RUBBER manufacturers association

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Dr. Ruth Lunn, Director
Office of the RoC
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By e-mail to: lunn@niehs.nih.gov.

Dear Dr. Lunn:

I. INTRODUCTION

The Rubber Manufacturers Association (RMA) is the national trade association representing every major domestic tire manufacturer including: Bridgestone Americas, Inc., Continental Tire the Americas, LLC; Cooper Tire & Rubber Company; The Goodyear Tire & Rubber Company; Michelin North America, Inc.; Pirelli North America; Toyo Tire (U.S.A.) Corporation and Yokohama Tire Corporation. RMA appreciates the opportunity to offer comments on the National Toxicological Program's ("NTP") request for comments on the potential nomination of carbon black for possible review for a future edition of the Report on Carcinogens (77 Fed. Reg. 2728, Jan. 19, 2012). Carbon black is one of the main ingredients in rubber tires. Therefore, RMA members have a significant interest in this proceeding.

These comments: (1) discuss whether it is cost-effective to prioritize a redundant review of the carcinogenicity of carbon black, given limited budgets and the number of chemicals that have not been evaluated previously; (2) summarize (and cite and incorporate by reference the summary of the toxicological literature provided in the comments of the International Carbon Black Association ("ICBA")); (3) discuss the issue of whether the rat study data are relevant to humans; and (4) provide data on human exposure in the tire manufacturing industry. We have not offered any names of scientists with expertise or knowledge about carbon black, as we believe the list of experts cited by the ICBA is appropriate.

In summary, for the reasons stated below, the proposal to consider the carcinogenicity of carbon black by the NTP is duplicative and a waste of the NTP's limited resources. Carbon black is not a known carcinogen nor is it reasonably anticipated to be a human carcinogen based on the NTP listing criteria.

II. THE NTP NOMINATION OF CARBON BLACK IS UNNECESSARY, REDUNDANT, AND WASTEFUL

The review and potential listing of carbon black is unnecessary and redundant because the carcinogenicity of carbon black has been classified by: (a) the International Agency for Research on Cancer (IARC);[1] (b) the State of California Office Environmental Health Hazard Assessment's (OEHHA);[2] and (c) the Environmental Protection Agency (EPA).[3] The Occupational Safety and Health Administration utilizes the IARC listing for hazard communication purposes.[4]

A listing by the NTP of carbon black would be redundant because carbon black is already regulated by OSHA, OEHHA, and EPA, and it would fail to further inform United States regulators about any unknown or underappreciated risks. Thus, there is no benefit to an NTP listing and it would waste limited NTP resources at a time when the federal government is being criticized for not addressing more chemicals.[5] The process of developing, peer reviewing, receiving and responding to public comment on a carbon black nomination would consume significant NTP and private sector resources with no demonstrable benefit. In sum, the most efficient and prudent course of action is simply not to include carbon black in the NTP nomination process.

III. IF THE NTP EVALUATES CARBON BLACK, THE WEIGHT OF THE EVIDENCE IS THAT CARBON BLACK IS NOT A KNOWN CARCINOGEN NOR REASONABLY ANTICIPATED TO BE A HUMAN CARCINOGEN

The NTP should not evaluate carbon black because the weight of the epidemiological evidence does not demonstrate that carbon black is a carcinogen, and the statistically significant increases in benign and malignant tumors in rats exposed to airborne carbon black particles at concentrations in excess of the level that overwhelms the natural lung clearance mechanism (*i.e.*, lung overburdening studies) are not relevant to humans (*see* ICBA submission, which is

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[1] IARC Monographs On the Evaluation of Carcinogenic Risks to Humans, Vol. 65, Printing Processes and Printing Inks, Carbon Black and Some Nitro Compounds at 241-243 (1996) ("IARC Carbon Black Monograph").

[2] "Carbon black (airborne, unbound particles of respirable size)" was listed in 2003. State of California, Chemical Listed Effective February 17, 2012 As Known To The State Of California To Cause Reproductive Toxicity, available at http://oehha.ca.gov/prop65/prop65_list/files/P65single021712.pdf.

