

Carbon Black Product Safety Studies

CITATION	TITLE (with ABSTRACT LINK)	SUMMARY
Bourdon JA, Saber AT, Jacobsen NR, Williams A, Vogel U, Wallin H, Halappanavar S, Yauk CL. 2013. <i>Cardiovasc Toxicol.</i> 13(4):406-12.	Carbon black nanoparticle intratracheal instillation does not alter cardiac gene expression	This animal study characterized heart gene expression profiles alongside plasma proteins associated with cardiovascular disease in C57BL/6 mice intratracheally instilled with vehicle or 0.162 mg Printex 90 carbon black nanoparticles (CBNPs). The authors reported an absence of changes in cardiac gene expression, but substantive changes in pulmonary and hepatic gene expression and other findings suggesting adverse cardiovascular effects following CBNP exposure.
Scientific Committee on Consumer Safety (SCCS). 2014. SCCS/1539/14, December	SCCS opinion for clarification of the meaning of the term "sprayable applications/products" for the nano forms of carbon black CI 77266, titanium oxide and zinc oxide.	This SCCS Opinion provides some clarifications to the opinion that use of various nanoparticles (ETH50, TiO ₂ , ZnO, Carbon Black) in sprayable formulations is not recommended. Regarding carbon black specifically, it concluded that "SCCS is of the opinion that the animal cancer data are relevant to humans and that the use of nano carbon black in sprayable applications that could lead to exposure of the consumer's lungs to nano carbon black by inhalation is not recommended."
Dell, L; Gallagher, A; Crawford, L; Jones, R; Mundt, K. 2014. <i>Occup. Environ. Med.</i> Jun;71 Suppl 1:A39. doi:10.1136/oemed-2014-102362.121.	0320 Evaluation of cumulative exposure to carbon black and lung cancer risk among US carbon black workers.	This conference abstract (there does not appear to be a full published paper available at this time) reported findings from an epidemiological study evaluating lung cancer mortality in relation to quantitative estimates of cumulative inhalable carbon black exposure among carbon black manufacturing workers. While noting that few lung cancer deaths occurred among the exposure sub-cohort, the study authors concluded that their findings showed no evidence of excess lung cancer mortality or association between lung cancer mortality and time-dependent cumulative inhalable carbon black exposure.
Epstein, M; Emri, I; Hartemann, P; Hoet, P; Leitgeb, N; Martínez, L; Proykova, A; Rizzo, L; Rodriguez-Farré, E; Rushton, L; Rydzynski, K; Samaras, T; Testai, E; Vermeire, T. 2014. <i>SCENIHR.</i> doi:10.2772/41391	Preliminary opinion: Guidance on the determination of potential health effects of nanomaterials used in medical devices.	This guidance document addresses the use of nanomaterials in medical devices and provides information for risk assessors regarding specific aspects that need to be considered in the safety evaluation of nanomaterials. It refers to carbon black as one of the various known forms of carbon that is frequently used in nanomedicine.
European Commission, Scientific Committee on Consumer Safety (SCCS). 2013. SCCS/1515/13. 75p.	Opinion on carbon black (nano-form)	This SCCS report provides an overall safety assessment for the cosmetics ingredient Carbon Black CI 77266 in nano-form. Based on its review of the available evidence, SCCS concluded "that the use of carbon black CI 77266 in its nano-structured form with a size of 20 nm or larger at a concentration up to 10% as a colorant in cosmetic products, is considered to not pose any risk of adverse effects in humans after application on healthy, intact skin." SCCS noted that "This opinion does not apply to applications that might lead to inhalation exposure to carbon black nanoparticles, where the preparation might lead to inhalable particles." This opinion was adopted by SCCS at its 4th plenary meeting on December 12, 2013.
Dell L et al. A Cohort Mortality Study of Employees in the US carbon black industry <i>J Occup Environ</i> 2006; 48: 1219-1229	A cohort mortality study of employees in the U.S. carbon black industry	The world's largest cohort study of mortality risks of carbon black manufacturing includes 5,011 workers at 18 plants in the United States. (2006 and 2014, completed manuscript) In 2006, a lower than expected lung cancer SMR* of 0.85 was observed, based on 127 cases; (95%-CI: 0.71, 1.00). (Dell et al. 2006) An update of this study with ascertainment of vital status through 2011 has recently been completed but not yet published at the time of preparation of this report. (Dec 2014). (Dell et al, 2014 in press) No excess in lung cancer or non-malignant respiratory disease was reported in the updated analysis.
