International Carbon Black Association

Recommendation for No Classification of Carbon Black for Carcinogenicity

Statement of Overall Conclusions

Carbon Black (CB) should not be classified for carcinogenicity according to the criteria of the Globally Harmonized System of Classification and Labelling of Chemicals. This recommendation is also valid for GHS implementation by different authorities such as the EU (Regulation (EC) No 1272/2008 (CLP)), United States 2012 OSHA Hazard Communication Standard (29 CFR 1910.1200) and the Canadian Hazardous Products Regulation (HPR) 2015. Human health studies show that exposure to carbon black does not increase the risk of carcinogenicity. Studies in laboratory animals show that lung tumors are induced in rats as a result of repeated exposure to inert, poorly soluble particles like carbon black and other poorly soluble particles. Rat tumors are a result of a secondary non-genotoxic mechanism associated with the phenomenon of lung overload. This is a species-specific mechanism that has questionable relevance for classification in humans. Thus a carcinogenicity classification for CB is not warranted.

GHS Classification System for Carcinogenicity

The categories for classification and labeling of carcinogenic substances under GHS are summarized in Table 1.

Table 1: Classification Criteria for Carcinogenicity under GHS

GHS, Chapter 3.6.2.1
Category 1: Known or presumed human carcinogens *The placing of a substance in Category 1 is done on the basis of epidemiological and/or animal data.*
Category 2: Suspected human carcinogens *The placing of a substance in Category 2 is done on the basis of evidence obtained from human and/or animal studies, but which is not sufficiently convincing to place the substance in Category*

1. Based on strength of evidence together with additional considerations, such evidence may be from either limited evidence of carcinogenicity in human studies or from limited evidence of carcinogenicity in animal studies.

The following sections provide data from epidemiological and animal studies on carbon black. Based on weight of evidence from these data, carbon black is not classified as a carcinogen under GHS.

A. Epidemiology

The most recent evaluation of possible human cancer risks due to carbon black exposure was performed by an IARC[a] Working Group in February 2006 (Baan *et al*. 2006). The Working Group identified lung cancer as the most important endpoint to consider and exposures of workers at carbon black production sites as the most relevant for an evaluation of risk.

Three epidemiological studies were undertaken to investigate lung cancer mortality in carbon black production plants and these were considered in great detail by IARC:

A UK cohort study on 1,147 workers at five plants (Sorahan *et al*. 2001) found an SMR[b] of 1.73 (61 cases, 0.95-CI[c]: 1.32, 2.22) but no trend across crudely assessed cumulative exposure, lagged up to 20 years. Elevated lung cancer SMRs were observed at two plants, the SMRs of the other three plants were unexceptionable. A German study on 1,528 workers at one plant (Wellmann *et al*. 2006, Morfeld *et al*. 2006, Buechte *et al*. 2006, Morfeld *et al*. 2006) estimated an SMR = 1.83 (50 cases, 0.95-CI: 1.34, 2.39) but could not find any positive trends with carbon black exposures. However, the German study identified smoking and prior exposures to known carcinogens as important risk factors that could explain the major part of the excess risk. A US cohort study on 5,011 workers at 18 plants (Dell *et al*. 2006) calculated an SMR = 0.85 (127 cases, 0.95-CI: 0.71, 1.00) and found no trend across time since first exposure and duration of exposure.

The Working Group at IARC concluded that the human evidence for carcinogenicity was ***inadequate*** (Baan *et al*. 2006).

Since this IARC 2006 evaluation, an extended follow-up of the UK study by Sorahan and Harrington (2007) applied a novel exposure metric ("lugging") while hypothesizing that carbon black may act as a late stage lung cancer carcinogen at plants with elevated SMRs. If so, the elevated SMRs of lung cancer should decrease substantially after cessation of exposure and positive associations should be found with "lugged" cumulative carbon black exposure ("lugging" the exposure by 15 years, say, means to count only exposures received during the last 15 years). Sorahan and Harrington 2007 observed both phenomena in those (and only those) two UK plant cohorts that had elevated lung cancer SMRs. In their paper, the authors asked for repetitions of their surprising finding in an independent study. Morfeld and McCunney 2007 thus tested the hypothesis of Sorahan and Harrington 2007 in the German study. Neither a decreasing

[a] IARC = International Agency for Research of Cancer
[b] SMR = standardized mortality ratio
[c] CI = confidence interval

SMR after cessation of exposure was observed nor a positive relationship with "lugged" cumulative carbon black exposure although the German cohort showed a clearly elevated lung cancer SMR. Therefore, Morfeld and McCunney 2007 were unable to lend support to the new hypothesis proposed by Sorahan and Harrington.

