September 12, 2011

Ms. Cynthia Oshita
Office of Environmental Health Hazard Assessment
California Environmental Protection Agency
P.O. Box 4010, MS-19B
Sacramento, CA 95812-4010

Subject: Public Comments - Prioritization: Chemicals Identified for Consultation with the Carcinogen Identification Committee

Dear Ms. Oshita:

Gowan Company appreciates an opportunity to provide a written statement on the carcinogenic potential of hexythiazox in advance of the October 12, 2011 meeting entitled “Prioritization: Chemicals Identified for Consultation with the Carcinogen Identification Committee” by the California EPA (Reproductive and Cancer Hazard Assessment Branch).

Hexythiazox was first approved for use in the US in 1989. Annual use of the active ingredient in California is currently around 23,000 kg, and as such Hexythiazox is not listed on the California Department of Pesticide Registration’s list of the top 100 pesticides (by weight) in the state.

Gowan Company is not aware of any published case report or epidemiological study indicative that its pesticidal use causes cancer in man.

The US EPA has reviewed the toxicological database on hexythiazox on multiple occasions; under the auspices of the HED Toxicology Branch Peer Review Committee in 1986, a FIFRA Scientific Advisory Panel in 1987, the HED Cancer Peer review Committee in 1987, and the Cancer Assessment Review Committee (CARC) in 2009.

As described in the memorandum\(^1\) from the CARC in 2009, results from long-term mammalian oncogenicity/toxicity bioassays have shown an increased incidence of liver tumors in female mice following dietary consumption of 1500 ppm hexythiazox (corresponding to 318 mg hexythiazox/kg body weight/day) as well as an elevation in the incidence of benign mammary gland tumors in male rats at dietary concentrations of 3000 ppm (corresponding to 163 mg hexythiazox/kg body weight/day).

However, there was no evidence of carcinogenicity in the opposite gender for rats or mice. In addition, the performance of a battery of genotoxicity studies has failed to show a mutagenic concern for hexythiazox. The CARC concluded “that the evidence as a whole was not strong enough to warrant the use of a linear low dose extrapolation model applied to the animal data (Q₈*) for a quantitative estimation of human risk”.

The US EPA has set the RfD for hexythiazox at 0.025 mg/kg body weight/day (based on a 100-fold safety multiple above the NOAEL of 2.5 mg hexythiazox/kg body weight/day from a one year dietary toxicity study in dogs). In 2009, the CARC indicated this RfD would be protective of all chronic effects including potential carcinogenicity in man. This RfD is almost 3 orders of magnitude (i.e. at least 920-fold) lower than the lowest no effect level (23.1 mg hexythiazox/kg body weight/day) observed in the rodent oncogenicity studies discussed above.

Based on the extensive toxicology database, minor use status and large safety margins, Gowan Company believes that no further hazard identification is necessary at this time for hexythiazox.

Sincerely,

[Signature]

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