

5. Summary of Data Reported

5.1 Exposure data

Thousands of chemical compounds are used in paint products as pigments, extenders, binders, solvents, and additives. The main organic solvents used are toluene, xylene, aliphatic compounds, ketones, alcohols, esters, and glycol ethers. Azo pigments that contain 3,3'-dichlorobenzidine are common, although free aromatic amines are not present in significant quantities. Asbestos was used as a filler in paints and decorative coatings until the early 1990s. Several hazardous chemicals including benzene, some other solvents, phthalates (plasticizers), chromium and lead oxides have been reduced or replaced in paint, although they are still used in some countries. The increasing use of water-based paints and powder coatings has promoted this trend. New formulations contain lower-toxicity solvents, neutralizing agents, such as amines, and biocides.

Workers in the painting industry are potentially exposed to the chemicals found in paint products during their application and removal. Exposure to dichloromethane occurs during paint stripping from wood and metal surfaces. Diisocyanate is present in some binders and is released during painting. Silica is used in the preparation of surfaces. Painters may also be exposed to asbestos or crystalline silica as bystanders during construction activities. During the application of paint, workers are exposed primarily to solvents whereas the mechanical removal of paint leads mainly to exposure to pigments and fillers. In the past, exposure to hazardous substances frequently exceeded current occupational exposure limits, but exposure levels have generally decreased over time.

Inhalation is the predominant route of exposure, followed by dermal absorption to a much lesser extent; higher inhalation exposures are frequently accompanied by higher dermal exposures. Appropriate selection and use of personal protective equipment can substantially reduce uptake, although painters do not generally wear respirators or gloves. Biomonitoring of exposure to paint products reveals elevated levels of paint compounds or their metabolites in blood and urine.

5.2 Human carcinogenicity data

Seventeen cohort and linkage studies of painters have shown consistent and significant, although moderate (36%), excesses of mortality from lung cancer. Three of these studies provided information on tobacco smoking which is strongly associated with this neoplasm. These excesses are consistent with case-control studies which largely controlled for smoking. Twenty-nine case-control studies of lung cancer in painters were evaluated. Although the results were heterogeneous, partially due to small numbers in

some studies, overall, a consistent excess risk of lung cancer was observed over time. Of the 29 studies, three had an odds ratio < 1 with large confidence intervals that included the null value, and the others had odds ratios > 1 , 14 of which showed a statistically significant or borderline significant increase. When all independent studies that appropriately adjusted for potential confounders were used in a meta-analysis, a statistically significant excess risk of 35% was obtained. When the analysis and results from the above and from population-based studies were restricted to smoking-adjusted estimates, the statistically significant excess risks were 34% and 41%, respectively.

A borderline significant excess of mortality from mesothelioma was observed in cohort studies and positive results were obtained in two case-control studies of this tumour, which is consistent with the presence of asbestos at some sites where painters work.

The 11 cohort and linkage studies of painters showed consistent, although moderate (21%), excesses of mortality from urinary bladder cancer. Two of these studies provided information on tobacco smoking which is strongly associated with this neoplasm. These excesses are consistent with case-control studies of painters that controlled for smoking in which an excess risk for urinary bladder cancer was seen. Most of the studies that were evaluated had odds ratios > 1 . When all independent studies that appropriately adjusted for confounding were used in a meta-analysis, a statistically significant excess risk of 28% was obtained. When the analysis and results from the above and from population-based studies were restricted to smoking-adjusted estimates, the statistically significant excess risks were 26% and 27%, respectively.

Other statistically significant excesses of mortality were observed in the cohort studies for cancers of the pharynx, oesophagus, and liver. Cancers at these sites are associated with tobacco smoking (pharynx and oesophagus) and alcoholic beverage consumption (pharynx, oesophagus, and liver), both of which have been shown to be increased among painters compared with the national populations typically used as referent groups; hence, these might act as positive confounders. However, there are inadequate supportive data from case-control studies of these cancers that control for these potential confounders to conclude that confounding can be excluded as a cause of these excesses. The data were insufficient for evaluation, but the Working Group noted some consistency between case-control and cohort studies for cancers of the pharynx and oesophagus.

More case-control studies evaluated the risk for lymphatic and haematopoietic cancers among painters than that for cancers at other sites. Although some excesses were observed, the data are inadequate to draw a conclusion because of inconsistency among results from these studies, and the lack of any excess mortality from these cancers in the cohort studies. A few case-control studies of cancers of the nose, nasopharynx, larynx, oesophagus, stomach, pancreas, small bowel, kidney, brain, prostate, ovary and breast, mesothelioma, melanoma, and soft-tissue sarcoma were conducted among painters.