More recent studies have also been published. (Morfeld and McCunney, 2009 and 2010). In a detailed analysis of the German carbon black cohort, additional analysis was conducted to address potential "lugging" effects. As noted above, "lugging" is a term introduced by Sorahan and Harrington (2007) to account for the most recent exposures with respect to health risk. Methods such as Bayesian analysis were employed to explore all potential risk factors and confounders that may have contributed to the results. These additional studies provide further support for the lack of a significant increased risk of cancer as a result of working in the carbon black industry.

The relationship between workplace exposure to carbon black and lung cancer risk was examined in two large population-based case-control studies carried out in Montreal, Canada (Parent *et al.* 1996; Ramanakumar *et al.* 2008). Interviews 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 CB. Lung cancer risk was analysed in relation to each exposure, adjusting for several potential confounders, including smoking. Subjects with occupational exposure to CB, titanium dioxide, industrial talc and cosmetic talc did not experience any detectable excess risk of lung cancer.

An update and extension of the retrospective mortality study of US carbon black workers evaluated a cohort of 6634 workers employed in the carbon black industry dating back to the 1930s (Dell *et al*. 2015). The mortality follow-up was extended until December 31, 2011 and a quantitative assessment of individual cumulative exposure to inhalable carbon black dust conducted. The results showed no increase in lung cancer or any other malignancy in either the total or inception cohorts: Lung cancer mortality was decreased in comparison to state-specific reference rates (184 observed deaths, SMR = 0.77; 0.95-CI: 0.67 to 0.89), and for all cancers (512 observed deaths, SMR=0.79, 0.95-CI: 0.72–0.86). Internal exposure-response analyses showed no convincing link between carbon black exposure and lung cancer mortality. In summary, the authors of the study concluded: "*Regardless of whether exposure was based on lagged, lugged, or total cumulative estimates, no consistent association was seen with lung cancer or non malignant respiratory disease."*

Excess mortalities were reported for diseases of the blood-forming organs and peritoneal and unspecified digestive organ cancers. No biological plausibility or mechanism can be discerned for these endpoints but the excesses may easily be explained by false positive findings due to the large number of comparisons performed (Morfeld 2015).

Overall, as a result of these further detailed investigations, no causative link of carbon black exposure and cancer risk in humans has been demonstrated. This view is consistent with the IARC evaluation in 2006.

B. Toxicology

Summary of Animal Data

In numerous studies, rodents, particularly rats, have been exposed by inhalation to carbon black. Based on the results from these studies a number of conclusions may be drawn.

First, prolonged inhalation of high levels of carbon black causes delayed alveolar lung clearance and marked retention of particles. This phenomenon is described as "lung overload" (IARC, 1996; Mauderly, 1996) and is common for a range of respirable insoluble dusts of low toxicity. The sequelae to these high lung burdens in rats include sustained inflammation, which leads to a range of changes in pro- and anti-inflammatory biochemical parameters (found in the BAL), epithelial hyperplasia, and pulmonary fibrosis.

Second, rats are more sensitive to the effects of carbon black overload than other species (mice, hamsters), with female rats having more pronounced reactions than male rats (ILSI, 2000). In long-term studies, only female rats were prone to a significant increase in the development of lung tumours. The lowest carbon black concentration used in a chronic inhalation study where lung tumours were induced was 2.5 mg/m^3, with rats being exposed for 16 hours/day, 5 days/week for 2 years (Mauderly *et al*. 1994). However, mice exposed to 11.6 mg/m^3 carbon black for 18 hours/day, 5 days/week for 13.5 months and observed for a further 9.5 months did not exhibit an increase in lung tumours (Heinrich *et al*, 1995).

