

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

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Comments on OCFP's "Pesticides Literature Review" **OCFP Review was incomplete and did not follow generally** **accepted review practices**

The Ontario College of Family Physicians (OCFP) review was limited to a review of a portion of the epidemiologic database, and the very significant toxicology database was ignored. Also ignored were studies that quantify the extent of exposure, if any, in various populations. Risk cannot be accurately determined in the absence of exposure data. Plausible mechanisms for cancer, or the lack thereof, were largely ignored. The review does not attempt to make "weight of the evidence" decisions, as required by sound science and regulatory agencies.

The literature review was limited to a relatively small portion of the total epidemiology database. For example, of the more than 140 studies that are pertinent to the phenoxy herbicides, the OCFP reviewers found only a handful suitable for their purposes. The criteria used to determine which studies would be reviewed are not clear. It appears that studies showing an association between pesticides and cancer or other health problems were given priority over studies showing no association. This creates a biased review.

Also, individual studies were selectively reported. Examples of this are Fleming (1999) and Morrison (1994). Fleming is a 20-year cohort study of 33,658 Florida pesticide applicators (3,503 females), both commercial applicators and farmers. This study found an association between the use of pesticides and prostate cancer, and this was included in the OCFP section on prostate cancer. The study found no association with cancers of the lungs, breast, stomach, pancreas, kidney, colorectal cancer, non-Hodgkin's lymphoma (NHL), leukemia etc. However, the study was not cited in those sections of the OCFP review. If the study showed a positive association, it was reported, while the equally important negative associations were not. This creates considerable bias in the report.

The OCFP authors state, "Morrison et al. (11) conducted a large study of 155,000 farmers in Canada and found a statistically significant increase in (non-Hodgkin's lymphoma) NHL (RR 2.11, CI 1.1-3.9), the risk increasing with acres sprayed." This is an extraordinary misrepresentation of the study. The study did not show a statistically significant increase in NHL, since the SMR (Standard Mortality Rate) for NHL was 0.79, indicating significantly fewer deaths from NHL compared to the Canadian population as a whole. The relative risk of 2.11 was only seen among farmers in both the 1971 and 1981 census that sprayed more than 380 acres in 1970.

Recent biomonitoring studies have demonstrated that pesticide application and number of acres applied is not a valid predictor of exposure. The study shows the SMR from all causes of death was 0.72, indicating that these farmers are living longer than the average Canadian. The SMR for all cancers was 0.76, indicating that these farmers have fewer deaths from cancer than the Canadian population as a whole. According to the OCFP review, this study is an indictment of pesticides.

The OCFP authors cite Schreimachers (1999) as evidence 2,4-D causes non-Hodgkin's lymphoma. That study compared a population of women living in "high yielding wheat counties" to a population of women living in urban counties. It assumed that the women living in the wheat areas were significantly more exposed to wheat herbicides than the urban women, and attributed various cancer deaths to that purported exposure. Interestingly, there was no increase in non-Hodgkin's lymphoma among men living in the same area. Also, women living in areas in which wheat and potatoes were grown, and areas in which corn and soybeans were grown (areas which also use 2,4-D) had no elevation of non-Hodgkin's lymphoma. Several actual exposure studies found no significant difference in herbicide exposure in women living in wheat producing areas compared to other areas. Exposure was negligible in both populations. If the basic assumption on which the study is based is wrong, the conclusions of the study are invalid. In spite of this, the OCFP authors determined that Schreimachers (1999) met their "criteria" and cited the study.

A number of recent exposure studies challenge the traditional surrogates or assumptions of pesticide exposure used in epidemiologic studies. The failure of the OCFP to include those studies in their review is another major flaw.

OCFP Review is at odds with U.S. National Cancer Institute

The U.S. National Cancer Institute has now spent 20 years and many millions of dollars testing the 2,4-D/non-Hodgkin's lymphoma hypothesis. They recently pooled the data from their three 2,4-D case-control studies, making one large study, and concluded in their analysis (DeRoos, 2003) that there is no association between NHL and "ever having used 2,4-D." The authors of the section on non-Hodgkin's lymphoma in the OCFP review chose to ignore this. Apparently, DeRoos, 2003 is another study which fails to meet the OCFP reviewers' "criteria".

OCFP Review is at odds with current science

The OCFP review attempts to make a case that populations exposed to pesticides can expect a higher incidence of cancer and other health problems compared to the general population. Yet, it simply ignores a significant number of studies that do not support this hypothesis. The two Fleming studies (a mortality and a cancer incidence) are again examples. Those studies found the overall incidence of cancer among the pesticide

applicators to be significantly lower than the general Florida population adjusted for age, and the applicators to be in significantly better health. The authors of the OCFP review chose not to include these findings, or similar findings in other studies. These studies have shown that populations of applicators, farmers and chemical workers who manufacture or formulate 2,4-D products (and thus have a potentially higher exposure risk) have an overall mortality from cancer below that of the general population.

