicity and carcinogenicity are also critically reviewed with particular attention given to possible mechanisms of nickel carcinogenicity. The final section assesses effects on the human respiratory system, kidney, cardiovascular system, skin and eye. Evaluation of the potential for carcinogenicity draws upon increased rates of nasal and lung cancer reported in several epidemiological studies of exposed workers. These studies provide evidence that inhalation of nickel dust and some soluble and insoluble nickel salts carries a risk of carcinogenicity.

**Reference:** Environmental Health Criteria No. 108, 1991, 383p, ISBN 924157108X.

## Nitrogen oxides

Evaluates the risks to human health and the environment posed by exposure to nitrogen oxides. Combustion processes provide the major source of nitrogen oxides in both indoor and outdoor air. Fossil fuel power stations, motor vehicles and domestic combustion appliances emit nitrogen oxides, mostly in the form of nitric oxide accompanied by some nitrogen dioxide. Once in indoor or outdoor air, chemical reactions oxidise nitric oxide into nitrogen dioxide and a suite of other nitrogenous species. The evaluation concentrated on nitrogen dioxide, which is the most extensively investigated nitrogenous species, the most toxic and the one most suitable for risk assessment from a public health perspective.

In view of the complex behaviour of these compounds in the environment, the many factors that affect the conditions of human exposure and the difficulty of correlating specific exposures with direct effects on health, the report gives particular attention to methods, logical problems that help resolve inconsistencies in reported results. The overriding aim is to establish reliable health based guidance values for both peak daily concentrations and average annual exposures that are sufficient to protect public health and susceptible population. Well over 1300 references to the literature are included in this cautious and carefully documented assessment. The opening chapter reviews data on both ambient and indoor sources of nitrogenous compounds, their emissions, and the resulting concentrations that may directly affect human health. Also considered are indirect effects that arise from the participation of nitrogen containing compounds in the production of photochemical smog, ozone depletion in the stratosphere and ozone depletion in the stratosphere. The next chapter concerned with the effects of atmospheric nitrogen compounds on plants, cites abundant evidence that increased pollution with nitrogen compounds has had major adverse effects on many plant species and has contributed to a loss of biodiversity.

The most extensive chapter evaluates the large body of evidence from animal studies designed to duplicate as closely as possible typical patterns of human exposure. Toxic effects consistently observed in several laboratory species support the conclusion that exposure to nitrogen dioxide causes adverse effects on lung metabolism and biochemistry, lung function and lung structure and can result in dysfunction of respiratory tract host defences, causing increased susceptibility to infectious respiratory diseases. Animal studies also clearly demonstrate that chronic exposure can cause emphysema of the type seen in human lungs.

The evaluation of effects on human health first considered findings from several well designed studies of controlled exposure conducted in young, healthy adult males, asthmatics and patients with chronic obstructive pulmonary disease, children and elderly. These findings support the conclusions that exposure to nitrogen dioxide causes decrement in lung function and results in increased airway responsiveness to bronchoconstrictive agents. Exposure of asthmatics causes in some subjects increased airway responsiveness to a variety of provocative mediators. An evaluation of the large number of epidemiological studies confirms that asthmatics are the population most susceptible to

adverse effects on health, children aged 5 to 12 years were identified as a sub-population potentially susceptible to increased respiratory morbidity as associated with exposure.

The report recommends a 1-hour average daily maximum nitrogen dioxide concentration of 200 mg/m<sup>3</sup> (0.11ppm) as a short term guideline value. An annual guideline value of 40mg/m<sup>3</sup> (0.023 ppm) was also proposed although a no effect level for subtonic or chronic exposure to nitrogen dioxide concentration has not yet been determined.

**Reference:** Environmental Health Criteria No. 188, 1997, xxiv, 550p, ISBN 9241571888.

## 2-Nitropropane

Evaluates the risks to human health and the environment posed by 2-nitropropane an important industrial chemical used as a solvent for printing inks, paints, varnishes, adhesives and other coatings such as beverage container linings 2-Nitropropane is also used in printing links for flexible food packaging and food processing primarily for the separation of oleic acid from polyunsaturated fatty acids. Though smokers are regularly exposed to low concentration, exposure of the general population from other sources is very low.

The most extensive section evaluates data from laboratory studies of toxicity. Studies show moderate acute toxicity for mammals with considerable variation in the sensitivity of different laboratory animals. Studies conducted in the rat provide clear evidence of destructive changes in the liver, including hepatocellular carcinoma. The report found no conclusive evidence that 2-Nitropropane causes cancer in the laboratory species.

Concerning effects on humans the report notes that exposure to high concentration, which are acutely toxic is largely or entirely confined to the occupational setting. An evaluation of toxic effects draws upon seven reports of industrial fatalities attributed to inhalation of 2-Nitropropane fumes, with death due to acute hepatic failure in all causes. Although more research on long term effects is needed the report notes that available data provide no indication that chronic occupational exposure at concentrations usually encountered in the workplace induce hepatic or other neoplasm's or other long term effect. Because 2-Nitropropane is a potential carcinogen in rats. The report recommends that occupational exposure to the solvent and its presence in consumer products be minimized and replaced with a less toxic solvent whenever practical. The report recommends against the use of 2-Nitropropane in food processing.

**Reference:** Environmental Health Criteria No. 138, 1992, 108p, ISBN 9241571381.

## Occupational exposures in insecticide application and some pesticides

Evaluates the carcinogenic risk of humans posed by occupational exposure during the spraying and application of insecticides. The book also features separate monographs evaluating the carcinogenicity of 17 individual pesticides, including several that have been banned by industrialized countries yet are still used in the developing world. Although some of these pesticides have been in use of more than four decades evaluation of carcinogenicity were hindered by the separatism of well designed epidemiological studies.

The first and most extensive monographs evacuated data from descriptive and ecological studies cohort studies and case control studies suggesting in increased risk of cancer, most notably lung cancer,, multiple myeloma and other tumours of B-cell origin, in workers exposed to insecticides during their application on the basis of this evaluation the book concludes that the spraying and application of nonarsenical insecticides entail exposures that the probably carcinogenic to humans



The remaining monographs evaluate the carcinogenicity of aldicarb, atrazine, captafol, chlordane, DDT, deltamethrin, dichlorvos, fenvalerate, heptachlor, monuron, pentachlorophenol, permethrin, picloram, simazine, thiram, triflurain and ziram.

Of these captafol, a fungicide used on plants for seed treatment and as a wood preservative, was classified as probably carcinogenic to humans. Atrazine, chlordane, DDT, dichlorvos, heptachlor, and pentachlorophenol were classified as possibly carcinogenic to humans. The remaining pesticides could not be classified on the basis of available data.

**Reference:** IARC Monographs on the evaluation of carcinogenic risks to human volume 53, 1991, 612p, ISBN 9283212533.

### **Occupational exposures of hairdressers and barbers and personal use of hair colorants, some hair dyes, cosmetic colorants, industrial dyestuffs and aromatic amines**

A detailed assessment of the carcinogenic risk to humans posed by the professional and personal use of hair colorant. An additional 17 monographs evaluate the carcinogenicity of eight hair dyes, one cosmetic colorant, four industrial dyestuffs and four aromatic amines, three of which are used in dyestuff manufacture.

The first and most extensive monograph considers the carcinogenic risk posed by occupational exposures of hairdressers and barbers and personal exposure to hair colorants. Citing consistent evidence from live large European cohort studies of excess risk for cancer of the urinary bladder in male hairdressers and barbers, the monograph concludes that occupation as a hairdresser or barber entails exposure that are probably carcinogenic. The carcinogenic risk linked to the personal use of hair colorants could not be determined.

