From: "Gretchen Lee Salter" <Gretchen@breastcancerfund.org> To: <biomonitoring@oehha.ca.gov> CC: "Fabiola Lao" <flao@breastcancerfund.org> Date: Wednesday - December 3, 2008 5:02 PM Subject: New Chemical for Friday's meeting

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Hello,

I would like to add another chemical for the guidance panel's consideration to be included in CA biomonitoring program. I understand that this may have been included already under the CDC's list but I just want to make sure.

Thank you.

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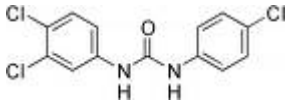
Triclocarban

Also known as TCC; 3,4,4´-trichlorocarbanilide;
Urea, N-(4-chlorophenyl)-N'-(3,4-dichlorophenyl)

($C_{13}H_9Cl_3N_2O$) CASRN: 101-20-2



Uses and extent of exposure:

Triclocarban (TCC) is a carbanilide chemical with a chemical structure similar to some pharmaceuticals and pesticides such as diuron (Ahn, 2008). It is a high production volume chemical which in 1998 was reported to be produced in volumes greater than 500,000 to 1,000,000 pounds/year (250 -500 metric tonnes/year). (EPA, 2002). TCC is widely used in toothpaste, soaps and other detergents where it is promoted for its antimicrobial properties, especially against gram positive bacteria (Ahn, 2008).
The major source of human exposure is thought to be through topical application and dermal absorption.

Because triclocarban is applied topically and excreted with an estimated half-life of 9 hours (Scharpf, 1975), it ends up in waste water. Waste water treatment plants are the major source of environmental contamination and TCC is found in both waste water effluent and biosolid waste. Recently published monitoring research has found TCC in 100% of river water samples collected downstream of wastewater treatment plants, as compared to 56% of those taken upstream (Sapkota, 2007). Concentrations of TCC (mean+/-standard deviation) downstream of sewage treatment plants (84+/-110 ng/L) were significantly higher than those of samples taken upstream (12+/-15 ng/L) (Sapkota, 2007). Compared to surface water, mean TCC concentrations found in dried, primary sludge obtained from municipal sewage treatment plants in five states were six orders of magnitude greater (19,300+/-7100 microg/kg) (Sapkota, 2007). This same group of researchers has suggested that approximately three-quarters of the TCC mass disposed of by consumers ultimately is released into the environment by application of municipal sludge (biosolids) on land used in part for agriculture (Heidler, 2006). It is currently unknown whether liquid or solid discharge of triclocarban is results in contamination of wildlife or whether food crops grown or cattle grazing in fields treated with biosolids will take up TCC.

Toxicity
TCC is a highly persistent chemical in the environment and does not degrade for over a decade. (O'Conner, 2008)

TCC has been described as a "new type" of endocrine disruptor that potentiates steroid hormone responses. Although TCC shows no endocrine activity by itself, in the presence

of natural ligands, TCC enhances the gene expression of several steroids, including androgens, estrogens and cortisol (Ahn, 2008; Lasley, 2008). Dietary exposure to 0.25% TCC for 10 days was found to increase male accessory sex organ weights (seminal vesicles, prostate and levator ani) in intact male rats and uterine weight in females without notable histopathology (Chen, 2007; Lasley, 2008).

Potential to biomonitor

Previous biomonitoring studies: There is limited biomonitoring information on TCC. Small studies have demonstrated that triclocarban is rapidly absorbed across the skin and can be measured in serum within minutes of topical application. Data presented recently at a scientific meeting showed TCC levels went from 0 to 75 ng/ml in serum after showering with a soap containing 0.6% TCC (Hammock, 2008). This is in contrast to older research using older methodologies for measuring radioactive uptake of topically applied triclocarban which did not find any radiolabel in the blood after topical application (Scharpf, 1975).