In primates (Nikula *et al*. 1997) and in humans (Mauderly, 1996), there are clear differences in particle deposition, clearance patterns, and tissue reactions, when compared to rats. These differences underline the uniqueness of the rat tumour development under conditions of lung overload and raise questions as to the validity of interspecies extrapolations of particle effects from rats to humans. In further support of the uniqueness of the rat response to particle overload are findings with another inert insoluble particle, namely TiO2. In a recent study, Bermudez, *et al.* (2004) exposed female rats, mice, and hamsters to aerosol concentrations of 0.5, 2.0, or 10 mg/m^3 uf-TiO_2 particles for 6 h per day and 5 days per week for 13 weeks. Animals were kept up to 52 weeks post-exposure. Mice and rats had similar retained lung burdens at the end of the exposures, when expressed as mg uf-TiO_2/mg dry lung, whereas hamsters had retained lung burdens that were significantly lower. Pulmonary inflammation was seen in rats and mice exposed to 10 mg/m^3 as well as progressive epithelial and fibro-proliferative changes. Importantly, these lesions became more pronounced with increasing time post-exposure. However, epithelial, metaplasia, and fibro-proliferative changes were not seen in either mice or hamsters. Under conditions wherein the lung uf-TiO_2 burdens were equivalent, rats developed a more severe inflammatory response than mice. A severe, persistent neutrophilic inflammatory response in the rat lung was believed to result in the development of progressive epithelial and fibro-proliferative changes. These data are consistent with the results of a companion study using

inhaled pigmentary (fine mode) TiO_2 (Bermudez *et al.* 2002) and demonstrate that the pulmonary responses of rats exposed to ultrafine particulate concentrations likely to induce pulmonary overload are different from the effects measured in similarly exposed mice and hamsters. Overall, these results remarkably parallel the interspecies findings seen in the Oberdoerster interspecies study with carbon black and further emphasise the uniqueness of the rat lung in its pathophysiological response (including neoplasia) to overload from inhaled poorly soluble inert particles such as carbon black.

Data on coal miners provides the best available human evidence with which to explore lung overload questions. Using eight studies conducted between 1956 and 1986 from a total of 1,225 miners in the US and UK, Mauderly (1994) converted the lung burden of coal dust into units of specific lung burden and showed that long-term coal miners commonly accumulated dust burdens in the range of 7 to 14 mg per g lung. This value indicates that the dust burdens in heavily exposed human lungs are in the same range as, or greater than, the heavily exposed experimental animals seen in chronic bioassays. In spite of these high lung burdens, coal dust exposure does not cause a significant increase in lung cancers among miners (IARC, 1996). This reasoning, although quite compelling, does not preclude the possibility that total particle surface area and particle number are also parameters pertinent to biological outcomes.

Third, results from genotoxicity studies suggest a direct association of mutation with inflammation and its sequelae in rat lung tumour development. Lung inflammation leads to the production of reactive oxygen species, and these mutational lesions seen in the *ex vivo hprt* assay can be prevented by experimental treatment with antioxidants (Driscoll *et al*. 1997). This study demonstrated that the increase in mutation frequency is caused by oxidative damage alone, typical of a secondary genotoxic mechanism.

The prevailing scientific consensus is that rat lung tumours induced by inert, poorly soluble particles (PSP's), such as carbon black, arise out of a background of chronic and persistent inflammatory changes; the corollary being that if these changes are avoided, then the tumours will not occur. In this respect, the studies of Driscoll *et al.* (1996 a) are of particular relevance because exposure to 1.1 mg/m^3 of respirable carbon black particles did not evoke inflammatory or mutational changes to female rats. A no observed adverse effect level (NOAEL) of 1 mg/m^3 (respirable) carbon black has been supported by more recent rodent findings by Oberdoerster, Driscoll, and colleagues (Carter *et al.* 2006; Elder *et al.* 2005; Driscoll *et al.* 2002).

Exposure protocols in experimental studies and relevance to occupational exposure

Exposure patterns and particle characteristics in experimental animal studies do not mimic conditions in the occupational environment. The duration of carbon black exposure in the chronic studies ranged from 16 to 18 hours per day (Mauderly *et al*. 1994; Heinrich *et al.* 1995), which does not simulate the workplace. Prolonged exposure does not give the animals the normal recovery period for lung clearance.

In contrast to the animal exposures, workplace exposure assessments in contemporary carbon-black manufacturing operations in Europe and in North America reveal typical 8-hour TWA exposures to well below 0.5 mg/m^3 respirable dust. In addition, industry workplace exposures are generally to large-size carbon black agglomerates that represent only part of the total dust exposure, with the remainder of workplace exposure being to non-carbon-black constituents. Thus, for both particle size and aerosol composition, workplace exposure characteristics are different from what has been used in the animal studies. Therefore, the applicability to human risk assessment of studies showing rat tumour development under conditions of lung overload is unclear.

