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

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Scientific Backgrounder

IARC* CLASSIFICATION OF THE HERBICIDE 2,4-D

(*International Agency for Research on Cancer)

Issue:

Pesticide regulatory agencies mandated with protecting public health that have reviewed the modern scientific data base regarding 2,4-D have all concluded there is no evidence of animal carcinogenicity and that 2,4-D is not a human carcinogen. These include: European Commission (2001), New Zealand (2003), World Health Organization (1996, 1997, 1998, 2003), United States Environmental Protection Agency (1994, 1997, 2004, 2005, 2007) and Health Canada's Pest Management Regulatory Agency (2005, 2006, 2007)[1].

In spite of these recent national and international evaluations by regulatory bodies responsible for protecting public health, news media coverage concerning the position of various advocacy groups on the "ornamental" use of pesticides in Canada has given rise to questions about the classification of pesticides by the International Agency for Research on Cancer (IARC), a classification based on research of 30 – 40 years ago.

As science-based organizations, the registrants of turf and lawn care products are equally concerned about the regulation and use of pesticides. All are in agreement that only pesticides that do not pose an unacceptable risk of cancer in humans are registered for use.

Background:

One Canadian advocacy group has had a position statement[2] on the "ornamental" use of pesticides for several years. In part, the position statement reads:

> "The Canadian Cancer Society is very concerned about the use of potentially carcinogenic (cancer-causing) substances for the purpose of enhancing the appearance of, for example, private gardens and lawns as well as parks, recreational facilities and golf courses (ornamental use). We base this concern on the conclusions of the International Agency for Research on Cancer (IARC) that state that some substances used in pesticides are classified as known, probable or possible carcinogens."

This statement gives rise to questions about the IARC classification of one class of compounds, chlorophenoxies, which are used in broadleaf herbicides for domestic, commercial and agricultural use. The herbicide 2,4-D is a chlorophenoxy.

IARC has <u>not</u> concluded that 2,4-D is a "possible" carcinogen (Group 2B). Furthermore, <u>not one</u> pesticide regulator in the world classifies 2,4-D as a human carcinogen. The facts pertaining to the IARC evaluation of <u>chlorophenoxy herbicides</u> are as follows.

- The IARC 1987 Supplement 7, which is frequently referenced, summarized previous 1977 and 1986 IARC evaluations. The 1977 IARC review was based on equivocal data from the 1960s and early 1970s.
- The 1977 IARC review examined the carcinogenic potential of two chlorophenoxy herbicides, 2,4,5-trichlorophenoxyacetic acid (2,4,5-T) and 2,4-D: "The results of the single cohort study of a small number of workers exposed to various herbicides, including 2,4-D, 2,4,5-T and 3-amino-1,2,4-triazole (amitrole) (IARC, 1986 - Vol. 41), are not sufficient to evaluate the carcinogenicity of 2,4-D to man [Because 2,4-D may be used with 2,4,5-T, which is contaminated with 2,3,7,8-tetradichlorodibenzo-*para*-dioxin, see also monograph on polychlorinated dibenzodioxins (IARC, 1997 – Vol.69)]."[3]
- The 1977 IARC review was on forms of 2,4-D no longer manufactured. As well, 2,4,5-T was withdrawn from the market in the early 1980s and is no longer used with 2,4-D.
- In 1986 IARC conducted a review of published studies on occupational exposures. That published monograph classified chlorophenoxy herbicides in Group 2B.
- In the original 1986 monograph – which is not available on the internet – Table 16[4], entitled "Chlorophenoxy herbicides and their major impurity considered in this monograph that have previously been evaluated in the IARC Monographs", 2,4-D was listed separately. The review concluded there was "inadequate" data to classify 2,4-D for carcinogenicity in animals or for genetic activity in short-term tests. The table is reprinted below.

