5. Evaluation – Aflatoxins

There is *sufficient evidence* in humans for the carcinogenicity of aflatoxins. Aflatoxins cause cancer of the liver (hepatocellular carcinoma).

There is *sufficient evidence* in experimental animals for the carcinogenicity of naturally occurring mixtures of aflatoxins, aflatoxin B1, G1, and M1. Aflatoxin B1 increases the incidence of liver cancer in rats, tree shrews, trouts, and mice. Aflatoxins G1 and M1 increase the incidence of liver cancer in rats.

There is strong evidence that the carcinogenicity of aflatoxins operates by a genotoxic mechanism of action that involves metabolic activation to a genotoxic epoxide metabolite, formation of DNA adducts, and modification of the *TP53* gene. In human hepatocellular carcinomas from areas of high exposure to aflatoxins, up to 50% of tumours have been shown to harbour a specific point mutation in the *TP53* tumour suppressor gene.

Overall Evaluation

Aflatoxins are *carcinogenic to humans (Group 1).*

5. Evaluation – 4-Aminobiphenyl

There is *sufficient evidence* in humans for the carcinogenicity of 4-aminobiphenyl. 4-Aminobiphenyl causes cancer of the urinary bladder.

There is *sufficient evidence* in experimental animals for the carcinogenicity of 4-aminobiphenyl. 4-Aminobiphenyl causes a significant increase in the incidence of malignant bladder tumours in dogs and mice, and of angiosarcomas (all sites) and liver tumours in mice.

There is strong mechanistic evidence indicating that the carcinogenicity of 4-aminobiphenyl in humans operates by a genotoxic mechanism that involves metabolic activation, formation of DNA adducts, and induction of mutagenic and clastogenic effects. Metabolic activation to DNA-reactive intermediates occurs by multiple pathways including *N*-oxidation in the liver, *O*-acetylation in the bladder, and peroxidative activation in the mammary gland and other organs.

Overall Evaluation

4-Aminobiphenyl is *carcinogenic to humans (Group 1).*

5. Evaluation – Benzene

There is *sufficient evidence* in humans for the carcinogenicity of benzene. Benzene causes acute myeloid leukaemia/acute non-lymphocytic leukaemia.

There is *limited evidence* in humans for a causal association of benzene with acute lymphocytic leukaemia.

There is *limited evidence* in humans for a causal association of benzene with chronic lymphocytic leukaemia.

There is *limited evidence* in humans for a causal association of benzene with multiple myeloma.

There is *limited evidence* in humans for a causal association of benzene with non-Hodgkin lymphoma.

There is *sufficient evidence* in experimental animals for the carcinogenicity of benzene. In mice, benzene causes tumours of the Zymbal gland, Harderian gland, lung, forestomach, liver, ovary, mammary gland, preputial gland, and of the haematopoietic system. In rats, benzene causes tumours of the oral cavity, Zymbal gland, forestomach, liver, and skin.

There is strong evidence that benzene metabolites, acting alone or in concert, produce multiple genotoxic effects at the level of the pluripotential haematopoietic stem cell resulting in chromosomal changes in humans consistent with those seen in haematopoietic cancer. Over more than three decades, in multiple studies, in different workforces in many countries a variety of genotoxic changes, including chromosomal abnormalities, have been found in the lymphocytes of workers exposed to benzene.

Overall Evaluation

Benzene is *carcinogenic to humans (Group 1)*.

5. Evaluation – Benzidine

There is *sufficient evidence* in humans for the carcinogenicity of benzidine. Benzidine causes cancer of the urinary bladder.

There is *sufficient evidence* in experimental animals for the carcinogenicity of benzidine. Benzidine causes malignant liver tumours in mice and mammary-gland tumours in female rats.

There is strong mechanistic evidence indicating that the carcinogenicity of benzidine in humans operates by a genotoxic mechanism that involves metabolic activation, formation of DNA adducts, and induction of mutagenic and clastogenic effects. Metabolic activation to DNA-reactive intermediates occurs by multiple pathways including *N*-oxidation in the liver, *O*-acetylation in the bladder, and peroxidative activation in the mammary gland and other organs.