Mechanism of tumour development in rats and species differences

1. Lung overload

The development of lung tumours occurs only in rats under lung overload conditions (IARC, 1996; Mauderly, 1996). Neither other rodents, such as mice and hamsters, nor humans develop lung tumours under similar conditions of lung overload from PSP's. The evidence to support this contention has been addressed above in the section summarising the most relevant experimental animal studies. All the interspecies investigations point to the same conclusion regarding the uniqueness of a very specific pathophysiological process operating in the rat, particularly the female rat, leading to the formation of primarily alveogenic tumours. The development of lung tumours at lung overload exposures is triggered by the inability of rats to effectively clear the particles from their lungs and a sustained inflammatory process.

2. Role of primary genotoxic effects caused by PAH's

The proposed mechanism of tumour induction in rats is not primary genetic damage caused by the particle. Numerous mutagenicity assays with carbon black showed no inherent particle genotoxicity. All carbon blacks are insoluble in water, biological fluids, and organic solvents. Soot particles generally contain a high percentage of tarry material, with large amounts of adsorbed PAH's. In contrast, only traces amounts of organic compounds are adsorbed on carbon black (typically less than 1,000 ppm or 0.1%) (Watson and Valberg, 2001). At these low levels, organic compounds are tightly bound to carbon black particles, and extensive solvent extraction procedures are needed to remove them. In a 2005 study, Borm and co-workers tested three carbon black particle exposure levels (1, 7, 50 mg/m^3) of Printex 90 and one concentration (50 mg/m^3) for Sterling V, as well as a sham exposure group specifically for PAH-DNA adduct forming properties. F344 rats were exposed by inhalation for 13 weeks and then DNA was extracted from whole lung DNA immediately after exposure. The lungs of the rats for DNA analysis were not lavaged but the vascular system was perfused. DNA was extracted and used to determine oxidative DNA damage. To determine whether PAHs were available and subsequently transformed into DNA-binding metabolites, lungs of three animals from each exposure group were analysed for DNA adducts, immediately after exposure. No adducts were found in DNA from lung homogenates isolated immediately after 13 weeks of inhalation of up to 50 mg/m^3 of Printex 90 and Sterling V, which resulted in lung burdens of 4.9 mg and 7.6 mg, respectively. Lung DNA from rats following inhalation of carbon black showed no "spots" relating to PAH-DNA adduct formation compared to sham-exposed animals.

Donaldson and co-workers (1998) postulate in their review on particle-mediated lung injury, that there is no evidence to support carbon black particles having direct mutagenic activity. They noted that diesel exhaust, carbon black and titanium dioxide (TiO_2), caused similar levels of overload tumours (Heinrich *et al*. 1995), despite the fact that the extractable organic component was 40% for diesel exhaust, 0.04% for carbon black and 0% for TiO_2. The results of Gallagher *et al*. (1994) support the findings of Heinrich and co-workers, because no PAH-DNA adducts were detected in rats with overload carbon black tumours. Examinations by Bond and co-workers (1990) and Wolff and co-workers (1990) showed similar results. Donaldson and co-workers (1998) concluded that the particles themselves cause recruitment of inflammatory cells, which release respiratory burst-derived oxidants and that these oxygen free radicals could induce mutations in particle-exposed lung of rats.

3. Role of secondary genotoxic effects caused by Reactive Oxygen Species

The lack of association between the inherent genotoxic activity of PSP's and the development of rat lung tumours after chronic inhalation exposure implies a secondary mechanism for this response. At an international workshop organized by the German Research Council / DFG (Deutsche Forschungsgemeinschaft) on particle and fibre evaluation (Greim *et al.* 2001), it was generally agreed that tumours in rat experiments are caused by a secondary, inflammatory / proliferative mechanism as opposed to direct genotoxicity. Lung overload leads to sustained inflammation, release of various biological mediators and oxidative stress. In addition to carbon black, high exposure levels of titanium dioxide (250 mg/m³) (Lee *et al.* 1985) and talc (10 or 20 mg/m³) (Hobbs *et al.* 1994) cause lung tumours in rats. Thus, the lung tumour response to inhaled inert particles observed in female rats is not particle specific.
"Particle overload" is the key factor leading to the development of tumours in rats, and it appears that oxidative stress is the primary event / mechanism critical for tumour pathogenesis. The susceptibility of the rat may reside in the fact that rat lungs show a far greater induction of several key pro-inflammatory processes and less induction of anti-inflammatory processes than other species (Driscoll and Carter, 1999).