[3] EPA, Memorandum from Bipin Gandhi, Inert Ingredient Assessment Branch, Registration Division, To Pauline Wagner, Chief, Inert Ingredient Assessment Branch, Registration Division; SUBJECT Reassessment of one Exemption from the Requirement of a Tolerance for Carbon Black (November 21, 2005), available at http://www.epa.gov/opprd001/inerts/carbonblack.pdf..

[4] 29 CFR §1910.1200(d)(4)(ii).

[5] General Accountability Office, Challenges Remain with EPA's Integrated Risk Information System Program (GAO-12-42, Dec 9, 2011), available at http://www.gao.gov/assets/590/586620.pdf. Also, "EPA … has not been able to complete timely, credible chemical assessments or decrease its backlog of 70 [as of 2008] ongoing assessments." See John B. Stephenson, Director, Natural Resources and Environment, Testimony before the Subcommittee on Investigations and Oversight, Committee on Science and Technology, June 11, 2009 .

incorporated by reference). Thus, carbon black is not a known carcinogen nor is it reasonably anticipated to be a human carcinogen based on the NTP listing criteria. [6]

The claim that the "lung overburdening" animal studies that resulted in statistically significant increases in lung tumors prove that carbon black causes cancer in humans is not biologically plausible. The only animal studies demonstrating the growth of tumors based on exposure to carbon black used exposure levels that overloaded the lung particle clearance mechanism in rats (*i.e.,* particles could no longer be removed from the lung tissue, so these particles caused inflammation). At very high levels of exposure, there was tumor growth in rats. This mechanism is not relevant to human exposure.[7]

EPA,[8] the American Conference of Government and Industrial Hygienists (ACGIH (2000)), the National Commission on Risk Assessment and Risk Management (1997),[9] a joint

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[6] NTP Listing Criteria, available at http://ntp.niehs.nih.gov/?objectid=03C9CE38-E5CD-EE56-D21B94351DBC8FC3.

[7] *See* ICBA submission. Prior submissions to the NTP concerning other substances have made the same point. Comments of John Addison and Arthur M. Langer, On the NTP Report on Carcinogens Background Document for Asbestiform Talc and Non-asbestiform Talc, at 11 (November 30, 2000), available at: http://dir.niehs.nih.gov/dirtob/rocpubcom/10throc/2000nominations/talcasbestiform-nonasbestiform/jaddison-11-30-00.pdf ("Addison and Langer") and. Gűnter Oberdörster, DVM, Ph.D., Comments on NTP Proposed listing of Talc Asbestiform and Non-Asbestiform, As Reasonably Anticipated to be a Human Carcinogen at 2-6 (November 20, 2000), available at http://dir.niehs.nih.gov/dirtob/rocpubcom/10throc/2000nominations/talcasbestiform-nonasbestiform/oberdorster-11-29-00.pdf, ("Oberdörster Comments"). These documents are in the NTP Talc Nomination document. RMA's submission is also in the NTP talc docket and is incorporated by reference herein. The NTP has not proceeded with its review of the carcinogenicity of talc.

[8] EPA, Toxic Chemical Release Reporting; Community Right-to-Know; Titanium Dioxide, 53 Fed. Reg. 23106, 23111 (1988), which concluded that titanium dioxide is not a carcinogen despite lung overburden rat study results. In 2002, EPA concluded that:

> The lung cancer response in rates from high-concentration exposures [to diesel exhaust] appear to be mediated by impairment of lung clearance mechanisms through particle overload, resulting in persistent chronic inflammation and subsequent pathologic and neoplastic changes in the lung. Overload conditions are not expected to occur in humans as a result of environmental and most occupational exposures to DE. Thus, the rat lung tumor response is not considered relevant to an evaluation of the potential human environmental exposure-related hazard. EPA, Health Assessment Document for Diesel Engine Exhaust at 7-139 (EPA/600/8-90/057F, May 2002).