Analytical methods

Researchers at UC Davis have developed a methodology for measuring TCC in serum: Bruce Hammock, Center for Watershed Resources, UC Davis or Dan Chang, Professor Emeritus, UC Davis.

Another methodology is described in this abstract:

Gruenke LD, Craig JC, Wester RC, Maibach HI, North-Root H, Corbin NC. A selected ion monitoring GC/MS assay for 3,4,4'-trichlorocarbanilide and its metabolites in biological fluids. J Anal Toxicol. 1987 Mar-Apr;11(2):75-80.

A selected ion monitoring gas chromatography/mass spectrometric method for the quantitative determination of 3,4,4'-trichlorocarbanilide (TCC) and its major metabolites (the 2'-hydroxy sulfate and the N- and N'-glucuronides) in human plasma and urine was developed using the deuterium-labelled compounds as internal standards. Limits of detection of 3 ng/mL in urine for the N-glucuronides and of 1.5 ng/mL in plasma for the 2'-hydroxy sulfate were attained. Use of the method was illustrated in a study in human subjects employing TCC-containing bar soaps.

Availability of adequate biospecimens

Previous research has shown that intravenous administration of radiolabeled triclocarban resulted in excretion primarily in feces (54%) and 21% of the dose in the urine with a urinary elimination half-life of ten hours (Scharpf, 1975). No radioactivity was detected in the saliva.

Recent research done at UC-Davis has found triclocarban can be measured in the serum. (Methodology not published but presented at recent meeting, Hammock, 2008)

References

Ahn KC, Zhao B, Chen J, Cherednichenko G, Sanmarti E, Denison MS, Lasley B, Pessah IN, Kültz D, Chang DP, Gee SJ, Hammock BD. In vitro biologic activities of the antimicrobials triclocarban, its analogs, and triclosan in bioassay screens: receptor-based bioassay screens. Environ Health Perspect. 2008 Sep;116(9):1203-10.

Chen, J., Ahn, K. C., Gee, N. A., Ahmed, M. I., Duleba, A. J., Zhao, L., Gee, S. J., Hammock, B. D., and Lasley, B. L. (2008). Triclocarban Enhances Testosterone Action: A New Type of Endocrine Disruptor? *Endocrinology* **149**, 1173-1179.

Hammock, B., "Triclocarban and Triclosan enzymatic assays" Presentation at 3rd annual Pacific Southwest Organic Residuals Symposium, University of California-Davis, October 1, 2008. (Bruce Hammock, Center for Watershed Resources, UC Davis).

Heidler J, Sapkota A, Halden RU. Partitioning, persistence, and accumulation in digested sludge of the topical antiseptic triclocarban during wastewater treatment. Environ Sci Technol. 2006 Jun 1;40(11):3634-9.

Lasley, B., "Triclocarban androgen- and estrogen receptor assays" Presentation at 3rd annual Pacific Southwest Organic Residuals Symposium, University of California-Davis, October 1, 2008. (Bill Lasley, Center for Health and the Environment, UC Davis)

O'Connor G. Fate of Biosolids-Borne Triclosan and Triclocarban. Presentation at 3rd annual Pacific Southwest Organic Residuals Symposium, University of California-Davis, October 1, 2008. (George O'Connor, University of Florida)

Sapkota A, Heidler J, Halden RU. Detection of triclocarban and two co-contaminating chlorocarbanilides in US aquatic environments using isotope dilution liquid chromatography tandem mass spectrometry. Environ Res. 2007 Jan;103(1):21-9.

Scharpf LG Jr, Hill ID, Maibach HI. Percutaneous penetration and disposition of triclocarban in man: body showering. Arch Environ Health. 1975 Jan;30(1):7-14.

U.S. EPA. High Production Volume (HPV) Chemical Challenge Program Data Availability and Screening Level Assessment for Triclocarban. Prepared for the HPV Challenge Program by: The TCC Consortium December 27, 2002. http://www.epa.gov/hpv/pubs/summaries/tricloca/c14186.pdf. [accessed October 7, 2008]