Overall Evaluation

Benzidine is *carcinogenic to humans (Group 1).*

5. Evaluation – Dyes metabolized to benzidine

There is *inadequate evidence* in humans for the carcinogenicity of dyes metabolized to benzidine.

There is *sufficient evidence* in experimental animals for the carcinogenicity of Direct Black 38 and Direct Blue 6. Direct Black 38 causes malignant liver tumours in rats. Direct Blue 6 causes malignant liver tumours in rats.

There is *sufficient evidence* in experimental animals for the carcinogenicity of dyes metabolized to benzidine.

There is strong mechanistic evidence indicating that benzidine-based dyes are converted by azoreduction to benzidine in humans and experimental animals and consequently produce DNA adducts and genotoxic effects similar to those of benzidine.

Overall Evaluation

Dyes metabolized to benzidine are *carcinogenic to humans (Group 1).*

In making the overall evaluation, the Working Group considered there is *sufficient evidence* in humans and in experimental animals for the carcinogenicity of benzidine, and the metabolism of benzidine-based dyes results in the release of free benzidine and the induction of chromosomal aberrations in humans, and in all experimental animal species studied.

5. Evaluation – BCME-CMME

There is *sufficient evidence* in humans for the carcinogenicity of bis(chloromethyl)ether and chloromethyl methyl ether (technical grade). Bis(chloromethyl)ether and chloromethyl methyl ether (technical grade) cause cancer of the lung.

There is *sufficient evidence* in experimental animals for the carcinogenicity of bis(chloromethyl)ether. In rats, bis(chloromethyl)ether causes tumours of the lung, nasal cavity, and skin. In mice, bis(chloromethyl)ether causes tumours of the lung, and skin.

There is *limited evidence* in experimental animals for the carcinogenicity of chloromethyl methyl ether.

There is moderate to strong evidence that bis(chloromethyl)ether and chloromethyl methyl ether, powerful alkylating agents, operate by a genotoxic mechanism. This mechanism is likely similar to that of other strong alkylating agents, involving modification of DNA and resultant mutations.

Overall Evaluation

Bis(chloromethyl)ether and chloromethyl methyl ether (technical grade) are *carcinogenic to humans (Group 1).*

5. Evaluation – 1,3-Butadiene

There is *sufficient evidence* in humans for the carcinogenicity of 1,3-butadiene. 1,3-Butadiene causes cancer of the haematolymphatic organs.

There is *sufficient evidence* in experimental animals for the carcinogenicity of 1,3-butadiene. In mice, 1,3-butadiene causes tumours of the haematopoietic system (lymphoma and histiocytic sarcoma), heart (haemangiosarcoma), lung, forestomach, Harderian gland, preputial gland, liver, mammary gland, ovary, and skin.

There is *sufficient evidence* in experimental animals for the carcinogenicity of D,L-diepoxybutane. D,L-Diepoxybutane causes skin tumours in rats.

There is strong evidence that the carcinogenicity of 1,3-butadiene in humans operates by a genotoxic mechanism that involves formation of reactive epoxides, interaction of these direct-acting mutagenic epoxides with DNA, and resultant mutagenicity. The metabolic pathways for 1,3-butadiene metabolism in experimental animals have also been shown in humans.

Overall Evaluation

1,3-Butadiene is *carcinogenic to humans (Group 1).*

5. Evaluation – Ethylene Oxide

There is *limited evidence* in humans for a causal association of ethylene oxide with lymphatic and haematopoietic cancers (specifically lymphoid tumours, ie, non-Hodgkin lymphoma, multiple myeloma and chronic lymphocytic lymphoma), and breast cancer.

There is *sufficient evidence* in experimental animals for the carcinogenicity of ethylene oxide. In rats, ethylene oxide increased the incidence of brain tumours (gliomas), peritoneal mesothelioma and mononuclear cell leukaemia. In mice, ethylene oxide increased the incidence of lung tumours (alveolar/bronchiolar adenoma and carcinoma), Harderian gland tumours (mainly cystadenoma), and mammary gland tumours (carcinoma).