Of the eight hair dyes considered only one HC blue No.1 could be classified as possibly carcinogenic to human. The cosmetic colorant D&C Red No.9 (CL Pigment Red 53:1) could not be classified. Of the four industrial dyestuffs, CL Direct Blue 15, CI Acid Red 114 and magenta containing CI Basic Ref 9 were classified as possibly carcinogenic to humans. The manufacture of magenta was classified as entailing exposures that are carcinogenic.

Of the four aromatic amines, 4,4'-Methylene bis (2-chloraniline) (MOCA) was classified as probably carcinogenic to humans para chloraniline and 2,6-dimethylaniline were classified as possibly carcinogenic, N,N-dimethyl aniline could not be classified.

**Reference:** IARC Monograph on the evaluation of carcinogenic risks to human, Volume 57, 1993, 427p, ISBN 9283212576.

### **Occupational exposures to Mists and vapours from strong inorganic acids and other industrial chemicals**

Evaluates the carcinogenic risk to humans posed by occupational exposure to mists and vapours from strong inorganic acids and by other industrial chemicals. The volume features six monographs concerning occupational exposures to mists and vapours from sulphuric acid and other strong inorganic acids, sulphuric acid and other strong inorganic acid, sulphuric acid and other strong inorganic acids sulfur dioxide and some sulfites, bisulfites and metabisulfites, hydrochloric acid, diethyl sulfate, disopropyl sulfate and 1,2,3-butadiene.

In the first and most extensive monograph evaluations draw upon numerous studies of occupational exposures in industries where the use of strong inorganic acid is particularly heavy. These include the manufacture of isopropanol, synthetic ethanol, phosphate fertilisers, lead batteries, soap and detergent, sulphuric acid and nitric acid and industries involving pickling and other acid treatment of demonstrated an excess of nasal sinus cancer, laryngeal cancer, and lung cancer. In all studies considered sulphuric acid mists were the most common exposure. On the basis the data, the monograph concludes that occupational exposure to strong inorganic acid mists containing sulphuric acid is carcinogenic to humans.

Concerning the other industrial chemicals evaluates in this volume, 1-3 butadiene and diethyl sulphate were classified as probably carcinogenic to humans. Disopropyl sulphate was classified as possibly carcinogenic to humans. Sulphur dioxide, sulphates, bisulfites, methabisulfites and hydrochloric acid could not be classified on the basis of currently available data.

**Reference:** IARC Monographs on the evaluation of carcinogenic risks to human, volume 54, 1992, 336p, ISBN 9283212541.

### Partially halogenated chlorfluorocarbons (Ethane derivatives)

Evaluate the environmental behaviour, toxic it ad ozone depleting and global-warming potentials of six partially halogenated ethane derivatives selected as candidates to replace the fifteen fully halogenated chlorfluorocarbons that are being phased out in line with the provisions of the Montreal Protocol on substances that Deplete the Ozones layer. The compound considered are 1,1-dichloro-1-fluoroethane (HCFC 141b), 1-chloro-1,1-difluoroethane (HCFC 142b), 1,2-dichloro-1,1 difluoroethane (HCFC 132b) 1-Chloro-1,2,2 trifluoroethane (HCFC 133a) 1,1-dichloro-2,2,2-trifluoroethane and 1-chloro-1,2,2,2 tetrafluoroethane

All compounds were judged to have ozone depleting and global warming potential considerably lower than those of CFC 11, the fully halogenated chlorfluorocarbon with the highest ozone depleting and global warming potential. Estimated atmospheric lifetimes range from 1,6 Years for HFC 123 to 19.1 years for HCFC 142b.

Because studies of HCFC 132b and HCFC 133a have documented a number of toxic effects these compounds could not be recommended as substitutes. Since the toxicity of HCFC 142b is low and the ozone-depleting and global-warming potentials are lower than those of fully halogenated chlorfluorocarbon, the report concludes that HCFC 142b can be considered as a transient substitute for the chlorfluorocarbons included in the Montreal Protocol. In view of paucity of toxicological data on HCFC141b, HCFC 123 and HCFC 125, no evaluation of the potential effects on human health could be made.

**Reference:** Environmental Health Criteria No.139, 1992, 130p, ISBN 924157139X.

### Partially halogenated chlorfluorocarbons (Methane derivatives)

Evaluates the risks to human health and the environment posed by two partially halogenated chlorfluorocarbons, dichlorfluoromethane (HCFC 21) and chlorldifluoromethan (HCFC 22), These two methane derivatives were selected for evaluation because of their potential use as substitutes for those fully halogenated chlorfluorocarbon that are being phased out as a result of the 1987 Montreal Protocol on substances that Deplete the Ozone layer. The evaluate is interned to assist industry in its urgent search for acceptable substitute chemicals, most notably for use as refrigerants, as propellants in aerosols, and as blowing agents for the production of polystyrene. While data on human toxicity are thoroughly reviews the greatest challenge is to find the most accurate models for predicting levels of release to the environment and estimating the potential of these chemicals to deplete the ozone layer.

Because HCFC 21 is no longer produced for any commercial purposes, most data assessed come from studies of HCFC –22. Current environmental levels of both chemicals are judged to be extremely low and highly unlikely to cause direct effects on human health. A review of models for estimating atmospheric residence time and routes of transport to the stratosphere concludes that the ozone depleting potential of both chemicals is considerably lower than that the fully halogenated chlorofluorocarbons, while HCFC 21 has the advantage of a much shorter troposphere lifetime, studies have linked exposure to liver damage. Concerning the toxicity of HCFC 22, evidence from the vast majority of studies is reassuring. The report concludes that HCFC22 is an acceptable transient substitute for the chlorofluorocarbon included in the Montreal Protocol. HCFC 21 could not be recommended due to this potential toxic effects on the liver.

**Reference:** Environmental Health Criteria No. 126, 1991, 97p, ISBN 9241571268.

## Permethrin

Evaluates the design and findings of over 250 studies concerned with the effects on human health and the environment posed by permethrin a photostable synthetic pyrethroid insecticide marketed since 1977, Because of its strong repellent properties and effectiveness as a stomach and contact insecticide, permethrin is widely used in the protection of several agricultural crops, in the control of insects in households and on cattle, in aerial application for forest pest control, as a fog in mushroom houses and as a wood preservative. Public health applications include the dissection of aircraft, treatment of mosquito nets, and human lice control.

In view of the uses of permethrin and its photostable properties, a section devoted to sources of human exposure concentrates on the large number of studies investigating residues in fruits. Vegetables, dairy milk, and grains. Finding from laboratory studies. indicating that permethrin is highly toxic to certain beneficial insects and natural enemies of pests are constricted with field investigations demonstrating the transitory nature of most toxic and repellent effects on non-target species.

The most extensive section reviews the finding of experimental studies concluded to assess toxicity. Particular attention is given to differences in study design, dose and mode of administration that can affect the validity of findings when extrapolated to humans. The final section draws upon a limited number of occupational and clinical studies to evaluate direct evidence of adverse effects on health.

On the basis of this review, the book concludes that most toxic effect are transitory that the likelihood of carcinogenic effects in humans is extremely low or non-existent and that permethrin, when used as recommended is not likely to present a hazard to the general public exposed workers, or the environment.

