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On Thursday, March 5th 2009 the California Environmental Protection Agency's Office of Environmental Health Hazard Assessment (OEHHA) released its screened candidate chemicals list. According to the process described, OEHHA identified 38 chemicals for review by the Carcinogen Identification Committee (CIC). At its next meeting, the CIC will provide OEHHA with advice on the prioritization of these chemicals for possible preparation of hazard identification materials. These materials will then be used by the CIC at future meetings to decide which chemicals to add to the Proposition 65 list. No listing decisions will be made concerning these chemicals at the May 29 meeting.

In response to this information, Ciba Inc. is providing this letter and supporting documentation for consideration by the CIC. It is our request that the CIC recommends against accepting triclosan for preparation of hazard identification materials for several reasons:

1. Recent scientific reviews of triclosan by the US EPA (2008), Australian NICNAS (2009), and the EU Scientific Committee for Consumer Products (2009) have not found sufficient evidence of carcinogenicity;
2. According to the 2004 Prioritization Process, it is unlikely a chemical will be proposed for CIC review that has been recently reviewed by a Proposition 65 authoritative body (e.g., US EPA) and found to have insufficient evidence of carcinogenicity;
3. Compared to most of the other 37 chemicals under consideration, triclosan warrants a "low" or "no" priority since the evidence of carcinogenicity is limited to liver tumors in one species, i.e., the mouse, via a mechanism of action not considered relevant to humans (peroxisome proliferation in the liver).

1. Recent Reviews by the US EPA, Australian NICNAS, and the EU Scientific Committee for Consumer Products

Triclosan has already been extensively reviewed by the US EPA, Australian NICNAS, and the EU Scientific Committee for Consumer Products within the past twelve (12) months. Each of these independent, globally respected regulatory agencies reached similar conclusions regarding the potential carcinogenicity and genotoxicity of triclosan. These publicly available opinions are herewith provided on the enclosed disk, with important excerpts listed below.

US EPA Reregistration Eligibility Decision (October 2008)

- **Carcinogenicity**

“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”.** [emphasis added] This decision is based on the weight-of-evidence that supports activation of peroxisome proliferator-activated receptor alpha (PPAR?) 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? activation and toxicokinetics. The quantification of risk is not required.” (Risk Assessment Chapter, page 7)

- **Genotoxicity**

“Triclosan has been tested for mutagenic activity in several assays, including bacterial reverse mutation tests (MRID 43533301 and MRID 44389705), an in vitro mammalian cell gene mutation test (MRID 44389704), two in vitro mammalian chromosome aberration tests (MRIDs 43740801 and 47276601), a mammalian bone marrow chromosomal aberration test (MRID 43740802), and an unscheduled DNA synthesis assay in mammalian cells in culture(MRID 47276602).” There are no data gaps for toxicology studies for triclosan at this time. (Toxicology Chapter, page 24).

Australian NICNAS: Priority Existing Chemical Assessment Report No. 30 (January 2009)

- **Carcinogenicity**

“Based on the available animal data triclosan does not meet the Approved Criteria (NOHSC, 2004) for classification as a carcinogen”, page 34.

“Neither of the carcinogenicity bioassay conducted in the rat or hamster provided evidence of a carcinogenic potential”, page 30

“While the mouse is the most sensitive species, there is evidence that (unlike the rat and hamster) it is sensitive to peroxisome proliferator-type effects in the liver that are not considered relevant to humans”, page xv.

- **Genotoxicity**

“Based on the available in vitro and animal data triclosan does not meet the Approved Criteria (NOHSC, 2004) for classification as a mutagen”, page 34.

EU Scientific Committee for Consumer Products, SCCP/1192/08 (21 January 2009)

- **Carcinogenicity**

“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 mouse liver”. (page 121)

- **Genotoxicity**

“Consequently, triclosan can be considered to have no relevant genotoxic potential in vivo.” (page 121)

2. According to the 2004 Prioritization Process, triclosan is an unlikely candidate for prioritization since it has been recently reviewed by a Proposition 65 authoritative body (e.g., US EPA) and found to have insufficient evidence of carcinogenicity.