There is strong evidence that the carcinogenicity of ethylene oxide, a direct acting alkylating agent, operates by a genotoxic mechanism. The direct reaction of ethylene oxide with DNA induces a dose-related increase in the frequency of ethylene oxide-derived haemoglobin adducts in exposed humans and rodents, induces a dose-related increase in the frequency of ethylene oxide-derived DNA adducts in exposed rodents, consistently acts as a mutagen and clastogen at all phylogenetic levels, induces heritable translocations in the germ cells of exposed rodents, and induces a dose-related increase in the frequency of sister chromatid exchange, chromosomal aberrations and micronucleus formation in the lymphocytes of exposed workers.

Overall Evaluation

Ethylene oxide is *carcinogenic to humans (Group 1).*

In making the overall evaluation, the Working Group considered that there is *sufficient*

evidence in experimental animals, and relied heavily on the compelling data on the genotoxic mechanism described above.

5. Evaluation – Formaldehyde

There is *sufficient evidence* in humans for the carcinogenicity of formaldehyde. Formaldehyde causes cancer of the nasopharynx.

There is *sufficient evidence* in humans for a causal association of formaldehyde with leukaemia.

There is *limited evidence* in humans for a causal association of formaldehyde with sinonasal cancer.

There is *sufficient evidence* in experimental animals for the carcinogenicity of formaldehyde. Formaldehyde causes nasal cavity tumours in rats.

The Working Group was almost evenly split on the evaluation of formaldehyde causing leukaemias in humans, with the majority viewing the evidence as *sufficient* for carcinogenicity and the minority viewing the evidence as *limited*. Particularly relevant to the discussions regarding sufficient evidence was a recent study accepted for publication which, for the first time, reported aneuploidy in blood of exposed workers characteristic of myeloid leukaemia and myelodysplastic syndromes with supporting information suggesting a decrease in the major circulating blood cell types and in circulating haematological precursor cells. The authors and Working Group felt this study needed to be replicated.

Overall Evaluation

Formaldehyde is *carcinogenic to humans (Group 1).*

5. Evaluation – MOCA

There is *inadequate evidence* in humans for the carcinogenicity of 4,4′-methylenebis(2-chloroaniline).

There is *sufficient evidence* in experimental animals for the carcinogenicity of 4,4′-methylenebis(2-chloroaniline). 4,4′-Methylenebis(2-chloroaniline) causes an increase in the incidences of malignant tumours in the lung, liver and mammary gland in rats.

There is strong mechanistic evidence indicating that the carcinogenicity of 4,4'-methylene-bis-(2-chloroaniline) involves a genotoxic mechanism that includes metabolic activation, formation of DNA adducts, and induction of mutagenic and clastogenic effects in humans. Metabolic activation to DNA-reactive intermediates occurs by multiple pathways including *N*-oxidation in the liver, *O*-acetylation in the bladder, and peroxidative activation in the mammary gland and other organs.

Overall Evaluation

4,4′-methylenebis(2-chloroaniline) is *carcinogenic to humans (Group 1).*

In making the overall evaluation, the Working Group considered that the genotoxicity of 4,4′-methylenebis(2-chloroaniline) is well documented and its toxicological profile is similar to that of *o*-toluidine, thus indicating a common mode of action. 4,4′-Methylenebis(2-chloroaniline) has been shown to interact with DNA to form adducts in urothelial cells, and with haemoglobin to form adducts in the blood of exposed workers. It has also been shown to cause the formation of sister chromatid exchange and micronuclei in urothelial cells and lymphocytes of exposed humans.

5. Evaluation – Mustard Gas

There is *sufficient evidence* in humans for the carcinogenicity of mustard gas. Mustard gas causes cancer of the lung.

There is *limited evidence* in humans for a causal association of mustard gas with cancer of the larynx.