**Reference:** Environmental Health Criteria No. 94, 1990, 125p, ISBN 9241542942.

## Peroxisome proliferation and its role in carcinogenesis.

Views and expert opinions of an IARC working group.

A state-of-the –art consensus report on what is known about peroxisome proliferation, the mechanisms involved and their relevance to carcinogens. Peroxisomes are single, membrane limited, cytoplasmic organelles that are found in cells of animals plants, fungi and protozoa. Peroxisome proliferators include certain hypolipidaemic drugs, phthalate ester plasticizers, industrial solvents, herbicides food flavours, leukotriene D4 antagonists and hormones. Numerous studies in rats and mice have demonstrated the hepatocarcinogenic effects of peroxisome proliferators and these compounds have been unequivocally established as carcinogens. Since humans are exposed to peroxisome proliferators to a significant

extent, assessment of the adverse biological effects of the group of compounds and particularly their potential carcinogenicity has become an important issue.

The report has two parts. The first records the consensus reached by a group of eleven experts, including several of leading investigators in this field. Questions addressed include the mechanism by which peroxisome proliferates exert their carcinogenic effects in rodents, the relevance of animal studies to the evaluation of carcinogenic risk in humans and the potential use of peroxisome proliferation as a biological marker for liver cancer. The report concludes that compounds including peroxisome proliferation in rats and mice have little, if any effect on human liver. The report also issues advice on the interpretation of peroxisome proliferation, demonstrated in animal studies when evaluating the carcinogenic risk to humans. The second part consist of three background papers presented by members of the working group.

**Reference:** IARC Technical report no. 24, IARc, 1995, 85p, ISBN 9283214390.

## Phenol

Evaluates risks to human health and the environment posed by exposure to phenol, a constituent of coal tar formed during the natural decomposition of organic materials. Phenol is the basic feedstock from which a number of commercially important materials are made. Including resins bisphenol. A carpolactam, alkyl phenols, and chlorphenols. The most important environmental emissions result from the use of phenolic resin. The residence of phenol in liquid manure and its formation following the atmospheric degradation of benzene may contribute significantly to atmospheric levels.

The most extensive section summarises toxic to data from studies in laboratory animals and in vitro test systems including special studies of neurotoxicity, myelotoxicity, immunotoxicology and biochemical effects. Neurotoxicity liver and kidney damage, respiratory effects as the main effects of short term exposure. An evaluation of effects on human health draws upon case report following accidental or intention ingestion, outbreaks of poisoning following the accidental contamination of drinking water and studies in occupationally exposed worker, while available data do not suggest a strong potential for cumulative health effects following chronic exposure, the report concludes that accidental high exposure can cause a number of local and systemic effects. Evidence of genotoxicity, and inadequate studies of carcinogenic potential, remain areas of concern,

Concerning risk to the environment, the report cites evidence of toxicity to freshwater and marine organisms. While phenol is judged unlikely to persist or bioaccumulate in the environment, the report warns that aquatic organisms may be at risk in any surface or sea water contaminated with this compound.

**Reference:** Environmental Health Criteria No. 161, 1994, 151p, ISBN 9241571616.

## Alpaha-Phenothrin

Evaluates the risks to human health and the environment posed by d-phenothrin, a synthetic pyrethroid insecticide used primarily for the household control of head lice and other insects and for the treatment of stored grain.

The opening sections review available data on world-wide industrial production and use are summarise studies conducted to assess residues in stored grain. A section devoted to the behaviour of d-phenothrin in the environment concentrates on investigations of photodegradation and transport, concluding the photodegradation under outdoor conditions is rapid, but that d-phenotrhin remains virtually intact for up to 12 months on grains store in the dark.

The most extensive section evaluates toxicological data from studies in experimental animals and in vitro test systems. The evaluation confirms a low toxicity for d-phenothrin and an absence of mutagenic, teratogenic, embryotoxic, oncogenic and neurotoxic effects. Concerning effects on human health, the book notes that d-phenothrin has not during more than a decade of use, been reported to have caused human poisoning or other toxic effects. The book concludes that d-phenothrin, when used as recommended is not likely to pose a hazard to either human health or the environment.

**Reference:** Environmental Health Criteria No. 96, 1990, 64p, ISBN 9241542969.

## Phosgene

Evaluates the risks to human health and the environment posed by exposure to phosgene initially important as an agent of chemical warfare, this extremely reactive gas is now widely used as a chemical intermediate, most often as the point of production. The principal use is in the production of aromatic diisocyanates. Such as methylene diphenyl diisocyanate and toluene diisocyanates, which are used to produce polyurethane foams and other polymers.

The report notes that most emissions are to the air and arise from the thermal degradation of chlorinated solvents and chlorinated polymers. Knowledge about the chemical properties of phosgene supports the conclusion that this chemical is unlikely to be detected in soil, vegetation, or food concerning sources of human exposure, the report concludes that inhalation is the principal route of exposure that the general population is exposed to extremely low levels and that occupational exposures though generally very low vary greatly depending on industrial hygiene practices.

The most extensive section evaluates findings from experimental studies. The lung is identified as the primary target organ in all species studies with pulmonary oedema consistently reported as the primary cause of death following acute poisoning. Available data were judged inadequate for the assessment of carcinogenicity, neurotoxicity and potential adverse effects on reproduction and development.

The review of effects on human health considers the consequences of high level, short term exposure to phosgene from reports of industrial accidents involving both individual workers and large numbers of the general population. These studies in line with the animal data confirm that the respiratory system is the primary target organ and that pulmonary oedema is the main cause of death following acute severe exposure. Studies show that survivors receiving proper medical support can recover completely.

On the basis of these evaluations, the report concludes that the extremely low levels of phosgene detected in air do not threaten the health of the general population. The report likewise found no evidence of adverse effects on the health of workers in closed system facilities employing good industrial hygiene. However firemen, welders and other occupational groups of workers with chlorinated solvents or exposed to chlorinated hydrocarbon polymers in contact with flames were noted to risk exposure to levels of phosgene known to cause adverse effects on human health.

**Reference:** Environmental Health Criteria No. 193, 1997, xvii, 70p, ISBN 9241571934.

## Platinum

Evaluates the risks to human health and the environment posed by the mining, refining, industrial use and recycling of platinum and selected platinum compounds. Because of its exceptional catalytic properties, resistance to chemical corrosion, and high mechanical strength, platinum is widely used in the chemical and petroleum industries, most notably in the production of catalysis, including devices for reducing hazardous gas emissions. The growing use of catalytic converters to reduce pollution from automobile exhausts has caused a sharp increase in the world demand for this metal. Compounds such as cisplatin also have important therapeutic applications.

The book opens with a review of the many sensitive techniques that can be used to detect and measure platinum in biological and environmental samples. A review of data on sources of human and environmental exposure concludes that all significant human exposures are occupational with the greatest potential health hazards posed by certain halogenated soluble salts that may be inhaled as dusts or come in to contact with skin during the later stages of refining or during the manufacturing of catalysts. The reclamation of platinum from scrap and used equipment may also entail hazardous exposures.

Concern about environmental contamination centres on the possible release of platinum in the exhausts of automobiles equipped with catalytic converters review of several well designed studies of automobile exhausts and roadside dust supports the conclusion that such emissions are unlikely to damage the environment or threaten the health of the general population. Concerning risks to human health, the book cites platinum salt hypersensitivity as the major health hazard for workers noting that symptoms of hypersensitivity may persist of lifetime and that allergic reactions can be provoked by very small quantities.