At and below carbon black concentrations of approximately 1 mg/m³ (respirable), it is highly unlikely that rats, other rodents, or humans are at risk for developing lung cancer (Oberdörster and Yu, 1997; Driscoll *et al.* 1995, 1996 a; ILSI [International Life Sciences Institute] Risk Science workshop, 2000). At the DFG workshop (Greim *et al.* 2001), the consensus was that preventing lung inflammation will prevent the development of lung tumours.
Evidence for an effect threshold has been demonstrated in that sub-chronic inhalation of 1.1 mg/m³ respirable carbon black did not elicit inflammation or increases in *hprt* mutation frequency in epithelial cells (Driscoll *et al.* 1996 a). In rats, a lung-tumour threshold has also been demonstrated for diesel-exhaust exposure (Valberg and Crouch, 1999). More recently, sub-chronic inhalation of carbon black over a range of concentrations has confirmed the absence of inflammatory responses following repeated exposures to 1 mg/m^3 (Carter *et al.* 2006; Elder *et al.* 2005; Driscoll *et al.* 2002). Thus, 1mg/m^3 of respirable-sized carbon black represents a clear

NOAEL for even the most sensitive of inflammatory markers in the most sensitive of test organisms, the female rat.

Conclusions, Animal Studies

At the DFG International Workshop Evaluation on Particle and Fibre Toxicity (Greim *et al.* 2001) a consensus was reached regarding the tumorigenic properties of inert, PSP's. The participants generally accepted that PSP's caused lung tumours in rats by a secondary genotoxic (inflammatory/proliferative) mechanism. The group concluded that, *"Studies to date have not demonstrated primary genotoxicity of carbon black with low PAH contamination using appropriate in vitro assays. DNA adducts related to associated organic compounds so far have not been found in lung tissue from rats exposed chronically to carbon black, although in the same studies adducts were found in diesel exhaust-exposed rats."*

Implicit in the inflammatory / proliferative mechanism is the existence of a non-linear, dose-related effect with a threshold. That is, particle exposures that do not overwhelm host defence mechanisms (*e.g.,* anti-oxidants, DNA repair) and hence do not elicit inflammatory and proliferative responses, should not pose an increased risk of lung tumours in humans (Driscoll, 1996 b; Driscoll *et al.* 1996a). Using a meta-analysis approach, Valberg and Crouch (1999) demonstrated that the incidence of lung tumours was not elevated in rats with less than an average 0.6 mg/m^3 continuous lifetime exposure to diesel exhaust particles. Therefore, the use of linear models for dose-response extrapolation from "lung overload" conditions is not appropriate and should be replaced with non-linear models incorporating a threshold.

Driscoll *et al*. (1996 b) have demonstrated that sub-chronic inhalation of 1.1 mg/m³ (respirable) carbon black did not elicit any detectable adverse lung effects. The results from Oberdörster's and Driscoll's research groups (Carter *et al.* 2006; Elder *et al.* 2005; Driscoll *et al.* 2002) support this finding, with a carbon black NOAEL of 1 mg/m³ (respirable). Furthermore, participants at the ILSI workshop (2000) proposed that no uncertainty (safety) factor (for rat-to-human extrapolation) was required for neoplastic and fibrogenic endpoints associated with particle exposure, because the rat appears to be more sensitive in its responses to all particle-related effects than other species, including humans. This conclusion was also reached by ECETOC (ECETOC 2013), which concluded "*Since the ILSI 2000 report, there has been a vast amount of in vivo and in vitro work on poorly soluble particles of low toxicity but there have been no compelling studies or a weight of evidence that would allow the Task Force to conclude that the rat lung overload findings is a reliable predictive model, in particular for neoplasia, with regard to hazard or risk assessment for humans who are exposed to poorly soluble particles of low toxicity."*. The evaluation of carbon black by IARC (1996 and 2006) and Greim *et al.* (2001) as a suspect carcinogen is solely founded on the observation that rats develop tumours. The ILSI workshop (2000), which evaluated the relevance of the rat responses to particle overload for human risk assessment, concluded that at non-overload exposures, a lung-cancer hazard did not exist.

Furthermore, experimentally-induced lung tumours in rats occur in the alveolar and small airway regions of the lungs, unlike human lung cancers that tend to occur at the bifurcations of the major airways (bronchi), further questions the appropriateness of extrapolating the results in the rat studies to humans.