There is *limited evidence* in experimental animals for the carcinogenicity of mustard gas.

There is strong evidence that the carcinogenicity of mustard gas operates by a genotoxic mechanism that involves DNA alkylation leading to crosslink formation, inhibition of DNA synthesis and repair, point mutations, and chromosome and chromatid aberration formation.

Overall Evaluation

Mustard gas is *carcinogenic to humans (Group 1).*

5. Evaluation – 2-Naphthylamine

There is *sufficient evidence* in humans for the carcinogenicity of 2-naphthylamine. 2-Naphthylamine causes cancer of the urinary bladder.

There is *sufficient evidence* in experimental animals for the carcinogenicity of 2-naphthylamine. 2-Naphthylamine causes malignant bladder tumours in rats, dogs and rhesus monkeys, and liver tumours in mice.

There is strong mechanistic evidence indicating that the carcinogenicity of 2-naphthylamine operates by a genotoxic mechanism that involves metabolic activation, formation of DNA adducts, and induction of mutagenic and clastogenic effects. Metabolic activation to DNA-reactive intermediates occurs by multiple pathways including *N*-oxidation in the liver, *O*-acetylation in the bladder, and peroxidative activation in the mammary gland and other organs.

Overall Evaluation

2-Naphthylamine is *carcinogenic to humans (Group 1).*

5. Evaluation – Dioxins

There is *sufficient evidence* in humans for the carcinogenicity of 2,3,7,8-TCDD. The strongest evidence in humans for the carcinogenicity of 2,3,7,8-TCDD is for all cancers combined.

There is *limited evidence* in humans for a causal association of 2,3,7,8-TCDD with soft-tissue sarcoma, non-Hodgkin lymphoma, and cancer of the lung.

There is *sufficient evidence* in experimental animals for the carcinogenicity of 2,3,7,8-TCDD. In rats, 2,3,7,8-TCDD causes malignant tumours of the liver (cholangiocarcinoma and hepatocellular carcinoma), lung, and oral cavity. In mice, 2,3,7,8-TCDD causes malignant tumours of the skin, liver, and haematopoietic system (lymphoma).

There is strong evidence to support a receptor-mediated mechanism for 2,3,7,8-TCDD carcinogenesis in humans where the primary mechanism is the promotion of carcinogenesis through the modification of cellular replication and apoptosis with a secondary mechanism related to increases of oxidative stress causing DNA damage. The conservation of the AhR and the related signalling pathways and responses across species, including humans, adds additional strength that this mechanism is active in humans.

Overall Evaluation

2,3,7,8-TCDD is *carcinogenic to humans (Group 1).*

2,3,4,7,8-PeCDF is *carcinogenic to humans (Group 1).*

PCB 126 is *carcinogenic to humans (Group 1).*

In making the second and third evaluations, the Working Group considered the following mechanistic arguments:

There is strong evidence to support a receptor-mediated mechanism for 2,3,4,7,8-PeCDF and PCB 126 carcinogenesis in humans based upon evidence of carcinogenicity in experimental animals and upon extensive evidence showing activity identical to 2,3,7,8-TCDD for every step of the mechanism described for 2,3,7,8-TCDD carcinogenesis in humans including receptor binding, gene expression, protein activity changes, cellular replication, oxidative stress, promotion in initiation-promotion studies and complete carcinogenesis in laboratory animals.

5. Evaluation – *o*-Toluidine

There is *sufficient evidence* in humans for the carcinogenicity of *o*-toluidine. *o*-Toluidine causes cancer of the urinary bladder.

There is *sufficient evidence* in experimental animals for the carcinogenicity of *o*-toluidine. In mice, *o*-toluidine causes an increase in the incidences of haemangiosarcomas and haemangiomas. In rats, it increases the incidence of malignant tumours of the skin (subcutaneous fibromas and fibrosarcomas), the mammary gland (fibroadenomas and adenomas), the urinary bladder, and of the spleen.

There is moderate mechanistic evidence indicating that the carcinogenicity of *o*-toluidine involves metabolic activation, formation of DNA adducts, and induction of DNA damaging effects.