**Reference:** Environmental Health Criteria, No.125, 1991, 167p, ISBN 924157125.

## Polybrominated Biphenyls

Evaluate the risks to human health and the environment posed by exposure to polybrominated biphenyls (PBBs). These chemical were introduced as flame retardant in the early 1970;s and used in the manufacture of small appliances and in automotive applications, coating, lacquers and polyurethane foam.

Research on these chemical has been especially intense following a 1973 poisoning disaster in Michigan, USA caused when the flame retardant Fire master was inadvertently confused with magnesium oxide based cattle feed supplement. The flame retardant was added to animal feed and widely distributed to farms within there State. The ensuing contamination of farm animals resulted in the destruction of tens of thousands of cattle, pigs and sheep and more than a million chickens. Since the cause of contamination remained un-detected for almost a year, thousands of farmers and other consumers were exposed to PBBs through the consumption of contaminated meat, eggs and dairy products.

Although production of PBBs has been halted or severely restricted in many parts of works these chemicals remain of enduring concern due to their extreme persistence in the environment, their concentration in the food chain, their marked tendency to bioaccumulate in living organisms. Including humans and potential for adverse health effects following long term exposure to very low levels. Close to 600 studies were critically assessed in an effort to reach definitive conclusions concerning the risks posed by these highly persistent chemicals

Citing overwhelming evidence from several sources, the report concludes that humans and the environment should not be exposed to PBBs and that commercial use of this compound should cease

**Reference:** Environmental Health Criteria No. 152, 1994, 577p, ISBN 9241571527.

## Polychlorinated Biphenyls and Terphenyls

Evaluates the vast body of evidence demonstrating the serious threat to human and environmental health posed by polychlorinated biphenyls(PCBs). These chemicals which are now ubiquitous in the environment, have been used commercially since 1930 as dielectric and heat-exchange fluids and in a variety of other applications. Over 1,300 studies were critically assessed. The book also contains a brief review of the limited data on polychlorinated terphenyls.

A section on the environmental assesses the mechanisms by which these highly persistent chemicals previously introduced into the environment are gradually being redistributed towards increased contamination of the marine environment. For the general population the most important sources of exposure are food items and for babies, breast milk. The well documented sign of poisoning in occupationally exposed workers are also reviewed. A section on metabolic fate cites evidence of accumulation in the liver and the adipose tissues of various organs, placental transport, foetal accumulation and distribution to milk.

The most extensive section, which runs some 100 pages, evaluates findings from studies of toxicity in experimental animals and in vitro system. Findings suggest that PCBs are immunosuppressive and act as tumour promoters. An assessment of effects on humans draws upon studies of two large outbreaks of poisoning from contaminated food, and occupational exposures. The report cites reproductive failure in sea mammals as the most important environmental hazard, further concluding that the predicted redistribution of residues towards the Marie environment will pose an increasing hazard for sea mammals in the future. A review of the hazards of polychlorinated terpenyls concludes the report.

**Reference:** Environmental Health Criteria No. 140, 1993, 682p, ISBN 9241571403.

### **Polychlorinated Dibenzo-paradioxins and Dibenzofurans**

Evaluates the risks to human health and the environment posed by exposure to polychlorinated dibenzo-para-dioxins (PCDDs) and polychlorinated dibenzofurans (PCDFs) these compounds which are not produced intentionally are formed as an undesired side reaction during the manufacture of chemical products used extensively as insecticides, herbicides, antiseptics, disinfectant and wood preservatives.

The main part of the book evaluates data linking these compounds and especially the PCDD 2,3,7,8 tetrachloro-dibenzo-p-dioxin, to adverse effects on health. The assessment also draws upon studies following industrial accidents, mass outbreaks of poisoning caused by consumption of contaminated rice oil in Japan and Taiwan and the widespread use of contaminated Agent Orange in Viet Nam. Despite the number of clinical and follow-up studies and despite the high incidence of hepacocellular carcinoma observed in some animal species, the report concludes that for occupational and accidental exposures, no clear cut persistent effects other than chloracne have been observed

**Reference:** Environmental Health Criteria No. 88, 1989, 409p, ISBN 9241542888.

### **Polychlorinated Dibenzo-para-Dioxins and polychlorianted Dibenzofurane**

Evaluates the carcinogenic risks to humane posed by exposure to polychlorinated dibenzo-para dioxins (PCDDs) and polychlorinated dibenzofurane (PCDFs).PCDDs are formed as inadvertent by products. Sometimes in combination with PCDFs during the production of chlorophenols and chlorophenoxy herbicides and have been detected as contaminants in these products. PCDDs and PCDFs may also be produce in thermal processes such as incineration and metal processing and in the bleaching of paper pulp with free chlorine. Of the PCDDs 2,3,7,8-tetrachlorodibenso-para-dioxin (2,3,7,8-TCDD) or dioxin has attracted the greatest concern.

PCDDs and PCDFs are ubiquitous in soil, sediment and air persist in the environment and accumulate in animal fat. Excluding occupational and accidental exposure most human exposure to these compounds, occurs from the consumption of meat, milk, eggs, fish and related products, Occupational exposures at higher levels have occurred since the 1940 as a result of the production and use of chlorphenol and chlorphenoxy herbicides and for PCDFs in metal production an reclining. Even higher exposures have occurred in sporadic industrial accidents and following incident s of rice oil contamination.

The evaluation, which considered abundant human and animal carcinogenicity data found strong evidence from epidemiological studies in humans that exposure to 2,3,7,8-TCDD produces increased risks for all cancer combined rather than for any specific site, suggesting that 2,3,7,8-TCDD is an unprecedented multi-site carcinogen with no single site predominating. Citing data from animal studies and other lines of evidence the monograph concludes that 2,3,7,8-TCDD is carcinogenic to human. Other polychlorinated dibenzo-para-dioxins and dibenzo-para-dioxin could not be classified as to their carcinogenicity to human.

For PCDFs the evaluation considered evidence from two large poisoning incidents involving rich oil contamination in Japan and Taiwan. Although excessive mortality from liver cancer was observed in long-term follow-up of the Japanese cases, the report cited other factors including a high prevalence of chronic hepatitis B infection in the geographical area concerned as possible explanations. Evidence of carcinogenic to human was judged inadequate in the absence of convincing data from experimental animals. PCDF;s could not be classified as to their carcinogenicity to humans.

**Reference:** IARC Monograph on the evaluation of carcinogenic risks to humans Vol. 69, 1997, ix, 666p, ISBN 928321269X.

## Printing processes and printing inks, carbon black and some nitrocompounds

Evaluates the carcinogenic risk to humans posed by exposures in printing processes and to printing inks, to carbon black and to selected in to compounds many of which are used in the production of dye and colorant intermediates. The first monograph evaluate occupational exposures in printing processes and to printing ink. Exposures in the printing industry are assessed according to their occurrence in printing ink manufacture and in printing operations such as letterpress, lithography, flexography, graver and screen printing. Although many epidemiological studies have demonstrated some evidence of cancer risk in printing trades and printing industries the assessment found several important problems in the design of these studies. Occupational exposures in printing processes were classified as possibly carcinogenic to humans. Printing ink could not be classified.

The second monograph evaluates the carcinogenicity of carbon black an intense black pigment mainly used in tyres and other rubber automotive products and in many other rubber products. Although the evaluation found sufficient evidence in experimental animals that exposure to carbon black causes lung tumours data on carcinogenicity to human were judged inadequate. Carbon black was classified as possibly carcinogenic to humans.