Several case-control studies evaluated the risk for childhood cancer and parental occupation as a painter or parental exposure to paints. Seven studies focused on

leukaemia. Five showed significant excesses associated with occupational or non-occupational exposure to paints, primarily among mothers. Despite this relatively small amount of data, the Working Group considered that there was some evidence that maternal occupational or other exposure to paints is associated with childhood leukaemia. The risks tended to be greater when mothers were exposed before or during pregnancy rather than after birth of the child, and two studies showed some evidence of an exposure–response relationship with duration of exposure.

Overall, a weakness of both the cohort and case–control studies is the lack of information on exposure–response trends, and few studies included analyses by duration of work as a painter.

There is also little information on specific work settings. One cohort, one case–control and one proportionate mortality study of artistic painters all showed excess mortality from urinary bladder cancer. Insufficient information is available to judge whether trends for risk for cancer have decreased over time with the changes in components of paints; for example, the levels of solvents, such as benzene, and pigments, such as lead chromates in paints, have decreased over past years. Data from studies carried out since the previous evaluations of painters still involve primarily painters who were exposed in the 1960s and the 1970s before many changes in paint components had taken effect.

Nevertheless, when the cohort and case–control studies were taken together, the Working Group concluded that there is consistent evidence in humans that occupational exposure as a painter causes lung and urinary bladder cancer. It does not appear that the excess mortality from these cancers is caused by the principal potential confounder, which is tobacco smoking.

No particular agent can be identified from epidemiological studies as the cause of excess of lung and urinary bladder cancer. It is improbable that the presence of asbestos would completely explain the excess of lung cancer; if this had been the case, a more pronounced excess of mesothelioma would have been observed. There is little information from epidemiological studies on the risk associated with the use of paint pigments that are known lung carcinogens, such as chromium or cadmium.

5.3 Animal carcinogenicity data

No data were available to the Working Group.

5.4 Other relevant data

Painters and paint industry workers are exposed to solvents (such as benzene, toluene and dichloromethane), paint pigments (such as lead, cadmium and chromium compounds) and many other compounds. Solvents are absorbed by inhalation and through the skin, and are generally rapidly metabolized and excreted as conjugated metabolites. Metal compounds that are used as paint pigments are predominantly

absorbed in the lung. Dermal absorption is generally low and depends on the chemical properties of the compound, the vehicle, and the integrity of the skin. Absorbed metals are distributed to the organs and, in the case of lead, are concentrated in the bone. Elimination of metals varies from several days to several years.

Overall, six of the eight studies on chromosomal aberrations among painters showed consistent and significant elevated frequencies. Of these six positive studies, three reported an association with years of employment while the other studies did not report analyses on duration of employment. Five of six studies reported significant increases in the frequencies of micronucleus formation among painters. Two of these five studies reported a dose gradient with years or weeks worked and levels of micronuclei. Chromosomal aberrations and micronucleus formation were found in both cultured lymphocytes and buccal cells. Four of seven studies on sister chromatid exchange among painters reported significantly increased frequencies. Exposure–response relationships with duration of employment were reported in three of these four studies. Three of the four studies on DNA single-strand breaks reported increased levels among painters.

Haematological changes were observed in several studies of painters. These included decreased levels of total white blood cells, T-cells and natural killer cells. Furthermore, an increased prevalence of leucopenia, anaemia and granulocytopenia was observed among painters. Immunological changes were also observed among painters in several studies. These effects included specific immunoglobulin (G and E) responses to hexamethylene diisocyanate and increased proliferation of lymphocytes after in-vitro stimulation with hexamethylene diisocyanate.

Most cytogenetic studies among painters that measured a variety of cytogenetic end-points and markers of genotoxicity reported elevated levels of genetic damage. Several of these studies showed a dose-gradient with years or weeks worked and the cytogenetic end-point. Stratified analyses by tobacco smoking status generally showed consistent results among smokers and nonsmokers. These data strongly suggest that occupational exposures in painting lead to increased levels of DNA damage. Furthermore, mechanistic data reviewed by the Agency for Toxic Substances and Disease Registry and in previous evaluations by the IARC Monographs on selected specific chemicals that had been or still are prevalent in exposures encountered by painters indicate strong support for the induction of haematopoietic (benzene, trichloroethylene, 1,3-butadiene), liver (trichloroethylene), and lung (asbestos, cadmium, chromium) cancers.