Overall Evaluation

o-Toluidine is *carcinogenic to humans (Group 1).*

5. Evaluation – Vinyl Chloride

There is *sufficient evidence* in humans for the carcinogenicity of vinyl chloride. Vinyl chloride causes angiosarcoma of the liver, and hepatocellular carcinoma.

There is *sufficient evidence* in experimental animals for the carcinogenicity of vinyl chloride. Vinyl chloride increases the incidence of hepatic and extra-hepatic angiosarcomas in mice and rats. Vinyl chloride increases the incidence of hepatocellular carcinomas and Zymbal gland carcinomas in rats. Vinyl chloride increases the incidence of lung carcinomas, and the incidence of mammary carcinomas in mice.

There is *sufficient evidence* in experimental animals for the carcinogenicity of chloroethylene oxide.

There is strong evidence that the carcinogenicity of vinyl chloride operates by a genotoxic mechanism that involves metabolic activation to reactive metabolites, binding of the metabolites to DNA, promutagenic action of these adducts leading to mutations on proto-oncogenes and tumour-suppressor genes. Many of these key events that have been demonstrated in experimental animals have also been demonstrated in humans.

Overall Evaluation

Vinyl chloride is *carcinogenic to humans (Group 1).*

5. Evaluation – Benzo[*a*]pyrene

[No epidemiological data on benzo[*a*]pyrene alone were available to the Working Group.]

There is *sufficient evidence* in experimental animals for the carcinogenicity of benzo[*a*]pyrene. In mice, benzo[*a*]pyrene causes lymphomas, sarcomas (at injection site) and tumours in the lung, respiratory tract, gastrointestinal tract, oesophagus, forestomach, liver, and skin. In rats, benzo[*a*]pyrene causes sarcomas (at injection site), and tumours in the lung respiratory tract, gastrointestinal tract, oesophagus, and mammary gland. In hamsters, benzo[*a*]pyrene causes sarcomas (at injection site) and tumours in the lung, nose, larynx, trachea, pharynx, oesophagus, stomach, and forestomach.

The genotoxic mechanism of action of benzo[*a*]pyrene involves its metabolism to highly reactive species that form covalent adducts to DNA. These *anti*-benzo[*a*]pyrene-7,8-diol-9,10-oxide-DNA adducts induce mutations in the *K-ras* tumour oncogene and the *TP53* tumour suppressor gene in both human and mouse lung tumours. Benzo[*a*]pyrene and benzo[*a*]pyrene-containing complex mixture exposures also induce other genotoxic effects, including sister chromatid exchanges, micronuclei, DNA damage and 8-oxodeoxyguanosine formation, all which can contribute to the carcinogenic effects of benzo[*a*]pyrene and benzo[*a*]pyrene-containing complex mixtures in exposed humans.

Overall Evaluation

Benzo[*a*]pyrene is *carcinogenic to humans (Group 1)*.

In making the overall evaluation, the Working Group took into consideration the following:

The strong and extensive experimental evidence for the carcinogenicity of benzo[*a*]pyrene in many species supported by the consistent and coherent mechanistic evidence from experimental and human studies provide biological plausibility to support the overall classification of benzo[*a*]pyrene as *carcinogenic to humans (Group 1).*

5. Evaluation – Soot, as found in occupational exposure of chimney-sweeps

There is *sufficient evidence* in humans for the carcinogenicity of soot as found in occupational exposure of chimney-sweeps. Soot, as found in occupational exposure of chimney-sweeps, causes cancer of the skin (observed in the scrotum), and of the lung.

There is *limited evidence* in humans for a causal association of soot as found in occupational exposure of chimney sweeps with cancer of the bladder.

There is *inadequate* evidence in experimental animals for the carcinogenicity of soot.

There is *sufficient* evidence in experimental animals for the carcinogenicity of soot extracts. Soot extracts cause malignant tumours of the skin in mice.