The remaining monographs evaluate selected nitro compounds. Of these 3,7 and 3,9 dinitrofluoranthene, 2,4 and 2,6-dinitrotoulenes, 2, nitroanisole, nitrobenzene and tetranitromethane were evaluated as possibly carcinogenic to humans. Chloronitrobenzenes, 3,5-dinitrotoulene, nitrotoluene, 2,4,6-trinitrotoluene, and musk xylene and musk ambrette could not be classified.

**Reference:** IARC Monograph on the evaluation of carcinogenic risk to human, Vol.65, IARC, 1996, v, 578p, ISBN 9283212657.

## Propachlor

Evaluates the risks to human health and the environment posed by propachlor, a pre-emergence an early post-emergence herbicide in use since 1965. Derived from acetanilide propachlor is used in agriculture to control annual grasses and some broad level weeds in several crops including corn, sorghum, pumpkins, flax and flowers.

A section devoted to the environmental behaviour of propachlor cites rapid degradation by micro-organism in soil and water and concludes that this chemical does not bioconcentrate or biomagnify.



Studies of metabolic fate in different mammalian species point to rapid elimination of propachlor and its metabolites.

The remaining sections evaluate findings from toxicological investigations in experimental animals and for humans the limited data available from cases of contact and allergic dermatitis reported in farmers and production workers exposed to propachlor. For experimental animals, the liver and kidneys are identified as the target organs. For human exposures the report found no evidence of symptoms or diseases reported for either occupationally exposed workers or the general population, with the exception of scattered reports of dermatitis in workers.

On the basis of these evaluations, the report concludes that under conditions of normal use exposure of the general population is unlikely. For occupationally exposed workers the report recommends the use of adequate safety and hygienic precautions to protect the skin, eyes and respiratory tract. Though propachlor is judged to pose a low hazard to birds, earthworm and honey bees evidence indicates high toxicity to some aquatic organisms supporting the conclusion that direct contamination of water courses should be avoided.

**Reference:** Environmental Health Criteria No. 147, 1993, 110p, ISBN 9241571470.

## 1-Propanol

Evaluates the risks to human health and the environment posed by the production, use and waste disposal of 1-propanol, a colourless, highly flammable liquid used primarily as the multipurpose solvent in industry and in the home the compound which has antiseptic as well as solvent properties is also used in drug and cosmetics. The evaluation concludes that under normal conditions of use 1-propanol is unlikely to pose a serious risk to either the general population or the environment.

**Reference:** Environmental Health Criteria No. 102, 1990, 98p, ISBN 9241571020.

## 2-Propanol

Evaluates the risk to human health and the environment posed by the production and use of 2-propanol, a liquid widely used as a low cost solvent in industry and in the home. Because of its cooling antipyretic, rubefacient, cleaning and antiseptic properties. 2-propanol is used to produce a large number of household and personal products, including topically applied pharmaceutical products and cosmetics.

The report notes that the strong acid production process, which has been causally linked to an increased risk of paranasal sinus cancer in workers, has been largely replaced by a less hazardous process, thus reducing the health risks to workers. Experimental studies point to toxic effects similar to those of acute ethanol intoxication. A review of sources of human exposure draws attention to reports of life threatening intoxication following the sponging of febrile children with 2-propanol preparations. While noting the need for further studies of carcinogenic activity, the report concludes that 2-propanol is unlikely to pose a serious health risk under normal conditions of exposure.

**Reference:** Environmental Health Criteria No. 103, 1990, 132p, ISBN 9241571039.

## Selected synthetic organic fibres

Evaluates the risks to human health posed by occupational and environmental exposure to selected synthetic organic fibres. Fibres covered include carbon and graphite fibres, aramid fibres and polyolefin fibres. Carbon and aramid fibres are used mainly in advanced composite material to improve strength, stiffness, durability, electrical conductivity or heat resistance. Since these fibres improve properties

without adding much weight, they are used primarily in the aerospace industry, for military purposes and in the manufacture of sports equipment. Polyolefin fibres are used in carpet pile, upholstery, bedding, curtains and other household tactile applications. The largest use of polyolefin fabric in clothing is in disposable diapers and antithetic socks.

Basic information on chemical and physical properties and methods of production is followed by a review of data from studies of exposure in the occupational environment. Where operation such as fibre forming, winding, chopping weaving, cutting and machining and composite formation release fibre dusts in to the workplace. The most extensive cheaper housed on the results of toxicological studies in laboratory animals and in vitro test systems, reviews the many important methodological problems, including choice of exposure route that make it difficult to assess effects and extrapolate findings to humans. Although data from human studies are limited the report concludes that occupational exposure to these synthetic organic fibres may have adverse effects on the respiratory system. The report further concludes that the health risk associated with exposure in the general environment is likely to be very low.

**Reference:** Environmental Health Criteria No. 151, 1993, 100p, ISBN 9241571519.

### **Silica, some silicates, coal dust and para-Aramid fibrils**

Evaluates the carcinogenic risks to humans posed by exposure to crystalline and amorphous silica, some silicates (palygorskite, sepiolite, wollastonite, and zeolites and other than erinoite), coal dust and para-aramid fibrills. The volume opens with a discussion of the many complexities involved in assessing the cancer risks associated with occupational exposure to inhaled mineral dusts and the special toxicological considerations required when evaluating the results of experimental studies. Against this background, the first and most extensive monograph evaluates human and animal carcinogenicity data on silica, concentrating on evidence of an increased risk for lung cancer. On the basis of this evaluation, crystalline silica inhaled in the form of quartz or cristobalite from occupational sources was classified as carcinogenic to humans. For amorphous silica, evidence from both epidemiological and experimental studies was judged inadequate and amorphous silica could not be classified.

For palygorskite, the evaluation found sufficient evidence from studies in rats that long fibres were carcinogenic studies of exposure to short fibres showed no significant increase in the incidence of tumours. The few studies in humans were judged inadequate. long palygorskite fibres were classified as possibly carcinogenic to humans. Short fibres could not be classified.

For coal dust, several limitations in human studies, largely concerned with excessive mortality from lung and stomach cancer, hindered interpretation of the epidemiological literature. The few adequate experimental studies showed no increase in tumours. Coal dust therefore could not be classified. Para-Aramid fibrils like wise could not be classified in view of inadequate in both the epidemiological and experimental data.

**Reference:** IARC Monographs on the evaluation of carcinogenic risks to human Vol. 68, 1997, iv, 506p, ISBN 9283212681.

### **Some flame retardants and textile chemicals and exposures in the textile manufacturing industry**

Evaluates the carcinogenic risk to humans posed by exposure to selected flame retardant and other chemicals used in the textile manufacturing industry. Agents were selected for evaluation on the basis of the availability for data on carcinogenicity and on human exposure. The book also includes an extensive monograph addressing the question of whether employment in the textile manufacturing industry exposes workers to carcinogenic risks.

Monographs cover six flame retardant (Chlorendic acid, chlorinated paraffins, decarbromodiphenyl oxide, dimethyl hydrogen phosphite, tetrakis (hydroxy methyl phosphonium salts and tris (chloroethyl) phosphate ) five textile dyes para-chlorethyl phosphate, five textile dyes (para-chloro-ortho-toluidine) and nititriacetic acid and its salts. Para-chloro-orthotoluidine and strong acid salts were classified as probably carcinogenic to humans and chloredic acid, chloronited paraffins. Disperse Blue-1 and nitrogluciwetic acid and its salts were classified as possibly carcinogenic to humans. The remaining chemical could not be classified.

