

Ontario Vegetation Management Association Update on 2,4-D

2,4-D Research Task Force
September 26, 2007

Today's Agenda:

- What is GLP Research
- What is 2,4-D
- Chronology of major milestones
- Most recent research by the International Agency for Research on Cancer
- A brief review of what really happened in Quebec
- Dealing with a few of the common questions
- Value & Benefits of phenoxy herbicides
- Buffer Zones

What is GLP Research?

- The Pest Management Regulatory Agency (PMRA) requires Good Laboratory Practice (GLP) studies from registrants.
- All aspects of research covered by strict government regulation as established by the OECD.
- Research must follow specified protocols with each step documented.
- Only GLP qualified facilities and personnel can be used.
- GLP research is demonstratively valid. In other words, if anyone wishes to conduct the research – then the results should be the same.
- An unintentional GLP violation can invalidate the study.
- An intentional GLP violation can be a criminal offense, as provided for under the Pest Control Products Act (2002).
- If studies that make the headlines in the news media today were of GLP quality, quite likely the debate we are witnessing in Canada would not be occurring.
- See: http://www.oecd.org/about/0,2337,en_2649_34381_1_1_1_1_1,00.html

Separating GLP Research from “Headline” Science in the Daily Newspaper

The studies and articles picked up by the news media typically have one or more design flaws:

- Ignore or downplay the conclusions of expert panels and regulatory agencies which have considered the weight of scientific evidence and data generated by means of Good Laboratory Practice (GLP) toxicological studies.
- Place greater emphasis on those epidemiological studies which show a positive association and often ignore studies which have a negative association.
- Ignore follow-on studies that have reassessed the original data or added additional study subjects.
- Misrepresent the findings of studies and/or selectively report certain data in isolation of overall findings.
- Manipulate the data to reach predetermined conclusions.
- Do not consider exposure, or lack thereof.
- Ignore biological plausibility.

What is 2,4-D?

- The original patent on 2,4-D was issued in 1945 to Dr. Franklin Jones, a plant physiologist. Dr. Jones was working with the naturally occurring plant auxin, indole acetic acid (IAA). IAA is present in all plant matter and humans ingest it daily whenever fruit, vegetables and cereals are consumed.
- 2,4-D, one of the most widely used herbicides worldwide, is applied to crops such as wheat, corn, rice, soybeans, sugar cane, pome fruits, stone fruits. It protects lawn and turf grass from invasive and damaging weed species.
- In 2004, The Henry Ford organization in Dearborn, Michigan identified 2,4-D as one of the 75 most important innovations in the previous 75 years. Few scientific innovations have done as much to increase food production throughout the world.
- If it was discovered today, it might well be classified as a “low risk” pesticide.

Page 5

Expert Reviews of 2,4-D

Dec.
2004

United States Environmental Protection Agency:

“In 1996, HED reviewed additional studies and concluded that they were not sufficient to change the conclusions drawn by the Science Advisory Panel/Scientific Advisory Board. Since the 1996 review, very few new studies have examined the relationship between exposure to 2,4-D and cancer. Review of the additional studies cited by BP [Beyond Pesticides] (and not previously considered) indicate that the studies add very little to our understanding of the cancer epidemiology specifically related to 2,4-D. **HED concludes there is no additional evidence that would implicate 2,4-D as a cause of cancer.**”

Feb.
2005

Health Canada's Pest Management Regulatory Agency:

“The PMRA is not aware of any new evidence from epidemiological studies that would challenge these conclusions, and more recent animal data lend further support for this classification. Furthermore, inadequate exposure characterization in the majority of these studies precludes the establishment of any causal link between 2,4-D and human carcinogenicity. Because of the inconsistent epidemiological associations and the fact that the animal studies designed to show causality were consistently negative, the PMRA concurs that 2,4-D cannot be classified as to its human carcinogenicity on the basis of all available and relevant data.”

Page 6

Expert Reviews of 2,4-D

Aug.
2005

United States Environmental Protection Agency:

"The Agency has twice recently reviewed epidemiological studies linking cancer to 2,4-D. In the first review, completed January 14, 2004, EPA concluded there is no additional evidence that would implicate 2,4-D as a cause of cancer (EPA, 2004). The second review of available epidemiological studies occurred in response to comments received during the Phase 3 Public Comment Period for the 2,4-D RED. EPA's report, dated December 8, 2004 and authored by EPA Scientist Jerry Blondell, Ph.D., found that none of the more recent epidemiological studies definitively linked human cancer cases to 2,4-D. cancer."

Short Term Risk Assessments for Residential Handlers: The Margins of Exposure (MOE) for various residential applications ranged from 1,800 for hose-end sprayers to 29,000 for fertilizer/herbicide granular mixtures. An MOE exceeding 1,000 is "not of concern".