In addition, Vanessa Vu of EPA's Office of Pollution Prevention and Toxics concluded in a paper reviewed and approved by EPA for publication that insoluble biochemically inert particles that cause fibrogenic and/or carcinogenic effects in rats at high exposure concentrations via particle overloading in the lungs of the animals due to excessive particle exposure were generally not of high concern. V. Vu, Use of Hazard and Risk Information in Risk Management Decisions: Solid Particles and Fibers Under EPA's TSCA and EPCRA at 10, in Proceedings of MIT Toxicology Symposium (March 1995).

EPA requires that where a "hypothesized mode of action is sufficiently supported in the test animals," one should "identify critical similarities and differences between the test animals and humans." (EPA, Final Guidelines for Cancer Risk Assessment at 2-47 (EPA/630/P-03/001F, March 2005) (EPA Cancer Guidelines), available at http://www.epa.gov/raf/publications/pdfs/CANCER_GUIDELINES_FINAL_3-25-05.PDF. A classification of "Not Likely to Be Carcinogenic to Humans" is appropriate when there is "convincing and extensive experimental evidence showing that the only carcinogenic effects observed in animals are not relevant to humans," "convincing

workshop on talc sponsored by the FDA and International Society of Regulatory Toxicology and Pharmacology;[10] IARC,[11] and other reputable scientific bodies and individual scientists[12] have concluded that the rat lung overburdening studies are not relevant to cancer in humans. A statistically significant increase in malignant and benign lung tumors in humans exposed to particles in lung overburdening conditions has not been observed in other test animals nor in humans. [13] The physiology of rat and human lungs is different and the rat reaction to lung overburdening is species-specific.[14]

EPA's Office of Prevention, Pesticides and Toxic Substances concluded:

> There is a **safe history of carbon black when used in tires**, plastics, automobile components, inks, adhesives, paints, dyes and ceramics. ... Taking into consideration all available information on carbon black, EPA has determined that there is a reasonable certainty that no harm to any population subgroup will result from aggregate exposure to carbon black when used as inert

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evidence that carcinogenic effects are not likely by a particular exposure route," or there is "convincing evidence that carcinogenic effects are not likely below a defined dose range." EPA Cancer Guidelines at 2-57 to 2-58.

[9] Presidential/Congressional Commission on Risk Assessment and Risk Management, Risk Assessment and Risk Management in Regulatory Decision-making, Volume II at 65 (1997) ("National Risk Commission Report"), available at www.riskworld.com/Nreports/ 1997/risk-rpt/volume2/html/v2epaa.htm.

[10] The Executive Summary of this joint FDA and International Society of Regulatory Toxicology and Pharmacology workshop on talc states: "In regard to the NTP talc bioassay in rodents, it [the unanimous expert panel] found that because of the extreme doses and the unrealistic particle sizes of the talc employed, because of the negative results in mice and male rats, because of the lack of tumor excess at the low doses, and because of the clear biochemical and cytological markers of excessive toxicity in female rats, the positive talc bioassay results in female F344/N rats are likely experimental artifact and non generic response of dust overload of lungs and not a reflection of a direct activity of talc." Workshop on Talc: Consumer Uses and Health Perspectives, cosponsored by International Society of Regulatory Toxicology and Pharmacology and the US Food and Drug Administration, Bethesda, MD, January 31- February 1, 1994, J. Reg. Tox. and Pharm. 21 211, at 215 (1995) ("Talc: Consumer Uses and Health Perspectives").

[11] Comments of Roger McClellan, DVM, DABT, DABVT, Critique of "Draft Report on Carcinogens Background Document for Talc; Asbestiform and Non-Asbestiform" at 6 (December 1, 2000), available at: http://dir.niehs.nih.gov/dirtob/rocpubcom/10throc/2000nominations/talcasbestiform-nonasbestiform/mcclellan-12-1-00.pdf ("McClellan Comments").

[12] Cogent summaries of the evidence that lung overburden studies in rats are not relevant to human exposure are provided in A. Watson and P. Valberg of Gradient Corporation, Particle-Induced Lung Tumors in Rats: Evidence for Species-Specificity in Mechanism, in Proceedings of MIT Toxicology Symposium (March 1995) ("Valberg Paper") and McClellan Comments, *supra* note 11, at 6.