Basing human lung cancer risk predictions on the rat response to the inhalation of PSP's, including carbon black under conditions of lung overload is not valid. Several independent, expert, scientific advisory groups have cautioned against using tumorigenic data from rats exposed to high ("lung overload") concentrations of insoluble particles for quantitative risk assessment. In the United States, the Presidential / Congressional Commission on Risk Assessment and Risk Management (CRARM, 1997) noted that the response of rat lungs to high concentrations of inhaled, PSP's (specifically carbon black and titanium dioxide) are not likely to be predictive of human cancer risks. For diesel exhaust, the Clean Air Scientific Advisory Committee (CASAC, 1995 and 1998), a peer-review group for the U.S. Environmental Protection Agency (EPA), has commented on two drafts of the EPA´s Health Assessment Document on Diesel Exhaust. On both occasions, CASAC emphasized that the data from lung-overloaded rats are not relevant for human risk assessment. Likewise, the Health Effects Institute (1995) also has concluded that rat data should not be used for assessing human lung-cancer risk from diesel-exhaust exposure.

A comprehensive review on translational toxicology focusing on dust exposure and on carbon black as one example was published in Morfeld *et al*. 2015.

C. Recommendation for Classification of Carbon Black according to GHS Criteria:

Although lung tumours are induced in rats when exposed to carbon black, it is generally acknowledged that these tumours are produced because of a phenomenon known as "lung overload". When exposed to a poorly soluble particle such as carbon black in high concentrations, laboratory rats cannot adequately clear carbon black from their respiratory tract, so lung tumours are induced by a secondary non-genotoxic mechanism. Lung tumours were not observed in mice and hamsters under similar study conditions. The relevance of the rat tumour data to human risk assessment is highly questionable (ILSI, 2000). A review by ECETOC (2013) also concluded that the rat represents a unique model with regard to lung neoplastic responses under conditions of lung overload. Thus, based on these findings and the guidance from authoritative bodies, the ICBA and the Carbon Black REACH Consortium have reached the opinion that it is not appropriate to classify carbon black as "Category 2 Carcinogen" under the GHS Regulation.

In support of this opinion, it should be noted that in the EU CLP Guidance for Specific Target Organ Toxicity – Repeated Exposure (STOT RE) (ECHA, **2015),** the issue of lung overload is mentioned under section 3.9.2.5.3 Mechanisms not relevant to humans (CLP Annex 1, 3.9.2.8.1.(e)) as *"The relevance of lung overload in animals to humans is currently not clear and*

is subject to continued scientific debate". Also section 3.9.2.8 (e) of the CLP regulation states that *"Substance – induced species specific mechanisms of toxicity, i.e. demonstrated with reasonable certainty to be not relevant for human health, shall not justify classification"*. **Further,** Section 3.6.1.1 of the CLP regulation states *"Substances which have induced benign and malignant tumours in well performed experimental studies on animals are considered also to be presumed or suspected human carcinogens* ***unless*** *there is strong evidence that the mechanism of tumour formation is not relevant for humans."* The ACGIH® has also designated carbon black a category A3 carcinogen, Confirmed Animal Carcinogen with Unknown Relevance to Humans. This designation by the ACGIH® is consistent with the ICBA and the Carbon Black REACH Consortium conclusion not to classify carbon black.

The United States 2012 OSHA Hazard Communication Standard's (29 CFR 1910.1200) (HCS) section on carcinogenicity is consistent with GHS, except that it provides classifiers with the option of relying on the classification listings of IARC and National Toxicology Program (NTP) to make classification decisions regarding carcinogenicity, rather than applying the criteria themselves. Using IARC and NTP listings for carcinogen classification is provided as an option, and is not mandatory. Therefore, the weight of evidence evaluation shown in this document is also acceptable under HCS.

In conclusion, the evaluation of carbon black as a suspect carcinogen is based solely on the observation that rats develop lung tumours under condition of "lung overload". The reliability of lung tumours induced in rats by inert poorly soluble particles, such as carbon black, as a predictor of hazard to humans is uncertain. Overall, the epidemiological evidence from well-conducted investigations has not shown that exposure to carbon black has a carcinogenic potential for humans.

Therefore, we recommend that no classification of carbon black is required based on the fact that data from rat lung overload studies, as described above and fully discussed in our statement, cannot be extrapolated to humans.

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