Triclosan is an unlikely candidate for prioritization. The 2004 Prioritization Process states:

“It is unlikely that chemicals will be proposed for CIC or DART IC review that have been recently reviewed by an authoritative body and found to have insufficient evidence of carcinogenicity or reproductive toxicity, respectively. Exceptions to this generalization may occur, for example, if an authoritative body has evaluated a chemical but failed to review all relevant data, or compelling new data have become available since the evaluation.”¹

As noted earlier, the potential carcinogenicity of triclosan was reviewed by US EPA, a Proposition 65 authoritative body, in a report published in October 2008. 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.” US EPA has reviewed all relevant data, and no new data have become available since US EPA’s evaluation. Preparing hazard identification materials for triclosan would contradict the guidance provided in the 2004 Prioritization Process and would represent a poor use of the valuable resources of OEHHA.

¹ OEHHA (2004) Process for prioritizing chemicals for consideration under Proposition 65 by the “State’s Qualified Experts.” December, 2004. p. 4.

3. Triclosan warrants a “low” or “no” priority since the evidence of carcinogenicity is limited to liver tumors in one species, i.e., the mouse, via a mechanism of action not considered relevant to humans.

Relative to most of the other 37 chemicals under consideration for prioritization, triclosan should receive a “low” or “no” priority. The evidence of carcinogenicity of triclosan is limited to mouse liver tumors in a single study via a mechanism of action that is not considered relevant to humans. Triclosan produced an increased incidence of liver tumors in male and female mice via activation of peroxisome proliferator-activated receptor alpha (PPAR?), a mode of action that is not relevant to humans. Triclosan did *not* increase the incidence of tumors in carcinogenicity studies in two other species: rats and hamsters. The weight of the scientific evidence indicates that triclosan is not a genotoxic carcinogen. And, as noted by OEHHA, “no cancer epidemiology studies were identified.” Compared to the other 37 chemicals under consideration, triclosan warrants a “low” or “no” priority rating based on the profile of its weak evidence of carcinogenicity.

Ciba Inc. firmly believes that triclosan is safe and effective for its intended use as a nonprescription antibacterial ingredient in consumer products and as a major manufacturer of triclosan, has supported the safety and efficacy of triclosan for use in FDA topical applications, FDA oral drug applications, FDA medical device applications, and EU Consumer Products Applications, among others. The extensive database, collected over more than 40 years of study and real-world application, confirms that the ingredient is effective and safe for humans and the environment. The scientific data supporting the safety of triclosan stands clearly and consistently against misconceptions often presented in activist campaigns and the media. On the basis of this wealth of data triclosan is registered world-wide to support its use throughout the global market and has not been removed from the marketplace by regulatory restrictions in any country.

The OEHHA Summary of Nomination information states that triclosan passed the animal data screen, underwent a preliminary toxicological evaluation, and is being brought to the Carcinogen Identification Committee for consultation. The compilation of the relevant studies identified during the preliminary toxicological evaluation appears to be incomplete. There are robust data summaries available at the FDA Dockets, in the EU SCCP 2009 Opinion Report, and in the 2008 Australian NICNAS report. None of these reports are cited, as such, we are concerned that all of the available information may not have been reviewed and that *the overall request for consultation and assessment may be based on a deficient data set.*

In our review of the rationale for evaluating triclosan, we do not agree that the CIC prioritization of triclosan to a level requiring OEHHA Hazard Identification document preparation and subsequent CIC review will give more certainty or clarity to the safety profile of triclosan because our database of studies has been used worldwide to inform human health risk assessment for all routes of triclosan exposure, most notably from consumer products.

We repeat here, that Ciba is committed to ensuring triclosan is and is perceived as a safe and effective antimicrobial substance suitable for hygiene, health care and medical device products. We welcome the opportunity to further discuss the details of the robust data set available on triclosan and thank you for considering our comments and requests.

Sincerely,

A handwritten signature in blue ink that reads "Lisa J. Navarro". The signature is written in a cursive style with a large initial "L".

Lisa Navarro, PhD, DABT
Director, Product Safety, Toxicology, & Regulatory Affairs
Business Line Home & Personal Care

Enclosures