The most extensive monograph evaluates occupational exposures in the textile manufacturing industry. Evaluations of risk concentrate on epidemiological evidence of carcinogenicity at the oral and pharyngeal, oesophagus and stomach, nasal cavity, larynx, lung and bladder sites. In view of the strength of findings of bladder cancer among dyers and among weavers and of cancer of the nasal cavity among weavers and other textile workers the monograph concludes that working in the textile manufacturing industry entails exposures that are possibly carcinogenic to human.

**Reference:** IARC Monograph on the evaluation of carcinogenic risks to human Vol. 48, IARC, 1990, 345p, ISBN 928321287.

### **Some naturally occurring substances. Food items and constituents, Heterocyclic aromatic amines and mycotoxins**

Evaluates the carcinogenic risk to humans posed by the ingestion of several naturally occurring substances. Separate monographs are presented for two food items (salted fish and pickled vegetables), two naturally occurring plant substances (caffeic acid and d-limonene) four heterocyclic aromatic amines found in cooked meat and fish and selected mycotoxins including aflatoxins.

The monograph on salted fish concentrates on fish and traditional prepared in Southern China, where very high rates of nasopharyngeal carcinoma have been linked to the consumption of salted fish prepared in a manner which involves putrefaction. The monograph concludes that Chinese style salted fish is carcinogenic to humans. The second monographs concludes that pickled vegetables prepared according to traditional Asian methods are possibly carcinogenic to humans. Caffeic acid was judged to be possibly carcinogenic to humans. The report was unable to classify the carcinogenicity of d-limonene. For the heterocyclic aromatic amines present in cooked meat and fish. IQ was classified as probably carcinogenic to humans, MeIQ, MeIQx and PhIP were classified as possibly carcinogenic.

The most extensive monograph, on aflatoxins concludes that naturally occurring mixtures of aflatoxins are carcinogenic to humans and that aflatoxin M<sub>1</sub>, occurring in milk is possibly carcinogenic. Toxins derived from *Fusarium moniliforme* and ochratoxin A, which has been linked to Balkan endemic nephropathy, were classified as possibly carcinogenic to humans. The remaining mycotoxins could not be classified.

**Reference:** IARC Monographs on the evaluation of carcinogenic risks to humans Vol. 56, 1993, 599p, ISBN 9283212568.

### **Tetrabromobisphenol A and derivatives.**

Evaluates the risks to human health and the environment posed by tetrabromobisphenol A (TBBPA) the most widely used and commercially important brominated flame retardant. The compound is mainly used as a reactive intermediate in the manufacture of flame-retarded epoxy and polycarbonate resins. Tetrabromobisphenol A is also used as an additive flame retardant in various polymers. Laboratory pyrolysis studies have demonstrated that polymers containing TBBPA can form polybrominated dibenzofurans and to a lesser extent polybrominated dibenzodioxins, under scarring the need to ensure cautious disposal by incineration of industrial wastes are consumed products treated with TBBPA

Findings from studies in experimental animals demonstrate a very low acute and repeated dose toxicity. Citing these and other findings the report concludes that the health risk for the general, population posed by TBBPA is insignificant. Since most of the manufacturing process takes place in enclosed equipment, the report further concludes that occupational hazards are mainly confined to dust exposure during the packing processes and can be minimised through the use of local ventilation and other engineering methods.

The report also summarizes available environmental health criteria on five TBBPA derivatives used as flame retardants (tetrabromobisphenol A dibromopropyl ether, tetrabromobisphenol A bis(allylether) tetrabromobisphenol A bis (2-hydroxyethyl ether ), tetrabromobisphenol A carbonate oligomers, and tetrabromobisphenol A brominated epoxy oligomer ) and one derivate tetrabromobisphenol A diemthylether ) having no commercial applications but detected in environmental samples. For all these compound data were judged inadequate for evaluation.

**Reference:** Environmental Health Criteria No. 172, 1995, 139p, ISBN 9241571721.

### 1,1,2,2-tetrachloroethane

A concise assessment of the risks to human health posed by exposure to 1,1,2,2-tetrachloroethane, a chemical used primarily as an intermediate in the synthesis of other chlorinated hydrocarbons. The documented is a part of new series of brief report aimed at the characterisation of hazards and dose response for exposure to selected industrial chemicals.

Studies of environment behaviour and fate support the conclusion that 1,1,2,2-Tetrachloroethne has slight to moderate acute toxicity the liver is the principal target organ. studies of long term exposure demonstrated a significant increase in the incidence of hepatocellular carcinomas in mice, but not in similarly exposed rats. Because of the chemical declining use few recent evaluations of toxic effects in humans were available for evaluation.

**Reference:** Concise international chemical assessment, 1998, iv, 28p, ISBN 9241530030.

### Tetramethrin

Evaluates the risks to human health and the environment posed by tetramethrin, a synthetic pyrethroid insecticide used in aerosol formulations, emulsifiable concentrates and mosquito coils exclusively for indoor pest control. A review of data on the environmental behaviour of this insecticide points to rapid abiotic degradation in air and water.

Concerning effects on organisms in the environment, the report cites laboratory data demonstrating that tetramethrin is highly and acutely toxic to fish and toxic to bees, but have very low toxicity for birds. Because tetramethrin is rapidly degraded, and provided its use is limited to buildings are recommended this potential for environmental toxicity is unlikely to be realised

The most extensive section evaluates the results of experimental studies of toxicity and carcinogenicity relevant to the assessment of health effects in human. The report found no evidence of carcinogenicity or other adverse effects on health. On the basis of this evaluation the report concludes that tetramethrin when used as recommended for the indoor control of pests is highly unlikely to present hazard to the general population to workers or to the environment.

**Reference:** Environmental Health Criteria No. 98, 1990, 69p, ISBN 9241542985.

## Thallium

Evaluates the risks to human health and the environment posed by thallium, a natural occurring ubiquitous heavy metal present at low levels in drinking water, food and ambient air. Although the industrial production and uses of thallium are now limited thallium (1) sulphate was previously used in the treatment of tuberculosis and malaria and as a depilatory agent, resulting in numerous cases of poisoning.

Thallium has also been used within this century as a rodenticide and insecticide. While such uses have been banned in most parts of the world, thallium continues to be used as a low cost rodenticide in some developing countries. However, since thallium salts are tasteless, odourless, colourless, highly toxic and were easily obtained in the past, thallium probably qualifies as the World most frequently used agent for suicide, homicide and attempts at illegal absorption, resulting in vast body of clinical data on toxic effects in humans.

The most extensive sections review findings from toxicity studies in laboratory animals and from toxicity in laboratory animals and in vitro test systems and summarise the large body of clinical data drawn from case reports of accidental, suicidal and criminal poisoning in humans. These studies support numerous conclusions concerning the mechanisms of toxic action, target organs, the symptoms of acute and chronic intoxication, factors influencing clinical course and the degree of recovery the effectiveness of different therapies and estimated lethal doses in children and adults.

The report concludes that while the limited industrial uses of thallium are unlikely to pose a threat to the general population or the environment emissions from power generating plant, smelters, brickwork and cement plant should be strictly controlled and monitored. The report calls for a world-wide ban on the use of thallium as a rodenticide.

