

INDUSTRY TASK FORCE II ON 2,4-D RESEARCH DATA

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Issue Background

CANCER IN DOGS

Issue:

It is sometimes reported in the news media that lawn and turf herbicides containing 2,4-D are a cause of cancer in dogs. This is not supported by the simple fact that all regulatory agencies in the world that have examined the scientific data have arrived at the same conclusion: 2,4-D is not an animal carcinogen.

Background:

In 1991, the Journal of the National Cancer Institute published a study which purportedly showed a positive association between canine malignant lymphoma (CML), a form of cancer in dogs, and dog owners use of the herbicide 2,4-D, (Hayes 1991)¹. The authors claimed to have demonstrated that dogs whose owners used the herbicide 2,4-D on their lawns four or more times per year were twice as likely to develop canine malignant lymphoma compared to dogs whose owners did not use 2,4-D (please note that the maximum labeled use of 2,4-D on turf is two applications per year).

The study was immediately controversial in scientific circles since it was in direct conflict with the extensive 2,4-D toxicology database including rodent and dog feeding studies. There are also lifetime feeding bioassays in rodents (Charles, et al., 1996a)² and a chronic feeding study in the dog (Charles, et al., 1996b)³ that did not indicate oncogenic effects. These animal feeding studies were done under controlled conditions by EPA/GLP qualified laboratories. The current EPA toxicology profile shows 2,4-D to be "non-carcinogenic" in animals.⁴

The Hayes study received widespread coverage by the news media, with the story being carried by almost 200 newspapers across the United States and Canada. Today, the study is often cited by anti-pesticide groups as evidence supporting the suggested relationship of 2,4-D and non-Hodgkin's lymphoma (NHL), a human disease somewhat similar to canine malignant lymphoma. Some veterinarians advise dog owners not to use 2,4-D on their lawns.

The 2,4-D Task Force was curious how the dose-response of frequency of 2,4-D use was calculated. Since the Hayes dog study was publicly funded, the data file was given to Dr. John B. Kaneene, Director, Population Medicine Center, School of Veterinary Medicine, Michigan State University (MSU), for independent analysis. Neither the Task Force nor MSU were able to obtain additional information from the NCI investigators regarding exposure criteria or the dose response algorithm. Dr. Kaneene, using NCI's own data, found that the data would not support the CML conclusions reached by the author, and that there was no

association between 2,4-D and cancer in dogs. Dr. Hayes was offered an opportunity to defend his study, which he declined. The MSU reanalysis was then published in the peer-reviewed journal (Kaneene, et al., 1999)⁵. Subsequently, a second more recent epidemiological case-control study (Gavazza et al., 2001)⁶ failed to show any association between dogs whose owners used lawn care herbicides and canine malignant lymphoma. This study concluded, “Variables describing animal care and pesticide use were either not associated with the disease [CML] or were uninformative.”

Regulatory decisions around the world confirm that 2,4-D is not an animal carcinogen (WHO 1996⁷, EU 2001⁸, PMRA 2005⁹, EPA 2005⁴).

Reprints for “Re-Analysis of 2,4-D Use and the Occurrence of Canine Malignant Lymphoma” (Kaneene 1999)⁵, are available through this Task Force. For information on other NCI epidemiologic case-control studies involving 2,4-D, see the Epidemiology page on this web site.

About the Task Force

The Industry Task Force II on 2,4-D Research Data is organized to provide funding for some 300 Good Laboratory Practice (GLP) research studies required to respond to the EPA reregistration and PMRA pesticide re-evaluation programs. The 2,4-D Task Force is comprised of those companies owning the technical registrations on the active ingredient in 2,4-D herbicides. They are Dow AgroSciences (U.S.), Nufarm, Ltd. (Australia) and Agro-Gor Corp., a U.S. corporation jointly owned by Atanor, S.A. (Argentina) and PBI Gordon Corp. (U.S.).

¹ Hayes *et al.* 1991. Case-control study of canine malignant lymphoma: Positive association with dog owner’s use of 2,4-dichlorophenoxyacetic acid herbicides. *J. Natl Cancer Inst* **83**(17):1226-1231.

² Charles, JM, Bond, DM, Jeffries, TK, Yano, BL, Stott, WT, Johnson, KA, Cunny, HC, Wilson, RD and Bus, JS. 1996a. Chronic Dietary Toxicity/Oncogenicity Studies on 2,4-Dichlorophenoxyacetic Acid in Rodents. *Fund. Appl. Toxicol.* 33: 166-172.

³ Charles, JM, Dalgard, DM, Cunny, HC, Wilson, RD and Bus JS. 1996b. Comparative Subchronic and Chronic Dietary Toxicity Studies on 2,4-Dichlorophenoxyacetic Acid, Amine, and Ester in the Dog. *Fund. Appl. Toxicol.* 29: 78-85.

⁴ U.S. EPA. 2005. Reregistration Eligibility Decision for 2,4-D. Docket # OPP-2004-0167
<<http://docket.epa.gov/edkpub/index.jsp>>

⁵ Kaneene, JB and R. Miller. 1999. Re-analysis of 2,4-D Use and the Occurrence of Canine Malignant Lymphoma. *Veterinary and Human Toxicology*, Vol. **41**, No. 2:164-170.

⁶ Gavazza, A, S Presciuttini, R Barale, G Lubas, and B Gugliucci. 2001. Association between Canine Malignant Lymphoma, Living in Industrial Area, and Use of Chemicals by Dog Owners. *J. Vet Intern. Med.* **15**: 190-195.

⁷ World Health Organization & Food and Agriculture Organization of the United Nations, Pesticide residues in food, Toxicological evaluations, 1996.

⁸ European Commission Health & Consumer Protection Directorate-General. 2001. Commission Working document. Review Report for the Active Substance 2,4-D Re-evaluation. 7599/VI/97-final. 1 October 2001.

<http://europa.eu.int/eur-lex/pri/en/oj/dat/2001/l_313/l_31320011130en00370039.pdf>

⁹ PMRA. (2005). Proposed Acceptability for Continuing Registration; Re-evaluation of the Lawn and Turf Uses of (2,4-Dichlorophenoxy)acetic Acid [2,4-D]. <www.pma-arla.gc.ca/english/consum/2.4-D-e.html>