July 21, 2021

Ms. Katherine Chalfant
Enterprise Quality Management Division
Office of Enterprise Information Programs
United States Environmental Protection Agency
1301 Constitution Ave NW
Washington, D.C. 20460

Dear Ms. Chalfant:

In his March 1, 2021 letter regarding the Request for Reconsideration (RFR #17002A) of the Chloroprene EPA IRIS Toxicological Review, Robert Holden (Counsel for Denka Performance Elastomer LLC) concludes that health data collected by the Louisiana Tumor Registry (LTR) indicate that St. John the Baptist Parish exhibited average or below-average rates of cancer incidence compared with cancer incidence rates for the state of Louisiana. He asserts that this comparison of cancer incidence rates is supportive of the validity of the PBPK model results from Ramboll Environ.

As a cancer epidemiologist, I have significant reservations with Mr. Holden's interpretation of the LTR data. **While the LTR is a valid source for assessing the overall burden of cancer in Louisiana for a defined period, the use of these data comparing the cancer incidence rates for an individual parish to the state overall to conclude that there is no increased risk due to chloroprene exposure is not valid**. I provide the following reasons as a basis for this assertion:

- Use of cancer rates to indicate an absence of an effect. A lack of statistically significant difference comparing age-adjusted cancer incidence rates for a parish compared to the state overall does not indicate a lack of an association with an exposure (i.e., cannot be used to say that chloroprene is not associated with increased risk of cancer). A lack of statistical significance may reflect limitations in LTR data (e.g., sample size, misclassification, missing data). Additionally, guidance from the LTR for Cancer Incidence in Louisiana by Census Tract, 2008-2017, states that "cancer rates alone neither prove a link between cancer and an industrial emission nor disprove such a link".

- LTR data are summary age-adjusted cancer incidence rates. While these rates account for differences in age distributions, they do not account for important confounders (e.g., smoking, access to healthcare, obesity) that may mask differences in cancer rates. Additionally, the age-adjusted rates reflect a summary measure across multiple age categories. If cancer incidence rates are different across age categories, then a summary measure would not be appropriate.

- Focus on total cancer incidence rate only does not capture cancer-specific risk. While Mr. Holden's letter highlights that the total cancer incidence rates for

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residents[1] are average or below-average in St. John the Baptist Parish compared to the state overall, the LTR data indicates significantly higher rates of prostate cancer and non-Hodgkin lymphoma in the parish compared to the state.

- Mr. Holden's statement reflects an ecological fallacy. Inferences at the parish-level may not reflect the biologic effect at the individual-level. The comparison of parish-level cancer incidence rates to the state overall assumes that all residents in St. John the Baptist Parish are exposed to the same level of chloroprene and that no individuals residing outside the parish have been exposed. This is likely not true.[1]

Given these considerations, the conclusion made by Mr. Holden cannot be scientifically supported by the Louisiana Tumor Registry data.

Sincerely,

Miranda Jones, PhD
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cc:
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Kelly Rimer, Office of Air and Radiation
Jaclyn Hotard Gaudet, St John the Baptist Parish President
Robert Holden, Counsel for Denka Performance Elastomer LLC

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[1] The LTR ignores, for example, incidence rates of cancer for employees of the DuPont/Denka Plant who do not reside in St. John the Baptist Parish.

This response represents my research and views and not those of the Johns Hopkins University or the Johns Hopkins Bloomberg School of Public Health.