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Table 16. Chlorophenoxy herbicides and their major impurity considered in this monograph that have previously been evaluated in the IARC Monographs[a]

Chemical	Evidence for carcinogenicity in animals	Evidence for genetic activity in short-term tests
2,4-D	inadequate	inadequate
MCPA[b]	no data	inadequate
2,4,5-T	inadequate	inadequate
TCDD	sufficient	inadequate

[a] From IARC (1982a, b) except where noted
[b] From IARC (1983)

It is also important to note that in the original 1987 monograph, Table 1[5] on page 60, 2,4-D was classified separately with no classification for human carcinogenicity and "I" (inadequate evidence) for animal carcinogenicity. Moreover, the footnote to Table 1 specifically states:

- "This evaluation applies to the group of chemicals as a whole and not necessarily to all individual chemicals within the group."

In 2002, IARC clarified its position[6] on the classification of 2,4-D:

- "At the time of the evaluation, the epidemiological data on 2,4-D as a separate compound were inadequate to evaluate its carcinogenicity to humans, because no data on human exposure to the single compound were available. The animal carcinogenicity data for 2,4-D were inadequate. The chlorophenoxy herbicides

> showed limited epidemiological evidence for increased occupational cancer risk in pesticide applicators, and were evaluated as possibly carcinogenic to humans, Group 2B. Because 2,4-D belongs to this group of substances, the compound has been given the same classification, in the absence of data that would make a full evaluation of 2,4-D possible."

IARC has not reviewed the more recent epidemiological or animal toxicological/oncogenicity data. Since IARC's limited and dated reviews of 1977 and 1986, there has been extensive 2,4-D toxicological data development for pesticide re-evaluation programs in many countries.

Furthermore, a multi-year study sponsored by IARC[7] concluded that workers exposed to the manufacture of chlorophenoxy herbicides, with minimal or no contamination by TCDD and higher chlorinated dioxins, did not have an elevated risk of cancer incidence. This type of occupational exposure is several orders of magnitude greater than that experienced by farmers, professional lawn care applicators and domestic class users.

In 2007 US EPA published an additional review of 2,4-D as to its human carcinogenicity:

> "Based on extensive scientific review of many epidemiology and animal studies, the Agency finds that the weight of the evidence does not support a conclusion that 2,4-D, 2,4-DB and 2,4-DP are likely human carcinogens. The Agency has determined that the existing data do not support a conclusion that links human cancer to 2,4-D exposure. This conclusion applies to 2,4-DB and 2,4-DP because they were considered for Special Review based solely on their similarity to 2,4-D. In addition, because they are used significantly less than 2,4-D, their contribution to exposure is minimal relative to 2,4-D. Because the Agency has determined that the existing data do not support a conclusion that links human cancer to 2,4-D exposure, the Agency is not initiating a Special Review of 2,4-D, 2,4-DB and 2,4-DP."[8] (emphasis added)

Pesticide regulatory agencies mandated with protecting public health that have reviewed the modern scientific data base from 2001 to the present have unanimously concluded there is no evidence of animal carcinogenicity and that 2,4-D is not a human carcinogen.

October 2007

References:

[1] Copies of these regulatory decisions may be viewed at: http://www.24d.org

[2] http://www.cancer.ca/ccs/internet/standard/0,2939,3172_335143__langId-en,00.html

[3] http://monographs.iarc.fr/ENG/Monographs/vol15/volume15.pdf

[4] IARC Monographs, Vol 41, 1986 (original printed version).

[5] IARC Monographs, Overall Evaluations of Carcinogenicity: An Updating of IARC Monographs Volumes 1 to 42, Supplement 7, 1987.

[6] Baan, RA. Private correspondence, October 31, 2002.

[7] Kogevinas *et al*. Cancer mortality in workers exposed to phenoxy herbicides, chlorophenols and dioxins. American Journal of Epidemiology, 1997.

[8] http://www.epa.gov/fedrgstr/EPA-PEST/2007/August/Day-08/p15109.htm