Harber P, Muranko H, Solis S, Torossian A, Merz B. Effect of carbon black exposure on respiratory function and symptoms. <i>J Occup Environ Med.</i> 2003; 45:144 –155.	Effect of carbon black exposure on respiratory function and symptoms.	This study evaluated over 1000 North American carbon black workers to assess relationships between exposure to carbon black and corresponding lung related symptoms and lung function. Results of this study had a major impact on the recently established ACGIH TLV for carbon black. Workers (1175) from 22 North American manufacturing facilities underwent a pulmonary function test and completed a health questionnaire. Analyses showed links between cumulative exposure and small reductions in lung function (FEV1). Recent exposures showed no effect on symptoms or lung function measurements. Results indicated that exposure to carbon black at 1.0 mg/m ³ , over a 40-year career, could result in a 27 ml decrement in FEV1 in addition to normal age related decline of ~ 30 ml per year or 1200 ml.
IARC 2010. IARC Monogr on Eval Carcinog Risks to Humans Volume 93: Carbon black, Titanium Dioxide and Talc. IARC, Lyon, France	Carbon black, Titanium Dioxide and Talc.	

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McCunney, RJ, Valberg P, Muranko H, Morfeld, P "Carbon Black" in Patty's Industrial Hygiene and Toxicology 2012; pp 429-453	"Carbon Black" in Patty's Toxicology 2012	
Ramanakumar AV, Parent ME, Latreille B, Siemiatycki J. Risk of lung cancer following exposure to carbon black, titanium dioxide and talc: results from two case-control studies in Montreal. Int J Cancer. 2008 Jan 1;122(1):183-9.	Risk of lung cancer following exposure to carbon black, titanium dioxide and talc	The relationship between workplace exposure to carbon black and lung cancer risk was examined in a population-based case-control studies in Montreal, Canada Interviews related to jobs and exposures for Study I were conducted in 1979–1986 (857 cases, 533 population controls, 1,349 cancer controls) and interviews for Study II were conducted in 1996–2001 (1,236 cases and 1,512 controls). Detailed lifetime job histories were elicited and a team of hygienists and chemists evaluated the evidence of exposure to a host of occupational substances, including carbon black. Lung cancer risk was analysed in relation to each exposure, adjusting for several potential confounders, including smoking. Subjects with occupational exposure to carbon black did not experience any detectable excess risk of lung cancer.
Crosbie, W.: Respiratory Survey on Carbon Black Workers in the U.K. and the U.S.; Archives of Environmental Health, 41:346-53, 1986.	Respiratory helath of carbon black workers	A major European morbidity study of carbon black workers. Among over 3,000 carbon black workers employed at 19 European plants with a mean work history of over ten years, weak associations were noted between exposure to carbon black (based on job titles) and chronic cough and sputum production. No data were available on dust levels, thus dose-response relationships could not be established. Minor exposure-associated declines in forced vital capacity (FVC) and forced expiratory volume in one second (FEV1) were noted.
Gardiner, K., N. Trethowan, J. Harrington, C. Rossiter, and I. Calvert: Respiratory Health Effects of Carbon Black: A Survey of European Carbon Black Workers; British Journal of Industrial Medicine, 50:1082-1096, 1993.	Respiratory helath effects of carbon black: a survey of European carbon black workers.	A long-term morbidity study was initiated in 1988 and designed to be conducted over a 10-year period with three distinct phases. The study included over 3000 workers at 18 carbon black plants in 7 Western European countries. Among the worker cohort, lung function measurements averaged more than 100% of that predicted for a person's age, height and gender for all categories of exposure, except for cigarette smokers in the highest exposure group (98.3% of the predicted value). When all results were analyzed in aggregate form, however, a small, but statistically significant relationship was noted between exposure to carbon black and decrements in FVC and FEV1. The authors described their findings as "consistent with a non-irritant effect on the airways"
Gardiner, K., van Tongeren, M., and J.M. Harrington: Respiratory Health Effects from Exposure to Carbon Black: Results of the Phase II and III Cross-Sectional Studies in the European Carbon Black Manufacturing Industry. Occupational and Environmental Medicine. 58:496-503. 2001.	Respiratory health effects from exposure to carbon black: results of the phase 2 and 3 cross sectional studies in the European carbon black manufacturing industry	The authors reported that carbon black exerted a significant effect on most respiratory symptoms and lung function, although they acknowledged shortcomings in the symptom data: "respiratory symptom results may have been biased and care should be taken in the interpretation of these results" (Gardiner et al., 2001). Although exposure related decrements in lung function were measured, the percentage of predicted lung function volumes, as noted above, exceeded 100% for FEV1 and FVC, the key parameters for evaluating lung function. These results suggest that conclusions regarding the health implications of carbon black exposure were based on the statistical significance of the results rather than the clinical relevance.