**Reference:** Environmental Health Criteria No. 98, 1990, 69p, ISBN 9241542985.

## Alpha-Toluidine

A concise assessment of the risks to human health posed by exposure to ortho-toluidine, a chemical used in the manufacture of dyestuffs and to lesser extent in the production of rubber, chemicals and pesticides, and as a curing agent for epoxy resin systems. The document is part of a new series of brief reports aimed at the characterisation of hazards and dose response for exposure to selected industrial chemicals with this goal in mind documents in the series focus on studies and findings considered critical for risk characterisation.

The document is primarily concerned with assessing the carcinogenic risk in occupationally exposed workers. A review of findings from studies in rats and mice, where oral administration of alpha toluidine has been linked to a significant increase in the incidence of benign and malignant tumours, supports the conclusion that alpha-toluidine may act as a genotoxic carcinogen. In humans limited epidemiological evidence suggests an increased risk of bladder cancer in occupationally exposed workers. In view of evidence that the chemicals carcinogenic action involves a genotoxic mechanisms the assessment was unable to identify a threshold at which exposure would not result in some risk to human health.

**Reference:** Concise international chemical assessment document No. 7, 1998, iv, 18p, ISBN 9241530073.

## Tributyltin compound

Evaluates risks to human health and the environment posed by the use of tributyltin compounds as molluscicides, as antifoulants and boats, ships, quays, buoys, and equipment in the fishing industry as wood preservatives and as slimicides on masonry. These compounds of a particular threat to the

marine equivalent view of these documented high toxicity to aquatic organisms, including commercially important shellfish.

Tributyltin compounds are observed to be toxic to micro-organisms and highly toxic to oysters, mussels, and other marine molluscs consumed by humans. A review of field observation which are in good agreement with laboratory findings, confirms the association between use of these compounds in the marine environment and mortality malformation and population decline of molluscs. The remaining sections evaluate findings from experimental studies and observations in occupationally exposed humans. The book concludes that tributyltin compounds are a severe irritant to human skin and an extreme irritant to the eye and that inhalation of aerosols can have especially hazardous effects on the respiratory tract. Despite the large body of experimental studies documenting toxicity the book was unable to quantify the risk to humans posed by the consumption of contaminated fish and shellfish.

**Reference:** Environmental Health Criteria No. 116, 1990, 273p, ISBN 9241571160.

## Trichlorfon

Evaluates the risks to human health and the environment posed by trichlorfon, a broad spectrum organophosphorus insecticide which act as a slow release source of dichlorvos in the mammalian body. Marketed since the 1950s. Trichlorfon is used to protect field and fruit crops to control forest insects and to control internal and external parasites in domestic and farm animals. Trichlorfon formulated as metrifonate has also been used for the pharmacological treatment of *Schistosoma naematobium* in millions of patients. The compound is under investigation as a treatment for Alzheimer's disease.

A review of environmental levels and human exposure concentrates on the significance of residues detected in crops, the milk of treated cows and other food items as possible sources of exposure for the general public. Nothing that detected levels are far below the established acceptable daily intake, the report concludes that trichlorfon does not constitute a health hazard for the general population. Concerning effects on environmental organisms the report cites evidence that trichlorfon is moderately toxic for fish and birds and moderately to highly toxic for aquatic arthropods, supporting the conclusion that this insecticide should never be sprayed over water bodies or streams.

The remaining sections evaluate data from toxicity studies from several hundred case reports of accidental or intentional human poisoning and from studies of schistosomiasis patients treated with metrifonate. Though poisoning may have serious effects, including delayed neurotoxicity, the report concludes that when good work practices and safety precautions are followed trichlorfon is unlikely to present a hazard for occupationally exposed workers the report further notes that in the millions of schistosomiasis patients treated with metrifonate, reported side effects have been minimal and rare.

**Reference:** Environmental Health Criteria No. 132, 1992, 162p, ISBN 9241571322.

## 1,1,1-Trichloroethane

Evaluates the risks to human health and the environment posed by 1,1,1-Trichloroethane a chlorinated hydrocarbon widely used in the cleaning and degreasing of metal and as a solvent in many industrial and consumer products. The abuse of this solvent has resulted in a large number of fatalities.

A review of data on the environmental behaviour of 1,1,1-Trichloroethane documents its ubiquitous presence in the atmosphere, its rapid transport to the troposphere, its long residence time. Its depletion of ozone and its contribution to global warming. Leaching into persistent contamination has been documented, while contamination of the atmosphere is judged to be the most important route of exposure for the general population, the report notes that indoor air may cause considerably higher exposures due to the use of numerous consumer products containing this solvent. Air is also noted to be the main source of exposure at the workplace.

An evaluation of effects on humans draws upon studies of occupationally exposed workers and cases of fatal exposure following accidents and intentional abuse. Both acute and long term inhalation exposures are noted to ranging from slight behavioural changes to unconsciousness. Exposure may also cause damage to the heart and liver. A review of accidentally at the workspace underscores the especially dangerous conditions in poorly ventilated area and confined spaces, such as tanks and vaults, caused by the compound's greater density than air. The final selection evaluates effects on organisms in the field. Concluding that environmental contamination is unlikely to pose a significant hazard for environmental organisms. Because of its many other hazards, including its ozone-depleting potential the report recommend that the release of 1,1,1-Trichloroethane be reduced to the greatest extent possible.

**Reference:** Environmental Health Criteria No. 136, 1992, 117p, ISBN 9241571365.

## Tricresyl Phosphate

Evaluates risks to human health and the environment posed by the production and use of Tricresyl Phosphate. Tricresyl Phosphate is used in industry as a plasticizer in vinyl plastic manufacture, as a flame retardant, as a solvent for nitro-cellulose, in cellulosic moulding composition and in the manufacture of fire resistant hydraulic fluids and lubricants.

Because of the physico-chemical properties of tricresyl-o -phosphate and its rapid biodegradation, the report concludes that use of compound does not threaten the environment though there is some evidence that crop plants can be affected by tri-o-cresyl phosphate released from plastic coverings. A section devoted to kinetics and metabolism concentrates on mechanisms of absorption, distribution, metabolism and delimitation that can help explain the well documented neuropathies actions of tricresyl phosphate and most notably its highly toxic isomer, tri-o-cresyl phosphate.

The most extensive section assesses findings from toxicity studies, emphasising the large number of studies documenting neurotoxic effects, often at very low doses. These effects are further characterised through a review of the numerous reported cases of large scale human poisoning following the ingestion of accidentally or deliberately contaminated medicine and foods stuffs. Readers are given detailed information on the clinical symptom of poisoning the characteristics of delayed neuropathy, long term prognosis and advice on the first aid treatment of victims. While the concluding section notes that use of tricresyl phosphate poses very little risk to either the environment or the general population, the report underscores the severity and long duration of the neuropathology caused by accidental poisoning noting that some victims never recover,

**Reference:** Environmental Health Criteria No.110, 1990, 122p, ISBN 9241571101.

## Tri-n-butyl phosphate

Evaluates risks to human health and the environment posed by the production and use of tri-n-butyl-phosphate. Tri-n-butyl-o -phosphate is widely used world wise as a solvent for cellulose esters, lacquers and natural gums as a primary plasticizer in the manufacture of plastics and vinyl resins in the formulation of fire resistant aircraft hydraulic fluids and as an antifoaming agent, mainly in paper manufacturing plants.

