



## LOMA LINDA UNIVERSITY

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Ms. Cynthia Oshita  
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Proposition 65 Implementation  
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Dear Ms. Oshita,

I have just learned from your web site that both triclosan and fluoride are being reviewed and evaluated for possible addition to the chemical list per Proposition 65, and there will be a hearing on the topic on May 29, 2009. As I will be out of country on May 29<sup>th</sup>, I would like to write to you expressing my concerns and opinions on the safety of triclosan and fluoride used for dental care.

I would like first to briefly introduce myself. Currently I am Professor of Restorative Dentistry and Director of Center for Dental Research at Loma Linda University School of Dentistry, responsible for research programs in the School. I am also Professor of Microbiology and Molecular Genetics at Loma Linda University School of Medicine. Prior to my appointments at Loma Linda University, I was a faculty at Indiana University School of dentistry. I also held a joint appointment in the Department of Pharmacology and Toxicology at Indiana University School of Medicine. During my career, I have served on numerous research, ethics, and faculty committees, and currently I am a voting member of the Food and Drug Administration (FDA) Dental Products Panel and serve as a consultant to the American Dental Association (ADA) and California Dental Association (CDA). Since 1998 I have been Chairman for SCDP subcommittee for Biological Evaluation of Dental Materials, which prepares the American National Standard/ADA Specification No. 41 for evaluation of biocompatibility of dental materials. My research has generated more than 200 publications, and I provide services to review grant applications and journal manuscripts, including *Food and Chemical Toxicology*, the *Journal of Dental Research*, among others.

If I understood correctly, both triclosan and fluoride are being reviewed because of speculative questions on their carcinogenesis. My PhD research was on genetic toxicity of fluoride, which generated nine articles. While the topic may still be confusing from an internet search, it has become

less controversial than it was in earlier years, and a careful assessment of credible scientific data does not support the unfounded claim of fluoride carcinogenesis in any forms of fluoride used for dental care. However, over years such confusion has been costly to the government, public and dental professional.

The available scientific data on triclosan is the same, that is, credible literature indicates a lack of evidence for its carcinogenicity. Triclosan safety has been reviewed by numerous regulatory agencies. These reviews have included an assessment of its potential of carcinogenicity. As you may know, the FDA conducted comprehensive reviews on studies of Total toothpaste, which contains 0.3% triclosan, and determined that the potential for human carcinogenicity was not a concern. More recently, an Australia chemical agency (NICNAS), the European Scientific Committee for Consumer Products (SCCP) and the US EPA all reviewed the issue of triclosan safety, including its potential for carcinogenicity and all reached the same conclusion that triclosan is not a carcinogen. A brief summary of these three documents is as follows.

- The NICNAS assessment of triclosan was published in 2009. After reviewing available literature, it concluded that based on the available animal data, triclosan does not meet the Approved Criteria (NOHSC, 2004) for classification as a carcinogen. The full report of the NICNAS assessment is available through the following link:  
[http://www.nicnas.gov.au/Publications/CAR/PEC/PEC30/PEC\\_30\\_Full\\_Report\\_PDF.pdf](http://www.nicnas.gov.au/Publications/CAR/PEC/PEC30/PEC_30_Full_Report_PDF.pdf).
- In its 2009 opinion on triclosan safety for use in cosmetic products, the SCCP reviewed all three studies on triclosan that reported carcinogenicity findings. The committee's conclusion (SCCP Opinion on Triclosan, Jan 21, 2009) is as follows: *“Three rodent lifetime bioassays have been conducted to evaluate the carcinogenic potential of triclosan. Triclosan produced hepatic effects and hepatic tumours in mice, but little evidence of toxicity and no tumours in rats. Hamsters showed increased liver toxicity relative to the rat, but no tumours. According to the EU classification system, triclosan is not considered classifiable as a carcinogen. It should be noted that triclosan is a peroxisome proliferator in mice liver.”* Relevant SCCP documents can be obtained from the following link:  
[http://ec.europa.eu/health/ph\\_risk/committees/04\\_sccp/docs/sccp\\_o\\_166.pdf](http://ec.europa.eu/health/ph_risk/committees/04_sccp/docs/sccp_o_166.pdf).
- EPA also assessed the data from the triclosan carcinogenicity studies during its 2008 review of triclosan for re-registration eligibility. In their *Risk Assessment for the Reregistration Eligibility Decision (RED) Document*, EPA states the following conclusion: *“On July 25, 2007, the Health Effects Division's Carcinogenicity Assessment Review Committee met to discuss the carcinogenicity classification for triclosan and additional data submitted conducted with triclosan in support of a mode of action involving peroxisome proliferation as a causative factor in the positive tumorigenic results observed in the mouse carcinogenicity study. In accordance with the EPA Final Guidelines for Carcinogen Risk Assessment (March 29, 2005), the CARC classified triclosan as “Not Likely to be Carcinogenic to Humans”. This decision is based on the weight-of-evidence that supports activation of peroxisome proliferator-activated receptor alpha (PPAR $\alpha$ ) as the mode of action for triclosan-induced hepatocarcinogenesis in mice. The data did not support either mutagenesis or cytotoxicity followed by regenerative proliferation as alternative modes of action. While the proposed mode of action for liver*

*tumors in mice is theoretically plausible in humans, hepatocarcinogenesis by this mode of action is quantitatively implausible and unlikely to take place in humans based on quantitative species differences in PPAR $\alpha$  activation and toxicokinetics. The quantification of risk is not required.*" This EPA document is available from the following link:

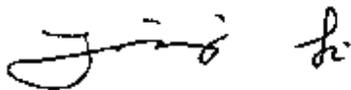
<http://www.regulations.gov/fdmspublic/component/main?main=DocumentDetail&o=0900006480741d39>)

As you know, triclosan and fluoride have been used in dentistry for many years, providing effective means for dental professionals and consumers to combat dental decay and gum diseases. The use of fluoride for preventing dental decay is one of the most successful public health measures and has been benefiting millions of ordinary people throughout the world for more than a half century. Further, triclosan at low concentrations in oral care products has clearly demonstrated its efficacy on preventing gum diseases and improving gum health. With success in controlling dental decay, the challenges we face in dental care has been increasingly the gum health. Triclosan provides an effective means to combat gum diseases for general consumers at an affordable cost. It would be unfortunate if the public is unnecessarily deprived of the access to the proven benefits of triclosan and fluoride for their oral care needs.

In summary, all credible data relating to the potential of triclosan to be a carcinogen have been reviewed by numerous regulatory bodies around the world with the conclusion that triclosan does not present a concern for human carcinogenicity. I believe that the available scientific evidence is adequate for the conclusion that neither triclosan nor fluoride used in dentistry is potentially carcinogenic. Therefore, I would like to urge you not to include triclosan and fluoride in the chemical list for consideration of its evaluation through public hearing per California Proposition 65, as this process may cause unnecessary misunderstanding and confusion, which can be costly to all the interested parties.

Thank you for taking the time to read my letter. Please do not hesitate to contact me if you need further information regarding my comments. My email address is yli@sd.llu.edu, and my other contact information is indicated on the first page of this letter.

Sincerely,



Yiming Li, Ph.D.  
Professor and Director

CC: Dr. Charles Goodacre, Dean, Loma Linda University School of Dentistry  
Dr. Clifford Whall, American Dental Association  
Dr. Wayne Wozniak, American Dental Association