Expert Reviews of 2,4-D

Aug.
2006

Pest Management Regulatory Agency:

"Animal data from various species including mice, rats and dogs indicated that 2,4-D was not carcinogenic in animals, in vitro data demonstrated that 2,4-D was not mutagenic, the chemical structure of 2,4-D does not correspond to known carcinogens, and there was no convincing evidence that 2,4-D adversely affects the immune system. A number of expert panels have examined a large body of human epidemiology studies involving phenoxy herbicides and have concluded that there is insufficient evidence to support 2,4-D as a human carcinogen. In other words, there is a lack of a positive human carcinogenicity findings. This is the basis for the USEPA classification of 2,4-D as a "Class D carcinogen - not classifiable with respect to human carcinogenicity". The PMRA concurs with the USEPA's classification."

Expert Reviews of 2,4-D



**Apr.
2007**

Ontario Pesticide Advisory Committee:

“OPAC has concluded, after in-depth consideration of the scientific evidence, that there is no reason for us to recommend additional restrictions on the use of 2,4-D. 2,4-D will continue to be classified according to the current classification guidelines.”

Expert Reviews of 2,4-D



**Jun.
2007**

Pest Management Regulatory Agency:

“The inconsistent epidemiological associations, the recognition that there are many other factors that may have contributed to the weakly positive associations and the fact that the animal studies designed to show causality were consistently negative have lead the PMRA scientists to concur that on the basis of all available and relevant data, 2,4-D cannot be classified as to its human carcinogenicity.”

In releasing this most recent assessment, the PMRA has again – the third time in three years – stated that 2,4-D is acceptable for use in Canada when label directions are followed.

Expert Reviews of 2,4-D

Aug.
2007

U.S. Environmental Protection Agency:

“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.”

Page 11

Is 2,4-D a human carcinogen?

- The WHO, EPA, European Commission and the PMRA all agree: 2,4-D not a human carcinogen.
- What about other pesticides?
- The International Agency for Research on Cancer (IARC) has recently report on attributable causes of cancer in France. This study is the first of several IARC will be undertaking into the subject matter; France is the first country. This most recent research adds to knowledge based on several earlier studies in other countries.
- With specific regard to pesticides, on page 139 IARC concludes:
 - "Very few currently available pesticides are established experimental carcinogens, and none is an established human carcinogen."
 - "Given the lack of evidence linking pesticide exposure to human cancer risk, no cases of cancer can be attributed to either occupational or non-occupational exposure to this group of agents."

Page 12

Percentage of cancer cases attributed to various factors since the seminal work of Doll & Peto, 1981

Risk Factors	Doll & Peto, US 1981	Olsen, Nordic countries 1997*	Harvard, US 2000	Doll & Peto, UK 2005	Danaei, high income countries 2005	IARC, France 2007
Tobacco	30	19	30	30	29	23.9
Alcohol	3	2	3	6	4	6.9
Infectious agents	10	2	5	5	1.5	3.7
Diet	[35	?	[30	[25	3	ni
Obesity		<1			3	1.6
Physical inactivity		ni			2	1.6
Occupation	4	3	5	2	ni	2.4
Environmental pollutants	2	1	2	2	1	0.1
Industrial products	<1	ni		ni	ni	ni
Food additives	<1	ni	1	ni	ni	ni
Medicines	[1	ni	1	[<1	ni	ni
Hormone replacement therapy		-			ni	0.9
Reproductive factors	7	-	3	15	ni	0.4
Non-medical ionizing radiation	[3	<1	[2	4	ni	ni
Ultraviolet light		4		1	ni	0.7
Man-made ionizing radiation	ni	2		<1	ni	ni

* : data for men only, study also considered women ni: factor not considered as being a risk factor by the study
Page 13

What Really Happened in Quebec?

- In July 2002, the draft Quebec Pesticide Management Code placed a number of pesticides on a prohibited list (Annex I)
- After requests from industry, Quebec released a background report titled "Methodology for Establishing the List of Prohibited Active Ingredients (Annex I)". This report is dated August 2002.
- MCPA, mecoprop, 2,4-D placed on the list. The report's conclusions drawn from the IARC review of phenoxy herbicides in 1986 are unfounded.
- The March 2003 report continued to recognize IARC as its basis for inclusion of the Active Ingredients in Annex I. However, the government changed its criteria:
 - "In fact, it is currently difficult to justify scientifically the introduction of these active ingredients taken individually, on the basis of this criterion. Given the doubt that persists, they are maintained on the list pending the outcome of the reassessments in progress."

What Really Happened in Quebec?

- Internal Quebec memorandum dated September 23, 2002:
 - "Certain herbicides in Annex I (2,4-D, MCPA, Mecoprop) cannot be prohibited on a scientific basis (carcinogenic risk and others). Briefs from companies producing these active ingredients emphasized this. These are active ingredients commonly used on lawns, and the prohibition of them has raised many objections and comments. However, we must rethink our position on this or base our argument on other items."
- Within one month after comments were received from industry, Quebec had acknowledged that it did not have a scientific basis to support the ban.
- As documented in several reports obtained under Access to Information, Quebec was considering removing the Active Ingredients from the list, but was concerned about the reaction of environmental groups.
- Memorandum to Cabinet dated February 4, 2003, from Environment Minister André Boisclair:
 - "There have been comments to the effect that the various 2,4-D, MCPA and Mecoprop molecules cannot be retained in Annex I because of the reference used, that of the International Agency for Research on Cancer (IARC) assessed the product family (chlorophenoxy) and not the products individually. **The prohibition cannot be scientifically defended on the basis of the criteria put forward**"

Page 15

The Precautionary Principle

- In Canada, and other OECD countries, pesticides are regulated on the basis of the Precautionary Principle:
 - "Fundamentally, the whole approach to pesticide regulation is precautionary. No pesticide may be used in Canada unless its health and environmental risks and its value have first been determined to be acceptable."
- Source: <http://www.hc-sc.gc.ca/pmra-arla/english/pdf/hlawns/hl-GovtResp-e.pdf>
- These compounds are well studied, their effects are well known, have been in use for 60 years.
 - The evidence of "harm" is not compelling.
 - The effects, even on the intended target pests, are reversible – the weeds and brush rapidly grow back.