Extracts of soot contain carcinogenic polycyclic aromatic hydrocarbons, are genotoxic, and based on limited numbers of human genotoxicity studies there is moderate evidence for a genotoxic mechanism for occupational exposures as a chimney-sweep. The detection of anti-benzo[*a*]pyrene-7,8-diol-9,10-epoxide-DNA adducts in the peripheral blood lymphocytes of exposed populations suggest the participation of benzo-[*a*]pyrene in the genotoxic mode of action of this exposure in humans.

Overall Evaluation

Soot, as found in occupational exposure of chimney-sweeps, is *carcinogenic to humans (Group 1).*

5. Evaluation – Coal Gasification

There is *sufficient evidence* in humans for the carcinogenicity of coal gasification. Coal gasification causes cancer of the lung.

There is *sufficient evidence* in experimental animals for the carcinogenicity of coal tars from gas works and manufactured gas plant residues. Coal tars from manufactured gas plants cause tumours of the skin, liver, and lung in mice.

There is strong evidence for a genotoxic mechanism for coal gasification samples based on experimental studies. Although there are no human studies, it is highly likely that genotoxicity is a mechanism for exposures to coal gasification, predominantly due to the presence of mutagenic PAHs.

Overall Evaluation

Coal gasification is *carcinogenic to humans (Group 1).*

5. Evaluation – Coal-tar Distillation

There is *sufficient evidence* in humans for the carcinogenicity of occupational exposure during coal-tar distillation. Occupational exposure during coal-tar distillation causes cancer of the skin (including but not limited to cancer of the scrotum).

There is *sufficient evidence* in experimental animals for the carcinogenicity of coal tars. Coal tars cause skin tumours in mice.

Studies in experimental systems and in tissues of humans provide strong evidence for a genotoxic mechanism for occupational exposures during coal-tar distillation in humans. The detection of *anti*-benzo[*a*]pyrene-7,8-diol-9,10-epoxide-DNA adducts in the peripheral blood lymphocytes of exposed populations suggest the participation of benzo[*a*]pyrene in the genotoxic mechanism of this exposure in humans.

Overall Evaluation

Occupational exposures during coal-tar distillation are *carcinogenic to humans (Group 1).*

5. Evaluation – Coke Production

There is *sufficient evidence* in humans for the carcinogenicity of coke production. Coke production causes cancer of the lung.

There is *sufficient* evidence in experimental animals for the carcinogenicity of samples of tar taken from coke ovens. Tar from coke ovens causes malignant tumours of the skin and lung in mice.

There is strong evidence for a genotoxic mechanism for occupational exposures during coke oven production based on both experimental and human studies. The detection of anti-benzo[a]pyrene-7,8-diol-9,10-epoxide-DNA adducts in the peripheral blood lymphocytes in exposed populations suggests the participation of benzo[*a*]pyrene in the genotoxic mechanism for this exposure in humans.

Overall Evaluation

Coke production is *carcinogenic to humans (Group 1).*

5. Evaluation – Coal-tar pitch

There is *sufficient evidence* in humans for the carcinogenicity of coal-tar pitch as encountered in paving and roofing. Coal-tar pitch as encountered in paving and roofing causes cancer of the lung.

There is *limited evidence* in humans for a causal association of coal-tar pitch as encountered in paving and roofing and cancer of the bladder.

There is *sufficient evidence* in experimental animals for the carcinogenicity of coal-tar pitch. Coal-tar pitch and extracts of coal-tar pitch cause skin tumours in mice.

There is strong evidence from experimental data that coal tar pitch has a genotoxic mechanism of action. There is moderate evidence in humans for a genotoxic mechanism for occupational exposures during roofing and paving with coal tar pitch, based on one study.

Overall Evaluation

Coal-tar pitch is *carcinogenic to humans (Group 1).*

5. Evaluation – Mineral oils

There is *sufficient evidence* in humans for the carcinogenicity of untreated or mildly treated mineral oils. Untreated or mildly treated mineral oils cause cancer of the skin (observed in the scrotum).