Sorahan, T., L. Hamilton, M. van Tongeren, K. Gardiner, and J. Harrington: A Cohort Mortality Study of U.K. Carbon Black Workers 1951-96; American Journal of Industrial Medicine, 39:158-170, 2001.	A cohort mortality study of U.K. carbon black workers, 1951-1996	The mortality of a cohort of 1,147 male manual workers from five U.K. factories manufacturing carbon black was investigated for the period 1951-1996. All subjects were employed in the carbon black industry for 12 months or more, and all were first employed before 1975. Limited work histories were used to calculate estimates of individual cumulative exposure to carbon black, using a job-exposure matrix derived by the study team. Based on serial rates for the general population of England and Wales, significantly elevated mortality was observed in the main study cohort for all causes (Obs 372, Exp 328.7, SMR 113, P < 0.05) and for lung cancer (Obs 61, Exp 35.3, SMR 173, P < 0.001). There were highly elevated lung cancer SMRs at two of the factories, and unexceptional SMRs at the remaining three factories. There was no indication of lung cancer SMRs increasing with period from first employment. Poisson regression analyses failed to find significant trends of lung cancer risks increasing either with cumulative exposure to carbon black (4 levels) or with duration of employment at the participating factories (4 levels). Confident interpretation of the elevated SMRs found for lung cancer in two of the factory subcohorts is not possible but the study has been unable to link cumulative exposure to carbon black with elevated risks of lung cancer.



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<p>Hamm, S., Weinand, R., Frey, T., Moninot, G., Petiniot, N. Investigations on the Extraction and Migration Behavior of Polycyclic Aromatic Hydrocarbons (PAHs) From Cured Rubber Formulations Containing Carbon Black as Reinforcing Agent; Rubber Chemistry and Technology, Vol. 82, 2009</p>	<p>Investigations on the extraction and migration behavior of Polycyclic Aromatic Hydrocarbons (PAHs) from cured rubber formulations containing carbon black as reinforcing agent</p>	<p>Potential release of polycyclic aromatic hydrocarbons (PAHs) from cured rubber materials containing carbon black as reinforcing agent was studied on the basis of seven standard formulations prepared with different loadings of a carbon black grade specifically selected for its high PAH content. A specific test method involving Soxhlet extraction with toluene was developed and validated for quantification of the US-EPA and EU priority PAHs in the rubber materials containing up to 350 ppm of these compounds. PAH migration into aqueous media was assessed by total immersion of rubber sheets into drinking water, artificial sweat, saliva and rainwater for 7 days at 30 °C. GC/MS and internal deuterated standards were applied for PAH determination in all tests. Migration of PAHs from the cured rubber into aqueous media was not detected for the EU PAHs including benzo(a)pyrene and proved to be very low for the combined US-EPA PAHs, not exceeding 1.2 µg/dm². Migration-derived PAH concentrations for drinking water were at least 105 lower than those in the rubber compounds. This study demonstrates that once incorporated into a rubber matrix, the PAHs originating from carbon black are scarcely available to aqueous media. These results should be considered while developing PAH exposure assessments for rubber articles.</p>
<p>Bott, J; Störmer, A; Franz, R; 2014. Food Addit. Contam. Part A, Chem. Anal. Control Expo. Risk Assess. 1-14.</p>	<p>Migration of nanoparticles from plastic packaging materials containing carbon black into foodstuffs</p>	<p>This study investigated the possibility that nanoparticles might migrate out of plastic materials used in the food packaging industry by incorporating two types of carbon black in low-density polyethylene (LDPE) and polystyrene (PS) at 2.5% and 5.0% loading (w/w) and then conducting migration studies. Based on both experimental findings that showed no evidence of carbon black migrating from the packaging material into food stimulants as well as theoretical considerations, the study authors concluded that "carbon black does not migrate into food once it is incorporated into a plastics food contact material."</p>
