National Toxicology Program
U.S. Department of Health and Human Services

NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES
111 T.W. ALEXANDER DRIVE
P.O. BOX 12233
RESEARCH TRIANGLE PARK, NC 27709

DATE: December 1, 2021

TO: NTP Board of Scientific Counselors

FROM: Designated Federal Official for the Board

SUBJECT: Public Comments from the American Wood Council

Please find attached public comments received from Stewart E. Holm, Chief Scientist, American Forest & Paper Association, American Wood Council.

The Division of the National Toxicology Program at the National Institute of Environmental Health Sciences has conducted toxicity and carcinogenicity studies with the monoterpene, α-pinene, a common indoor air pollutant that is emitted from a number of plants (e.g., pine trees, cannabis, rosemary) and is widely used as a fragrance and flavor ingredient in consumer products. We are currently reviewing findings from these studies for publication in an NTP Technical Report in 2022.

[redacted]

Mary S. Wolfe, Ph.D.

AMERICAN WOOD COUNCIL

December 1, 2021

NTP Board of Scientific Counselors
530 Davis Drive
Durham, NC 27713

RE: α-Pinene Research Request

Dear Members of the Board:

We are writing to recommend that the NTP Board of Scientific Counselors (the Board) consider advising NTP to undertake an assay of α_{2u}-Globulin accumulation in the male rat kidney upon exposures to α-Pinene. As the Board is aware, NTP has underway a rodent cancer bioassay of α-Pinene.

Two other monoterpene bioassays that have been conducted by NTP, for d-Limonene[1] and beta-Myrcene[2], were found to produce male rat kidney tumors along with associated α_{2u}-Globulin nephropathy. In its three-month study of α-Pinene[3], NTP found exposure-related male rat kidney granular casts and hyaline droplet accumulation. Such accumulation is known to be associated with increases in α_{2u}-Globulin. (We note here of interest, that all three chemicals have the same chemical formula: $C_{10}H_{16}$).

If the NTP cancer bioassay of α-Pinene shows male rat kidney tumors, there will likely arise questions concerning mode of action and human relevance. NTP should be prepared in advance to address a possible α_{2u}-Globulin nephropathy mode of action. Accordingly, we encourage the forementioned assay to be initiated as soon as possible.

We recommend the Board place this matter on its December 8, 2021 meeting agenda.

Please contact me if you have any comments or questions.

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[1] NTP (National Toxicology Program) Tech Rep ser. 347 (1990).
[2] Complex Histopathologic Response in Rat Kidney to Oral Beta-myrcene: An unusual dose-related nephrosis and low-dose Alpha2U-Globulin Nephropathy. (Toxicologic Pathology, 41: 1068-1077, 2013).
[3] Toxicity Studies of Alpha-pinene administered by inhalation to F344/N Rats and B6C3F1/N Mice. (Toxic Rep. ser. 2016 May; NTP-Tox-81).

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Thank you,

Sincerely,

/s/ Stewart E. Holm

Stewart E. Holm
Chief Scientist
American Forest & Paper Association
American Wood Council
[redacted]