[13] MRC IEH, Workshop on *Approaches to predicting toxicity for occupational exposure to dusts* (IEH, 1999); IARC Monographs On the Evaluation of Carcinogenic Risks to Humans, Vol. 68, Silica, Some Silicates, Coal Dust and Para-armid Fibrils 34 (1997) ("IARC Silica Monograph"); IARC Monographs On the Evaluation of Carcinogenic Risks to Humans, Vol. 65, Printing Processes and Printing Inks, Carbon Black and Some Nitro Compounds at 241-243 (1996) ("IARC Carbon Black Monograph"); Valberg Paper, *supra* note 12 and McClellan Comments, *supra* note 11, at 6.

[14] P. Valberg, Gradient, Public Review Comments On U.S. EPA's "Health Assessment Document For Diesel Emissions Vols. I and II" (April 1995).

ingredient in pesticide formulations when considering the dietary exposure and all other non-occupational sources of pesticide exposure for which there is reliable information.[15]

According to EPA, even if the lung overburdening data are relevant to humans, these studies "support the existence of a nonlinear response if it is assumed that inflammation is a prerequisite for lung tumor induction."[16]

In summary, there is little reason given the existing data on carbon black to perform another duplicative assessment of carcinogenicity.

IV. THERE IS LITTLE OR NO EXPOSURE OF THE PUBLIC TO CARBON BLACK

The NTP should not formally evaluate carbon black for inclusion in the Report on Carcinogens because the actual exposure to carbon black in the U.S. is not "significant," as required. Carbon black is tightly bound with the material with which the product is made, such as rubber. The animal studies relied upon by IARC and OEHHA relate solely to carbon black particles, not to rubber, rubber particles or any other particles.

As you and I discussed earlier today, RMA plans to submit data on measurements of carbon black in the tire manufacturing industry following the close of the comment period.

V. CONCLUSION

In summary, the weight of the epidemiological evidence does not demonstrate that carbon black is a carcinogen (as defined by the NTP) and the statistically significant increases in benign and malignant tumors in rats exposed to airborne carbon black particles at concentrations in excess of the level that overwhelms the natural lung clearance mechanism (*i.e.*, lung overburdening studies) are not relevant to humans.

If, nonetheless, the NTP concludes that as a matter of policy, it must nominate carbon black, RMA urges the NTP limit the review to "carbon black (as unbound airborne particles of respirable size under conditions of lung overload in humans)." The rationale for this language is that the only condition under which carbon black causes tumors in rats is when the airborne concentration of particles overwhelms the natural lung clearance mechanism. Such an assessment should review the relevance of these lung overburden data to humans and/or whether there is an applicable threshold.[17]

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[15] EPA, Memorandum from Bipin Gandhi, Inert Ingredient Assessment Branch, Registration Division, To Pauline Wagner, Chief, Inert Ingredient Assessment Branch, Registration Division; SUBJECT Reassessment of one Exemption from the Requirement of a Tolerance for Carbon Black (November 21, 2005), available at http://www.epa.gov/opprd001/inerts/carbonblack.pdf.. See also Memorandum from E. Fertich, Inert Ingredient Assessment Branch, Registration Division to P. V. Shah, Chief, Inert Ingredient Assessment Branch, Registration Division , Subject Decision Document for Carbon Black (CAS Reg. No. 1333-86-4) Petition No. 8E7484) p. 2 (March 31, 2009).

[16] Diesel Exhaust IRIS Listing, available at http://www.epa.gov/IRIS/subst/0642.htm.

[17] The NTP seeks information on exposure, the extent and nature of the scientific evidence for evaluating carcinogenicity in humans and experimental animals, and "any major relevant issues." NTP, Process for Preparation of the Report on Carcinogens, available at http://ntp.niehs.nih.gov/NTP/RoC/Thirteenth/Process/FinalRoCProcesswithFig.pdf.

RMA again thanks NTP for the opportunity to provide comments on the nomination of carbon black. Please contact me at (202) 682-4836 if you have questions or require additional information.

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Respectfully Submitted,
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Rubber Manufacturers Association