<p>Dell L et al. Carbon Black Exposure and Risk of Malignant and Nonmalignant Respiratory Disease Mortality in the US Carbon Black Industry Cohort; <i>Journal of Occupational and Environmental Medicine</i> 2015; 57: 984-997.</p>	<p>Cohort Study of Carbon Black Exposure and Risk of Malignant and Nonmalignant Respiratory Disease Mortality in the US Carbon Black Industry.</p>	<p>To evaluate lung cancer and respiratory disease mortality associations with cumulative inhalable carbon black exposure among 6634 US carbon black workers. This analysis was performed using standardized mortality ratio (SMRs) and Cox regression analyses. Lung cancer mortality was decreased overall (SMR = 0.77; 95% confidence interval [CI], 0.67 to 0.89) but less so among hourly male workers (SMR = 0.87; 95% CI, 0.71 to 1.05). No exposure-response association was observed with time-dependent cumulative inhalable carbon black: hazard ratio [HR] = 1.0 (95% CI, 0.6 to 1.6) for 20 to less than 50 mg/m³-yr; HR = 1.3 (95% CI, 0.8 to 2.1) for 50 to less than 100 mg/m³-yr; and HR = 1.4 (95% CI, 0.9 to 2.1) for 100 mg/m³-yr or more compared with referent (<20 mg/m³-yr). No consistent associations were observed between cumulative inhalable carbon black exposure and respiratory disease mortality. Quantitative carbon black exposure estimates were not related to lung cancer or nonmalignant respiratory disease mortality.</p>
<p>Public Comments for Substances Nominated to the Report on Carcinogens, National Toxicology Program</p>	<p>http://ntp.niehs.nih.gov/pubhealth/roc/noms/index-2.html#carblack</p>	
<p>International Carbon Black Association. Unsuitability of the ZEK/AfPS test method for the quantification of PAHs in Carbon Black.</p>	<p>http://www.carbon-black.org/files/ICBA-Statement_Unsuitability-of-ZEK-test-method-for-CB_01_2016.pdf</p>	

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<p>Morfield, P.; Mundt, K.; Dell, L.; Sorahan, T.; and Mccunney, R.: Meta-Analysis of Cardiac Mortality in Three Cohorts of Carbon Black Production Workers, <i>International Journal of Environmental Research and Public Health</i>. 2016, 13(3), 302.</p>	<p>http://www.mdpi.com/1660-4601/13/3/302</p>	<p>Epidemiological studies have demonstrated associations between airborne environmental particle exposure and cardiac disease and mortality; however, few have examined such effects from poorly soluble particles of low toxicity such as manufactured carbon black (CB) particles in the work place. We combined standardised mortality ratio (SMR) and Cox proportional hazards results from cohort studies of US, UK and German CB production workers. Under a common protocol, we analysed mortality from all causes, heart disease (HD), ischemic heart disease (IHD) and acute myocardial infarction (AMI). Fixed and random effects (RE) meta-regression models were fit for employment duration, and for overall cumulative and lagged quantitative CB exposure estimates. Full cohort meta-SMRs (RE) were 1.01 (95% confidence interval (CI) 0.79–1.29) for HD; 1.02 (95% CI 0.80–1.30) for IHD, and 1.08 (95% CI 0.74–1.59) for AMI mortality. For all three outcomes, meta-SMRs were heterogeneous, increased with time since first and time since last exposure, and peaked after 25–29 or 10–14 years, respectively. Meta-Cox coefficients showed no association with lagged duration of exposure. A small but imprecise increased AMI mortality risk was suggested for cumulative exposure (RE-hazards ratio (HR) = 1.10 per 100 mg/m³-years; 95% CI 0.92–1.31), but not for lagged exposures. Our results do not demonstrate that airborne CB exposure increases all-cause or cardiac disease mortality.</p>