



California Society of
ANESTHESIOLOGISTS
Physicians for Vital Times



January 27, 2020

Julian Leichty
Office of Environmental Health Hazard Assessment
Proposition 65 Implementation
P.O. Box 4010, MS-12B
Sacramento, California 95812-4010

Dear Mr. Leichty,

The California Society of Anesthesiologists and the Society for Pediatric Pain Medicine are deeply concerned about the process underway by the California Environmental Protection Agency's Office of Environmental Health Hazard Assessment (OEHHA) to consider adding acetaminophen as a medicine listed under Proposition 65.

Tylenol, or Acetaminophen, is one of the most common over-the-counter drugs to treat pain and fever. It has been found to be low risk in pregnant patients and has become a popular and important alternative to opioids during the opioid epidemic. Unfortunately, there is now a misguided effort that could add acetaminophen to the Proposition 65 list, labeling the medicine as a carcinogen, in a similar fashion as to how the weed killer Roundup was labeled in 2017. This is not justified by scientific evidence and instead could actually prove detrimental to patient safety.

When used appropriately, the benefits of acetaminophen outweigh rare or potential risks. Based on review of the literature and information presented, it is the opinion of the California Society of Anesthesiologists and the Society for Pediatric Pain Medicine that labeling acetaminophen as a carcinogen is misleading the public, and we are opposed to current attempts to add it to the Proposition 65 list. Furthermore, we believe this could create an incentive for trial attorneys to increase erroneous claims linking acetaminophen to cancer.

Statistical analysis of the literature does not show a clear causal relationship of acetaminophen with cancer. Studies are negative or mixed (Weiss). Most any drug, if misused or given in high doses, can be deleterious to the body. Individual patient differences also need to be accounted for. But after many studies and decades of use, acetaminophen has a strong body of evidence to support its safety and efficacy. The U.S. Food & Drug Administration has stated that "currently available data do not support a conclusion that exposure to acetaminophen in FDA-regulated products causes cancer," and that adding a Proposition 65 cancer warning on labeling of acetaminophen products would misbrand them and violate federal law. Furthermore, the International Agency for Research on Cancer evaluated

acetaminophen and found that the data was inadequate to classify the medicine as carcinogenic to humans.

Of additional interest, acetaminophen has shown some benefit in improving chemotherapy treatment in breast cancer. Japanese researchers have found in mice that aggressive, undifferentiated breast cancer stem cells become more differentiated with acetaminophen, which improves chemotherapy activity in killing these cancer cells (Takehara).

In summary, current literature does not support labeling acetaminophen as a carcinogen in humans at regular dosages. Acetaminophen is not only safe but it is also the best option for some special populations – for example it is the only pain reliever/fever reducer that is safe for infants under six months, it is the most appropriate option for patients with stomach conditions, heart disease, high blood pressure, asthma, or kidney disease, or who are pregnant. Additionally, in light of the opioid epidemic, acetaminophen is being positioned as a preferred first line of treatment for pain and an important alternative to opioids. Acetaminophen has been incorporated into many “Enhanced Recovery After Surgery” (ERAS) protocols as a core strategy to reduce dependence on post-operative opioids.

Research and good clinical judgement should be our compass in this evaluation. We believe a Prop. 65 listing for acetaminophen would confuse consumers and create concerns that would push them to other pain medications with a less favorable risk-benefit profile for their individual need.

CSA and SPPM strongly oppose the current proposal being considered by OEHHA to add a Proposition 65 warning to acetaminophen.

Sincerely,

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References:

- Takehara M, et al. Acetaminophen-induced differentiation of human breast cancer stem cells and inhibition of tumor xenograft growth in mice. *Science Direct. Biochemical Pharmacology* 81 (2011): 1124–1135.
- Weiss NS. Use of acetaminophen in relation to the occurrence of cancer: A review of epidemiologic studies. *Cancer Causes Control* (2016) 27: 1411–1418.
- Letter to OEHHA from Janet Woodcock, MD, Director, Center for Drug Evaluation and Research, Food and Drug Administration, November 4, 2019 (<https://oehha.ca.gov/media/dockets/19653/19710->

[u.s. food and drug administration fda/fda comments notice of availability of hazard identification materials for acetaminophen 1142019.pdf](#)

- International Agency for Research on Cancer (IARC) Monographs (<https://monographs.iarc.fr/>)

**CC: Christine Hironaka, Deputy Cabinet Secretary, Office of the Governor
Richard Figueroa, Deputy Cabinet Secretary, Office of the Governor**