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Peter T. Grass
President

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Via E-Mail and First-Class Mail

C. W. Jameson, Ph.D.
National Toxicology Program, Report on Carcinogens
79 Alexander Drive
Building 4401, Room 3118
P.O. Box 12233
Research Triangle Park, NC 27709
e-mail: jameson@niehs.nih.gov

Re: Comments on the Nomination of Asphalt Fumes for Listing in the
NTP Report on Carcinogens, 69 Fed. Reg. 28941 (May 19, 2004)

Dear Dr. Jameson:

The Asphalt Institute welcomes the opportunity to submit comments on the nomination of asphalt fumes for listing in the National Toxicology Program's Report on Carcinogens, 12th Edition. The Asphalt Institute is a U.S.-based association of international petroleum asphalt producers, manufacturers, and affiliated businesses. The Institute's mission includes the support of research into the potential health and environmental effects of asphalt and development of new and improved measurement and control techniques, work practices and education and training materials to characterize and reduce exposure in the workplace and environment.

Because the nomination of asphalt fumes for listing [Shelp 2001] was submitted almost three years ago, the purpose of our comments is to ensure that NTP is aware of ongoing scientific studies, initiated after the nomination, that are designed to fill major gaps in the existing epidemiological and toxicological data on the potential carcinogenicity of asphalt fumes.

Background

NTP last reviewed asphalt fumes in the late 1990s [NTP 1997, 1998], when its Interagency Committee for Chemical Evaluation and Coordination (ICCEC) recommended new research on the basis of NIOSH's nomination for comprehensive toxicological testing [NIOSH 1997a, b]. The Nomination concluded that because of confounding exposures and poor exposure information, the available epidemiologic studies are insufficient to make a judgment with respect to asphalt [NIOSH 1997b]. On the subject of the animal data, the Nomination pointed to the need to determine whether the laboratory-generated asphalt fumes tested in two NIOSH skin-painting studies [Thayer 1981, Niemeier 1988, Sivak 1989] are representative of workplace

EXECUTIVE OFFICES & RESEARCH CENTER
RESEARCH PARK DRIVE, P.O. BOX 14052
LEXINGTON, KENTUCKY 40512-4052
(859) 288-4960 • FAX (859) 288-4999
pgrass@asphaltinstitute.org
www.asphaltinstitute.org

exposures [NIOSH 1997a]. The Nomination also noted that “no significant animal inhalation studies to evaluate the risk for cancer have been reported” [NIOSH 1997a].

NTP’s Board of Scientific Counselors approved, and its Executive Committee directed, additional research based on the ICCEC recommendation and the NIOSH Research Nomination [NTP 1999]. NIOSH researchers have responded with several new findings [Ma 2002, 2003a. b; Wang 2001]. Two major studies that are intended to address the major epidemiological and toxicological data gaps are now underway.

The IARC Case-Control Study of European Asphalt Workers

IARC is conducting a large multi-country study of European asphalt workers that was initiated after IARC found the available human data to be insufficient for an evaluation of the potential carcinogenicity of asphalt fumes and determined that the proposed epidemiological study was feasible [Partanen 1994, 1995]. The first phase of the project, a retrospective cohort study of almost 30,000 European asphalt workers, was completed in 2001 [Boffetta 2001, 2003a, b]. The IARC investigators found a small increase in lung cancer risk but, because of the likelihood of confounding due to coal tar exposures and tobacco use, were unable to conclude on the presence or absence of a causal link between exposure to asphalt fumes and risk of cancer [Boffetta 2003b]. They recommended a follow-up nested case-control study of the lung cancer risk in the cohort with individual data on exposures to asphalt and confounders [Boffetta 2003a]. Approximately one year after the IARC Cohort Study was completed, Watkins, et al. reported on a study of U.S. asphalt roofing manufacturing and asphalt production workers, which found no apparent dose-response relationship between asphalt fumes and lung cancer when individual exposure data were evaluated [Watkins 2002].

As we understand it, the protocol for the IARC Case-Control Study has been finalized and approved, and the Study is fully funded and will begin this summer, 2004. The Study will collect more detailed information on occupational and non-occupational factors for all cohort members who died from or were diagnosed with lung cancer (the cases) and a sample of cohort members, matched by date of birth and country, who were free from lung cancer (the controls). The main hypothesis to be tested will be whether the risk of lung cancer is increased according to estimated exposure to asphalt fumes, coal tar or other agents occurring in the asphalt industry, while adjusting for the estimated carcinogenic effect of tobacco smoking and exposure to other known and suspected lung carcinogens. The Study is anticipated to be completed in three years.

The Fraunhofer Institute Inhalation Study in Rats

The other principal data gaps identified during NTP’s 1997-98 review are being addressed by the ongoing two-year inhalation carcinogenicity bioassay in Wistar rats being conducted by the Fraunhofer Institute of Toxicology and Experimental Medicine. In this study, which began in Spring 2003 with the in life portion to be completed less than a year from now. The rats are being exposed by nose-only inhalation to asphalt fume concentrations of 4, 20 and 100 mg/m³, based on the results of acute and 90-day toxicity studies which were completed prior to the bioassay.


The Fraunhofer investigators have devoted considerable effort to developing and validating a laboratory fume generation procedure that is designed to yield fumes representative of worker exposures [Fraunhofer 2003]. We understand these efforts included consultations with NIOSH. As NTP has recognized [NTP 1999], this is a crucial step to address various studies

indicating that the laboratory fume condensates tested in the NIOSH skin-painting studies are markedly different in composition and potential biological activity from asphalt fumes generated under field conditions [Kriech 1999, Kurek 1999, McCarthy 1999]. These concerns have taken on greater weight as a result of subsequent studies indicating that field fumes generated in U.S. asphalt paving and roofing operations appear to have even lower potential for genotoxic effects than the non-active fractions of the NIOSH laboratory fume condensates [Kriech 2002, 2004].

Conclusion

During the period since NTP last evaluated the data on asphalt fumes, no major studies have been reported that change fundamentally the conclusion that additional data are needed for a scientifically sound evaluation of the potential carcinogenicity of asphalt fumes. Subsequent authoritative reviews by ACGIH [2000, 2001], NIOSH [2000], Cal/OSHA [2003], and the WHO's International Programme on Chemical Safety [CICAD 2004] are all consistent with the NIOSH Research Nomination that NTP acted-on in 1997-98. The ongoing IARC and Fraunhofer studies directly address the primary data gaps identified at that time and are expected to be completed in the next several years. In light of these facts, we believe that the NTP should defer any formal review of asphalt fumes for listing in the RoC pending the completion of the ongoing studies.

Sincerely,



Peter Grass, President

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