There is *sufficient evidence* in experimental animals for the carcinogenicity of untreated vacuum distillates, acid-treated oils, and aromatic oils, including extracts from solvent treatment of distillates and the high-boiling fraction of catalytically cracked oils [classes 1, 2 and 6]. These increase the incidence of malignant skin tumours in mice.

There is *sufficient evidence* in experimental animals for the carcinogenicity of mildly hydrotreated oils [class 4]. Mildly hydrotreated oils [class 4] increase the incidence of malignant skin tumours in mice.

There is *sufficient evidence* in experimental animals for the carcinogenicity of used gasoline-engine oil [class 7.2]. Used gasoline-engine oil increases the incidence of malignant skin tumours in mice.

There is weak evidence on the mechanism of action of mineral oil exposures in humans. This evidence is based on genotoxic activity of mineral oils in bacteria and a single cytogenetic study of glassworkers exposed to aerosols of mineral oils.

Overall Evaluation

Untreated or mildly treated mineral oils are *carcinogenic to humans (Group 1).*

5. Evaluation – Shale oils

There is *sufficient evidence* in humans for the carcinogenicity of shale oils. Shale oils cause cancer of the skin (observed in the scrotum).

There is *sufficient evidence* in experimental animals for the carcinogenicity of shale oils. Various types or fractions of shale oils increase the incidence of malignant skin tumours in mice and rabbits, and of lung tumours in mice and rats.

Shale oils are genotoxic in experimental systems. There is weak evidence to determine a mechanism of action of shale oil exposures based on one *in vitro* human study.

Overall Evaluation

Shale oils are *carcinogenic to humans (Group 1).*

5. Evaluation – Aluminium Production

There is *sufficient evidence* in humans for the carcinogenicity of occupational exposures during aluminium production. Occupational exposures during aluminium production cause cancer of the bladder, and of the lung.

There is *sufficient evidence* for the carcinogenicity in experimental animals of airborne particulate polynuclear organic matter from aluminium production plants. [No target organ identified].

Emission samples from aluminium smelters were mutagenic in bacteria. There were mixed reports on the mutagenic activities of urines from exposed workers. DNA adduct studies of aluminium smelter workers also gave mixed results. There is weak to moderate evidence for a genotoxic mechanism based on both experimental and human studies for human exposures in aluminium production.

Overall Evaluation

Occupational exposures during aluminium production are *carcinogenic to humans (Group 1).*

5. Evaluation – Auramine Production

There is *sufficient evidence* in humans for the carcinogenicity of auramine production. Auramine production causes cancer of the urinary bladder.

There is *inadequate evidence* in humans for the carcinogenicity of auramine.

There is *sufficient evidence* in experimental animals for the carcinogenicity of auramine.

There is insufficient mechanistic data relevant to the carcinogenicity of auramine in humans. Magenta induces DNA strand breaks in experimental animals.

Overall Evaluation

Auramine production is *carcinogenic to humans (Group 1).*

Auramine is *possibly carcinogenic to humans (Group 2B).*

5. Evaluation – Occupational exposures during iron and steel founding

There is *sufficient evidence* in humans for the carcinogenicity of occupational exposures during iron and steel founding. Occupational exposures during iron and steel founding cause cancer of the lung.

[No data on the carcinogenicity to experimental animals of complex mixtures found in the iron and steel founding industry were available to the Working Group.]

There is moderate evidence that extracts of particles collected from a steel foundry have a genotoxic mechanism based on bacterial mutation studies. There is weak evidence for a genotoxic mechanism for exposures during iron and steel founding based on DNA adduct studies in humans.

Overall Evaluation

Occupational exposures during iron and steel founding are *carcinogenic to humans (Group 1).*

5. Evaluation – Isopropyl alcohol manufacture by the strong-acid process

There is *sufficient evidence* in humans for the carcinogenicity of isopropyl alcohol manufacture by the strong-acid process. Isopropyl alcohol manufacture by the strong-acid process causes cancer of the nasal cavity.

[No data in experimental animals for the carcinogenicity of isopropyl alcohol manufacture were available to the Working Group.]

