

Interoffice Memorandum

Date: 12/10/2018

To: Mr. Aaron Yeow, US EPA and Dr. Louis Anthony Cox, US EPA CASAC, Chair

From: Dr. Jack Harkema, DVM, PhD, DACVP, ATSF, Concerned Private Citizen

Subject: Personal comments on the US EPA, Integrative Science Assessment for PM, October 2018 Draft Document

My name is Jack Harkema. I am a Professor of Pathobiology at Michigan State University. I have conducted toxicology research on the health effects of air pollutants for over 30 years. I have served as a member of the chartered CASAC from 2012 to 2018, and as a member of the CASAC PM Review Panel from 2015 to 2018. My comments are as a concerned private citizen.

The EPA authors are to be commended for a clearly written and comprehensive first draft of the Integrated Science Assessment (ISA) for Particulate Matter (PM). The magnitude of the scientific literature to be reviewed since the last ISA is enormous and the authors have done an exceptional job in identifying pertinent data from a wide range of disciplines and incorporating it in a well-organized and integrative manner.

I have decided to focus the remainder of my comments on the review process for this ISA. I will provide only one specific example to illustrate my concern and recommendation.

One of the most striking changes in this draft ISA from the previous ISA is the determination that there is a *likely to be causal relationship* between nervous system effects and long-term PM exposure. This determination is based on new scientific findings that *neuroinflammation and morphologic changes in the brain, indicative of neurodegeneration, has been substantiated and coherent across experimental and epidemiologic studies*. This conclusion, however, is based on data from predominantly animal toxicology studies in laboratory rodents and not human epidemiological studies.

As an inhalation toxicologist and veterinary pathologist, I am impressed by the quality of the animal studies that have documented these neurological changes caused by controlled PM exposure. However as a comparative pathologist I know that the structure and function of the nose in laboratory rats and mice are markedly different than that of humans raising uncertainties in translating these findings in animals to people.

It has been documented in some animal studies that ultrafine particles depositing in the rodent nose can be directly transported to the brain by way of nasal olfactory nerves. Inhaled particles translocated to the brain could incite damaging neuroinflammation and neurodegeneration, but laboratory rodents can only breathe through their nose (they are obligate nose breathers) while we breathe through our nose and mouth. Therefore the dose of particles to the rodent nose during exposures could be substantially larger than that in humans making these animals more susceptible to nasal particle deposition, particle transport to the brain and subsequent injury to the central nervous system.

In addition, the anatomy of the rodent nose is more structurally complex allowing for much better filtration of inhaled particles compared to the human nose. Furthermore, greater than 50% of the rodent nasal passage is lined by olfactory epithelium compared to less than 5% in the human nose. Therefore the chances of particles depositing on olfactory epithelium and then translocating to the brain is much greater in laboratory rodents than in humans. These species differences again raise questions about how to translate nervous system findings in animals to the human condition.

My point is neither to reject nor accept the authors' conclusions in regard to the causality of nervous system effects and long-term PM exposure, but to emphasize the need for more deliberation among experts from multiple disciplines to properly assess the data and the conclusions made by the EPA authors. In this specific case, it is necessary to have not only toxicologists, epidemiologists and aerosol scientists, but also neuroscientists and comparative animal biologists at the table to properly assess the rigor of the science and the interpretation of the findings. I urge the CASAC to reinstate a PM review panel composed of recognized experts with different perspectives to ensure the best review.

In his recently released and heralded book *Factfulness*, Dr. Hans Rosling warns against the *Single Perspective Instinct*. He emphasizes that to control this dangerous instinct, *it is better to look at problems from many angles to get a more accurate understanding and find practical solutions*. I urge the CASAC to avoid falling into the trap of *single mindedness*. Thank you for your time.

Respectfully submitted,

Jack R. Harkema, DVM, PhD, DACVP, ATSF  
University Distinguished Professor of  
Pathobiology & Diagnostic Investigation  
The Albert C. and Lois E. Dehn Endowed  
Chair in Veterinary Medicine  
Institute for Integrative Toxicology  
College of Veterinary Medicine  
Michigan State University  
1129 Farm Lane, Room 212  
Food Safety and Toxicology Bldg.  
East Lansing, MI 48864  
Tel: 517/353-8627  
Fax: 517/353-9902  
Email: [harkemaj@msu.edu](mailto:harkemaj@msu.edu)