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May 5, 2009

Cynthia Oshita
Office of Environmental Health Hazard Assessment
Proposition 65 Implementation
P.O. Box 4010
1001 I Street, 19th floor
Sacramento, California 95812-4010

Submitted by e-mail: coshita@oehha.ca.gov

Re: Listing of Triclosan by OEHHA for Further Prioritization and Listing under California Proposition 65

Dear Ms. Oshita:

The Dial Corporation ("Dial"), a manufacturer of consumer and personal care products, welcomes the opportunity to provide comments regarding the California Environmental Protection Agency's Office of Environmental Health Hazard Assessment (OEHHA) public notice of March 5, 2009 regarding the review of 38 chemicals by the Carcinogen Identification Committee (CIC) for further prioritization and listing under Proposition 65. As a member of the Soap and Detergent Association (SDA), Dial also supports the comments submitted by the SDA regarding this matter.

As indicated in OEHHA's public notice of March 5th, OEHHA performed a preliminary toxicological evaluation of the chemicals identified via the application of epidemiology and animal data screens. In addition, literature searches were also employed to identify information relevant to carcinogenicity, such as studies on genotoxicity, mechanism of action, metabolism and pharmacokinetics. This information was then used to conduct a preliminary evaluation of the overall evidence of carcinogenicity for each of the chemicals identified by the data screens. Chemicals for which a preliminary evaluation of the available evidence indicated that carcinogenicity may be a concern were then proposed for CIC consideration.

As further announced by OEHHA on April 10, 2009, the next step of this process will include a recommendation by the CIC on May 29, 2009 regarding the priority ranking (i.e., high, medium, low, or no priority) assigned to each listed chemical for the purpose of preparing future hazard identification materials.

Dial would like to bring to OEHHA's attention that an extensive toxicological and human exposure database, collected over more than 40 years of study and real-world application, exists for triclosan, and that this data confirms that triclosan is safe for humans. As such, Dial does not believe that the preliminary toxicological evaluation conducted by OEHHA's supports the listing of triclosan for the following reasons:

- No epidemiology study exists which indicates that triclosan causes of health problems in human populations
- Triclosan has not been shown to be carcinogenic in two or more studies and there is no evidence to support the notion that triclosan is a human carcinogen

The Dial Corporation
15101 N. Scottsdale Road
Scottsdale, AZ 85254-2199
USA

www.dialcorp.com
www.henkel.us
Phone 480.754.3425
Fax 480.754.6284

- There is extensive data that demonstrates that triclosan is neither genotoxic nor mutagenic
- Triclosan's mechanism of action is different from other structural analogues that are tumorigens or P65 carcinogens
- Triclosan does not disrupt hormonal activity or function
- The metabolism and disposition studies of triclosan in multiple animal species suggest that the general disposition of triclosan is most similar between hamsters and humans and that triclosan is not likely to be a human carcinogen

Further details regarding each of these points is presented below.

1. Epidemiological Evidence

Triclosan has been used in a variety of consumer products since 1968. Extensive safety and efficacy data have been submitted to the USEPA and US Food and Drug Administration (FDA) in support of triclosan consumer and OTC drug product applications (e.g., topical OTC drugs, medical devices, toothpastes) at concentrations of up to 1.0 percent. No epidemiological studies of potential chronic or carcinogenic effects in workers or of the general population who use triclosan-containing products have been conducted. Thus, there are no epidemiological studies involving triclosan that are appropriate for application of OEHHA's Epidemiology Data Screens. The extensive database collected over more than 40 years of study and real-world application confirms that triclosan is safe for humans.

2. Triclosan Has Not Been Shown To Be Carcinogenic In Two Or More Studies

The preliminary toxicological evaluation for triclosan by OEHHA suggests that there are "two or more positive animal cancer studies" (first screen criteria). Across a number of studies conducted on triclosan, only one study presented positive findings – a mouse study which is not relevant to humans. There is sufficient weight-of-evidence to establish a mode of action for peroxisome proliferator-activated receptor alpha (PPAR α) for triclosan-induced hepatocarcinogenesis in mice. The proposed mode of action for liver tumors was found quantitatively unlikely to take place in humans.

Carcinogenicity studies in rats and hamsters indicate no carcinogenicity effects. A United States Environmental Protection Agency (EPA) Cancer Assessment Review Committee (CARC) review of the relevant carcinogenicity data on triclosan on March 19, 2005 concluded that:

"In accordance with the EPA Final Guidelines for Carcinogen Risk Assessment (March 19, 2005), the Cancer Assessment Review Committee (CARC) classified Triclosan as Not likely to be Carcinogenic to Humans".

In 2008, EPA concluded that triclosan should not be considered a human carcinogen for the following reasons:

- 1) Positive results in mice but not rats or hamster;
- 2) The absence of any mutagenic or genotoxic effects;
- 3) Difference in metabolism in mice compared to hamsters and humans; and
- 4) Clear evidence that triclosan produced liver tumors in mice by a mode of action that is not relevant to humans.

Based on EPA's conclusions, OEHHA should not include triclosan in their prioritization process as a chemical classified as a human carcinogen.