While it is plausible that areas of localized low pH from inhalation of inorganic acid mists could damage DNA and increase cancer risks, the evidence supporting DNA damage of any other mechanism as the cause of the observed cancers due to the inorganic acid mists is inadequate.

Overall Evaluation

Isopropyl alcohol manufacture by the strong-acid process is *carcinogenic to humans (Group 1).*

5. Evaluation – Magenta Production

There is *sufficient evidence* for the carcinogenicity of magenta production. Magenta production causes cancer of the urinary bladder.

There is *inadequate evidence* in experimental animals for the carcinogenicity of magenta.

There is *sufficient evidence* in experimental animals for the carcinogenicity of CI Basic Red 9. CI Basic Red 9 causes hepatocellular carcinoma in mice and subcutaneous fibroma, thyroid gland follicular cell adenoma and carcinoma, and Zymbal gland carcinoma in rats.

There is insufficient mechanistic data relevant to the carcinogenicity of magenta in humans or experimental animals.

Overall Evaluation

Magenta production is *carcinogenic to humans (Group 1).*

Magenta is *possibly carcinogenic to humans (Group 2B).*

5. Evaluation – Occupational exposure as a painter

There is *sufficient evidence* in humans for the carcinogenicity of occupational exposure as a painter. Occupational exposure as a painter causes mesothelioma, cancers of the urinary bladder, and lung.

There is *limited evidence* in humans for a causal association of maternal exposure to painting (including preconception and during pregnancy) with childhood leukaemia in the offspring.

No data in experimental animals on occupational exposure as a painter were available to the Working Group.

The multiple genetic and cytogenetic effects observed among workers employed as painters and the information on individual chemicals to which painters are exposed provide strong evidence to support genotoxicity as one mechanism for the observed increased cancer risk. However, due to the complexity and changing nature of the mixtures of exposures and the potential interactions between exposures as painters, other mechanisms are also likely. While it is clear that exposures to some agents as a painter have been reduced over time, recent genotoxicity studies and the exposure to multiple mutagens and carcinogens continue to raise concerns for cancer risks.

Overall Evaluation

Occupational exposure as a painter is *carcinogenic to humans (Group 1).*

5. Evaluation – Occupational exposures in the rubber manufacturing industry

There is *sufficient evidence* in humans for the carcinogenicity of occupational exposures in the rubber manufacturing industry. Occupational exposures in the rubber manufacturing industry cause leukaemia, lymphoma, cancers of the urinary bladder, lung, and stomach.

There is *limited evidence* in humans for a causal association of occupational exposures in the rubber manufacturing industry with cancers of the prostate, oesophagus, and larynx.

No data in experimental animals on the rubber manufacturing industry were available to the Working Group.

The multiple genetic and cytogenetic effects observed among workers employed in the rubber manufacturing industry provide strong evidence to support genotoxicity as one mechanism for the observed increased cancer risks. However, due to the complexity and changing nature of the exposure mixture and the potential interactions between exposures in the rubber manufacturing industry, other mechanisms are also likely. While it is clear that exposures to some agents in the rubber manufacturing industry have been reduced over time, recent cytogenetic studies continue to raise concerns for cancer risks.

Overall Evaluation

Occupational exposures in the rubber manufacturing industry are *carcinogenic to humans (Group 1).*

5. Evaluation – Mists from strong inorganic acids

There is *sufficient evidence* in humans for the carcinogenicity of mists from strong inorganic acids. Mists from strong inorganic acids cause cancer of the larynx.

There is *limited evidence* in humans for a causal association of mists from strong inorganic acids with cancer of the lung.

No data in experimental animals were available to the Working Group.

While it is plausible that areas of localized low pH from inhalation of inorganic acid mists could damage DNA and increase cancer risks, the evidence supporting DNA damage or any other mechanism as the cause of the observed cancers due to the inorganic acid mists is inadequate.

Overall Evaluation

Mists from strong inorganic acids are *carcinogenic to humans (Group 1).*