Page 16

What about exposure via inhalation?

2004 U.S. EPA risk assessment summary provides clear guidance:

- “Intermediate-term and long-term incidental oral, dermal, and inhalation exposures are not expected based on the 2,4-D use scenarios.” (page 6)
- “Potential inhalation exposures are not anticipated for the post application worker scenarios because of the low vapor pressure of 2,4-D ($2.0\text{e-}07$ torr at 20°C).” (page 11)

Source: EPA Overview of the 2,4-D Risk Assessments, June 18, 2004

Conclusion: inhalation of 2,4-D is not a risk factor because exposure is unlikely.

Page 17

Estimated Costs if 2,4-D was Withdrawn from Industrial Vegetation Management Sector

Current herbicide cost of 2,4-D	\$ 3.5 M	Total \$7 M
Current cost of application	\$ 3.5 M	
Incremental Costs	Calculation Method	Value (\$ million)
Cost of more expensive replacement herbicides + greater volume required	At least + 100% of the cost of the withdrawn 2,4-D	3.5
Costs of mowing, etc. To control remaining weeds	Four times the cost of applying herbicides (i.e. \$3.5 million x 4=)	14
Total incremental costs		\$ 17.50

150 % expected increase in IVM costs if 2,4-D withdrawn (\$7M to \$17.5M)

Page 18

PMRA Proposed Buffer Zones

Method of Application	Crop/Use	Buffer Zone (metres) Proposed by the PMRA for the Herbicides 2,4-D & Picloram			
		Aquatic Habitat (metres depth)(e.g., ponds, sloughs, prairie potholes, creeks, rivers, streams, wetlands, marshes, lakes)			Terrestrial Habitat*
		< 1 m	1 – 3 m	> 3 m	
2,4-D Field Sprayer	Cereals	1	0	0	4
2,4-D Aerial, fixed wing	Cereals	10	3	0	90
Tordon 101 Field Sprayer	Rights-of-way	4	3	1	-
Tordon 101 Aerial, fixed wing	Rights-of-way	450	400	175	-
Tordon 101 Rotary wing	Rights-of-way	275	225	100	-
2,4-D Aerial, fixed wing	Pastures, rangeland, grasslands, fallow land, crop stubble	30	10	3	200
2,4-D Aerial, fixed wing	Forestry (3.1 kg a.e./ha)	600	125	50	800

Page 19

Why registrants and users are equally concerned

- This policy has the potential to...
 - Substantially increase buffer zones on the big foundation molecules such as 2,4-D
 - Have a significant impact on aerial buffer zones
 - Extensive non-compliance:
 - Large buffer zones become impractical
 - Major economic impact on users
 - Significant reduction in ability to manage crops “corner to corner”
 - Raise questions about the scientific credibility of Canadian Regulatory system (see the fine print in the definitions)

Page 20

After 60 years of widespread use around the world, the science of 2,4-D is well understood

- After 60 years of wide-spread use and research, an unprecedented amount of scientific data on 2,4-D has been amassed around the world.
- After rigorous analysis of the relevant scientific data, experts all agree 2,4-D:
 - Is not a human carcinogen.
 - Does not cause cancer in animals.
 - Does not cause birth defects.
 - Does not cause genetic damage.
 - Does not bio-accumulate.
 - Does not metabolize, is rapidly excreted (half life <24 hours).
 - Is not persistent in soil, water or vegetation.
 - Breaks down rapidly into compounds of nontoxicological significance.
- Expert panels and government agencies mandated with protecting human health and the environment all reach the same conclusion: **2,4-D is acceptable for use according to label directions.**

Page 21

Important links for 2,4-D:

2,4-D Task Force website:

www.24d.org

PMRA Agriculture and other site uses decision:

<http://www.pmra-arla.gc.ca/english/pdf/pacr/pacr2007-06-e.pdf>

EPA fact sheet on 2,4-D:

http://www.epa.gov/oppsrrd1/REDs/factsheets/24d_fs.htm

PMRA buffer zone proposal:

<http://www.pmra-arla.gc.ca/english/pdf/pro/pro2005-06-e.pdf>

IARC causes of cancer in France:

<http://www.iarc.fr/IARCPress/pdfs/francecancer2000/CausesofCancerFrance2000.pdf>

UK Advisory Committee on Pesticides review of the OCFP report

<http://www.pesticides.gov.uk/acp.asp?id=1387>

Page 22