3. Triclosan Is Not Genotoxic Or Mutagenic

A battery of 24 in vitro and in vivo mutagenicity and genotoxicity tests were reviewed by EPA's CARC in 2008 as part of an evaluation of the carcinogenic potential of triclosan. These studies were designed to evaluate the full range of potential to produce mutagenic or genotoxic effects in prokaryotic and eukaryotic systems. Of these 24 experiments, only three yielded weakly positive responses for the endpoints evaluated. Two of these assays used in vitro systems, while the third was an in vivo test. The few weakly positive results are not consistent with respect to type of genetic alterations observed nor have the observations been duplicated in the same or equivalent assays. Accordingly, the overall weight-of-evidence from these experiments indicates that triclosan is not mutagenic or genotoxic.

Additionally, EPA's 2008 "Cancer Assessment Document: Evaluation of the Carcinogenic Potential of Triclosan concluded that:

"Triclosan has intrinsic mutagenic activity in vitro but this is not expressed in whole animals. Accordingly there is no mutagenicity concern for triclosan".

Based on the USEPA's conclusion and the overall weight-of-evidence from mutagenicity and genotoxicity studies conducted, triclosan should not be considered by OEHHHA as a mutagenic or genotoxic.

4. Triclosan's Mechanism Of Action Is Different From Other Structural Analogues That Are Tumorigens Or P65 Carcinogens

In 2008, the U.S. EPA classified triclosan as a member of the diphenyl ether class of chemicals and stated that no appropriate analogs were available for comparison. Polychlorinated biphenyls (PCBs), polybrominated diphenyl ethers (PBDEs) such as the decabromodiphenyl oxide (DBDE), and the mechanistic "analog" di(ethylhexyl)phthalate (DEHP), are structurally different. As such, the mechanisms of actions of these compounds are different and not relevant to triclosan.

We concur with USEPA's assessment that there is "no appropriate structural analogs were available for comparison".

5. Triclosan Does Not Disrupt Hormonal Activity Or Function

There are numerous hormonal systems in the body each with specific chemical messengers. The recent findings regarding triclosan's effects on thyroid hormone receptors, blood serum thyroxine (T4) and testosterone induced transcriptional activity have questions regarding the real world association to humans and animals. Studies in whole animal models show no effect of triclosan on endocrine organs or their functions.

6. Metabolism And Disposition Studies Of Triclosan In Multiple Animal Species Suggest That The General Disposition Of Triclosan Is Most Similar Between Hamsters And Humans and That Triclosan Is Not Likely To Be a Human Carcinogen

The pharmacokinetics of triclosan has been evaluated in animals and humans exposed by the oral and dermal routes. The metabolism and disposition studies of triclosan in multiple animal species (rats, mice, hamsters, dogs, and monkeys) suggest that the general disposition of triclosan is most similar between hamsters, monkeys, and humans. Data indicate that hamsters, monkeys and humans show triclosan glucuronide conjugates (parent and/or non-parent) as the major metabolites while the majority of triclosan detected is in the form of the parent sulfate conjugate in the mouse and the dog. In the rat and the mouse, enterohepatic recirculation and biliary excretion play a much larger role than in the hamster or the human.

Data indicate that both humans and hamsters show urinary excretion as the major route with the glucuronide conjugate as the major urinary metabolite. By contrast, the rat and the mouse show greater excretion in feces. Similar distribution patterns were noted in the hamster and the rat, with no evidence of accumulation in tissues. In the mouse there was evidence of accumulation in the liver. In humans, glucuronidation of the parent and excretion in urine appears to be the preferred clearance pathway for triclosan, resulting in limited free parent remaining for delivery to target organs. These results taken together indicate that significant differences in kinetics exist between mice and humans confirming a lack of relevance of the mouse carcinogenicity study to humans.

Furthermore, we concur with EPA's 2008 conclusion that there is sufficient evidence that triclosan is a PPAR α agonist and that triclosan is "Not likely to be a human carcinogen".

Concluding Remarks

In conclusion, an extensive database collected over more than 40 years of study and real-world application confirms that triclosan is safe for humans. Carcinogenicity studies in rats and hamsters indicate no carcinogenicity effects. The positive findings in the mouse study has been extensively reviewed and determined not relevant to humans. The review of the carcinogenicity studies by the EPA in 2008 resulted in the conclusion that triclosan is not a potential human carcinogen (*U.S. Environmental Protection Agency, 2008 Cancer Assessment Document: Evaluation of the Carcinogenic Potential of Triclosan. Cancer Assessment Review Committee, Health Effects Division, Office of Pesticide Programs*).

Dial appreciates the opportunity to comment on OEHHA's public notice regarding the review of 38 chemicals by the Carcinogen Identification Committee (CIC) for further prioritization and listing under Proposition 65. Based on the information presented, Dial does not believe that the preliminary toxicological evaluation conducted by OEHHA's supports the listing of triclosan. Therefore, we urge OEHHA to either remove triclosan from the list of chemicals being considered for prioritization or rank triclosan as no priority for further consideration as a human carcinogen.

Please feel free to contact the undersigned at 480.754.5788 or by e-mail at carl.druiz@us.henkel.com if you have any further questions or comments regarding this submission.

Sincerely,



Carl D'Ruiz, MPH
Regulatory Affairs