Although tri-n-butyl phosphate has been widely detected in air, water, sediment and biological tissues, the review notes that concentration is usually very low. Workers involving in air craft maintenance and exposed during the manipulation of hydraulic fluids are regarded as the largest occupational group at risk. In view of several weaknesses in available experimental data, the report was unable to reach firm conclusions concerning the risks posed by tri-n-butyl phosphate as a potential carcinogen, neurotoxic agent or dermal sensitise through a neurotoxic effect comparable to organophosphate induced delayed neuropathy was judged unlikely. The report concludes that the production and use of tri-n-butyl

phosphate pose a low risk for the environment and for the general postulations and that are likelihood of long term effects in occupationally exposed workers is small.

**Reference:** Environmental Health Criteria No. 112, 1991, 80p, ISBN 9241571128.

## Triphenyl phosphate

Evaluates risks to human health and the environment posed by the production and use of Triphenyl phosphate, a compound widely used as flame retardant in phenolic and phenylene oxide based resins for the manufacture of electrical and automobile components. Triphenyl phosphate is also used as a non-flammable plasticizer in cellulose acetate for photographic films and as a components of hydraulic fluids and lubricant oils.

Main sources of release in to the environment are identified as leakage or spills of hydraulic fluid, leaching from plastic and manufacturing processes. A review of data on effect on organism, in the environment concentrates on risks to the aquatic environment, concluding that triphenyl phosphate is the most acutely toxic of the various triarylophosphates to fish, shrimp and daphnia's. The remaining section evaluate toxic effects as determined through studies in experimental models and observation in humans. The book notes that triphenyl phosphate exhibits low toxicity in short term studies is not mutagenic and has not been shown in several well designed studies to cause delayed neurophathy or other neurotoxic changes. Studies of exposed workers found no evidence of neurological diseases or other abnormalities. Risk to the environment are likewise judged to be low, though spills of hydraulic fluid could result in fish kills.

**Reference:** Environmental Health Criteria No. 111, 1991, 80p, ISBN 924157111X.

## Tris (2,3-dibromopropyl)phosphate and Bis (2,3 dibromopropyl) phosphate

Evaluates the risks to human health and the environment posed by tris (2,3 dibromopropyl) phosphate (TBPP) a flame retardant with former, widespread use children, sleep wear. In 1977, concern that TBPP might be a human carcinogenic led the USA ban children's clothing treated with this compound. Several other countries have also banned the use of there restricted its use in other consumer products. Although available data indicate that TBPP is no longer produced for use in textiles, an evaluation of health and environmental hazardous was judged important in view of additional commercial applications, including the use of TBPP in polymers.

A discussion of production and uses concentrators on previous applications as a flame retardant for tricacetate and polyester fabrics. Release to the environment is noted to occur during the wearing or laundering of treated garments from textile finishing plants and following the disposal of solid wastes containing TBPP. Children wearing treated sleepwear are identified as the main group in the general population exposed to TBPP. In humans. TBPP applied to the surface of fabrics can be extracted by saliva. Absorption through human skin also was shown to occur.

Several studies in experimental animals have detected toxic effects on the kidney and liver and produced evidence that TBPP is teratogenic, mutagenic, genotoxic and carcinogenic in rats and mice. On the basis of these TBPP should no longer be used commercially. The report also assesses available data on bis (2,3-dibromopropyl) phosphate, a major breakdown product of TBPP which is no longer produced for commercial use. Data were judged inadequate for evaluation.

**Reference:** Environmental Health Criteria No. 173, 1995, 129p, ISBN 924157173X.



## Vinylidene chloride

Evaluates the environment hazards and risks to human health posed by the production and use of vinylidene chloride. Vinylidene chloride. Vinyl chloride copolymers are used for the packaging of foods, as metal coating in storage tanks, building structures and tapes and as moulded filters, valves and pipe fittings. Food packaging applications include both commercial packaging films and household wrap.

The most extensive section evaluate the design and findings of studies in experimental animals and in vitro test systems, attempting to link exposure to specific health hazards. Research including studies of possible carcinogenic and mutagenic effects indicates that the main health hazards associated with exposure are irritation of the skin and eye and depressed functions of the central nervous system. The report concludes that the general population is exposed to very low level of this chemical that risks associated with long term occupational exposure warrant special precautions and that an evaluation of carcinogenic risk to humans must await further epidemiological studies. The release of vinylidene chloride in to the atmosphere is not considered likely to contribute to the depletion of the stratospheric ozone layer.

**Reference:** Environmental Health Criteria No. 100, 1990, 187p, ISBN 9241543000.

## White spirit (Stoddard solvent)

Evaluates the risks to human health and the environment posed by exposure to white spirit a petrochemical solvent widely used in paints and varnishes, in cleaning products and as a degreasing and extraction solvent. These wide spread uses represent a correspondingly large potential for exposure of the general population, professional painters and workers in dry cleaning plants and other settings where white spirit is used. The report cites inhalation of vapours as the primary route of human exposure. Exposure of the general population is noted to occur during the domestic use of paints and lacquers habitation in recently painted rooms and during the washing of vehicles with products containing white spirit.

The most extensive section evaluate the large body of data from laboratory experiments and epidemiological studies in human. In humans signs of toxicity, identified in epidemiological studies of exposed workers include central nervous system effects ranging from dizziness and headache to impaired performance of neuropsychological tests. In sever cases of chronic toxic encephalopathy has been diagnosed. In its evaluation of effects on human health the report gives particular attention to findings from several epidemiological studies of cancer in potentially exposed painters metal machinists, construction workers and dry cleaners. Though increased relative risks for cancers of the lung kidney and prostate and for Hodgkin's lymphoma have been reported, the report concludes that inadequacies in the design of these studies preclude the establishment of a causal relationship between exposure to white spirit and an increased risk of cancer in human.

**Reference:** Environmental Health Criteria No. 187, 1996, 186p, ISBN 924157187X.

## Xylenes

Evaluates the risks to human health and the environment posed by exposure to xylene and its three isomeric forms, ortho, meta and para Xylene is an aromatic hydrocarbon blended in to petrol and used in variety of solvent application mainly in the paint and printing industries.

The opening section on sources of exposure and behaviour in the environment, note that most xylene present in the environment results from its use as solvent and its presence in motor vehicle exhaust. The majority of environmental xylene enters the atmosphere directly where it is readily degraded via photooxidation. The report cites evidence that xylene is rapidly biodegraded in soil and water, through o-

xylene is more persistent in soil than the other isomers. Limited evidence suggest low bioaccumulation by fish and invertebrates and low to moderate toxicity, supporting the conclusion that xylene is unlikely to endanger aquatic ecosystems except under the higher exposure conditions found in the vicinity of industrial discharges of following accidental spills.

A section on environmental levels and human exposure summarises data on concentrations detected in various environmental media. In door, air, near point source sand in occupational setting where workers are exposed. Data on levels in food were judged inadequate for evaluation, Inhalation was determined to be the most important route of human exposure. Concerning kinetics and metabolism in laboratory animals and humans. The report cites abundant evidence that xylene is rapidly and efficiently metabolised with more than 90% biotransformed to methylpuric acid and excreted in urine.

In view of numerous studies conducted in laboratory animal sand in vitro test system cites evidence of chronic effects on the central nervous system following exposure at moderate concentration. These findings support the limited data available on humans, where studies suggest that exposure to xylene may have an acute impairing effect on the sensory motor and information processing, functions of the central nervous system. The report found no evidence that xylene is mutagenic or carcinogenic.  
Reference: Environmental Health Criteria No.190,1997,xiv,147p,ISBN 924157190X

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