Some of these studies are shown in the following table. The OCFP review commented on only two of the studies listed below, and then failed to point that in both studies the overall cancer death rate was lower than for the general population. As stated in the footnote to the table, a Standard Mortality Rate below 1.00 indicates a lower than expected death rate. An SMR of 1.00 indicates no difference between the death rate of the group studied and the general population.

Cohort studies of farmers or workers potentially exposed to 2,4-D

Research study	Number of study participants/cases	Standardized Mortality Rates (SMR ¹)		
		All Causes	All Cancer Sites	Non-Hodgkin's Lymphoma
Swedish agricultural and forestry workers (Wiklund & Holm, 1986)	354,620		0.90	
Ontario Hydro forestry workers (Green, 1986)	1,222	0.95	1.10	
Saskatchewan farmers, (Wigle, 1990)	70,099	0.74	0.78	0.92
Manitoba, Saskatchewan & Alberta farmers, (Morrison, 1994)	155,547	0.72	0.76	0.79
Lawn care pesticide applicators, (Hoar Zahm, 1997)	32,600	0.69	0.76	1.14 ²
Florida pesticide applicators, (Fleming, 1998)	30,155	0.72	0.78	0.88
Phenoxy herbicide manufacturing workers, (Kogevinas, 1997)	21,853	0.91	0.96	1.00

Dow 2,4-D chemical workers 50 year update (Burns, 2001)	1,517	0.90	0.95	1.00
Agricultural Health study (National Cancer Institute, 2003)	55,332	0.50	0.60	0.90

1. An SMR below 1.00 indicates a lower than expected death rate, while values above 1.00 indicate a higher than expected death rate.
2. Four actual deaths versus 3.5 expected.

OCFP Review did not include recent major reviews of 2,4-D by World Health Organization, U.S. EPA, the European Commission and the New Zealand Environmental Risk Management Authority

Although the OCFP singled out the herbicide 2,4-D for special attention, recent reviews of 2,4-D by regulatory agencies, reviews that included all pertinent epidemiologic studies, the full toxicology database, considerable exposure and environmental fate data etc., were not included. The conclusions in these reviews are based on the weight of the total evidence, and are far more comprehensive than the somewhat cursory review of 2,4-D in the OCFP report. Example of such reviews are the World Health Organization (WHO) review of 2,4-D (1996), the U.S. EPA Carcinogenicity Peer Review Committee's fourth review of 2,4-D (1997), the European Commission (2001) and the New Zealand Environmental Risk Management Authority (2003).

These reviews came to conclusions very different from the conclusions reached by OCFP, which is perhaps why they were not included.

These four agencies – which are mandated to protect human health – are in agreement that 2,4-D is not an animal carcinogen, mutagen or teratogen, and that the epidemiology database did not present a convincing case that there is evidence of a causal relationship between exposure to chlorophenoxy herbicides and the development of non-Hodgkin's lymphoma (NHL) and other cancers in humans.

OCFP Review did not include major reviews by other researchers

The OCFP review failed to include the comprehensive literature reviews by researchers attempting to quantify the contribution of pesticides to the overall incidence of cancer. Such reviews include Sir Richard Doll (1981), Doll (1998), Ritter (1997) and Gold (2002). All four of these reviews conclude that the major causes of preventable cancer are smoking, alcohol consumption and life style (mainly diet) and that the contribution from pesticides is negligible. These conclusions are very considerably different from what is being suggested by OCFP, which is probably the reason they were not included.

The OCFP authors did not include comprehensive expert panel reviews of 2,4-D that do not support the conclusions reached in the OCFP review. Examples are Garabrant (2002), USDA/NAPIAP (1996), Munro (1992), the Canadian Centre for Toxicology, Guelph University (1991), Ibrahim (1991) and the Canadian Centre for Toxicology (1987).

An example of OCFP research?

Finally, page 2 of the OCFP review alleges that 2,4-D was developed as the result of chemical warfare research during World War II designed to “eradicate the Japanese rice crop.” This is complete nonsense. The inventor of 2,4-D, as shown on the original 2,4-D patent, was Dr. Franklin D. Jones. The author of this review worked for the same company and knew Dr. Jones. He was never even remotely involved in chemical warfare research, and concentrated his research efforts on improving crop yields or increasing food production. 2,4-D is a highly improbable herbicide to be used to “eradicate” rice. In fact, it very quickly became the world’s most widely used rice herbicide, used to protect rice from yield destroying invasive weeds. It is still extensively used by Japanese rice growers today. It has been an important tool used to increase rice production worldwide (and the production of wheat, barley, corn, oats, rye, etc.) having a significant impact on reducing world hunger.

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