

Summary of Regulatory Decisions and Expert Panel Reviews of 2,4-D August 2007

Larry E. Hammond
Technical Chairman
Industry Task Force II
on 2,4-D Research Data
Email: lhammond@indy.rr.com

What is an Industry Research 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. Other companies formulate 2,4-D into agricultural, commercial and consumer use products.
- Member companies are:
 - Dow AgroSciences (U.S.)
 - Nufarm, Ltd. (Australia)
 - Agro-Gor Corp., (U.S./Argentina)
- Many other Research Task Forces exist (e.g. MCPA & Mecoprop-p)

What is 2,4-D

- The original patent on 2,4-D was issued in 1945 to Dr. Franklin D. 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, potatoes, sugar cane, pome fruits, stone fruits and nuts. It controls weeds in turf grass and invasive species in aquatic areas and federally protected areas.
- 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 be classified as a “low risk” pesticide.

Expert Reviews of 2,4-D

1986

IARC concluded that there was limited evidence that occupational exposures to chlorophenoxy herbicides are carcinogenic to humans. Classification applies to the group of chemicals as a whole, not to the compound.

Mar.
1987

The Ontario Pesticide Advisory Committee of the Ontario Ministry of the Environment concluded the evidence was inadequate to classify 2,4-D as a carcinogen.

Apr.
1987

At its first meeting, the U.S. EPA Health Effects Division Carcinogenicity Peer Review Committee (CPRC) evaluated 2,4-D as a possible human carcinogen (interim **Group C**) based on borderline evidence of tumors in male F344 rats.

Expert Reviews of 2,4-D

Jun.
1987

U.S. EPA Science Advisory Panel (SAP) disagreed with the CPRC and placed 2,4-D in **Group D** (not classifiable as to human carcinogenicity).

Dec.
1987

At its second peer review, the CPRC disagreed with SAP and maintained its **Group C** decision.

1988

At its third peer review, the CPRC changed its conclusion to **Group D**, now in concurrence with the SAP.

1991

An expert panel, convened at the Harvard School of Public Health, concluded that a link between 2,4-D and cancer was far from established.

Expert Reviews of 2,4-D

Sep.
1996

FAO Panel of Experts and the World Health Organization concluded that the epidemiologic studies do not provide consistent evidence of human cancer risk related to 2,4-D. Stated in all animal feeding studies:
"There was no evidence of carcinogenicity."

1996

USDA/NAPIAP University Minnesota School of Public Health Review:
"No scientifically documented human health risks, either acute or chronic, exist from the approved uses of phenoxy herbicides."

Expert Reviews of 2,4-D

Jan.
1997

The Health Effects Division Carcinogenicity Peer Review Committee of the U.S. Environmental Protection Agency reviewed the updated animal and human evidence and for the 4th time concluded that 2,4-D should remain as classified:

Group D agent, not classifiable as to human carcinogenicity.

The European Commission Health & Consumer Protection Directorate-General completed the final review of 2,4-D:

- "...the review has established that the residues arising from the proposed uses, consequent on application consistent with good plant protection practice, have no harmful effects on human or animal health."

- "...under the proposed and supported conditions of use there are no unacceptable effects on the environment..."

- No evidence of carcinogenicity in mammals.

- **"...no clear association between cancer development and exposure to phenoxy herbicides could be established from the available epidemiological studies."**

Oct.
2001

Expert Reviews of 2,4-D

Nov.
2001

Handbook of Pesticide Toxicology, Chapter 72:

"The extensive database of metabolic, toxicological, and epidemiological studies on 2,4-D has **provided no evidence that 2,4-D poses any health risk to humans when used according to label instructions.**"

Drs. David H. Garabrant and Martin A. Philbert, University of Michigan School of Public Health after reviewing more than 160 toxicologic and epidemiologic studies concluded:

"Studies in rodents demonstrate a lack of oncogenic or carcinogenic effects following lifetime dietary administration of 2,4-D.

Jul.
2002

Epidemiologic studies **provide scant evidence that exposure to 2,4-D is associated with soft tissue sarcoma, non-Hodgkin's lymphoma, Hodgkin's disease, or any other cancer.** There is no human evidence of adverse reproductive outcomes related to 2,4-D."

Expert Reviews of 2,4-D

Sep.
2003

Re-analysis of data from three earlier NCI studies conducted in Kansas, Nebraska and Iowa-Minnesota during the 1980s and 1990s. The NCI researchers determined: "Whereas an indicated effect of 2,4-D exposure on NHL (non-Hodgkin's lymphoma) was reported in the NCI's Nebraska and Kansas studies, **this analysis of the pooled data found no association with having ever used 2,4-D.**"

Dec.
2003

New Zealand Environmental Risk Management Authority considered the carcinogenicity potential of chlorophenoxy herbicides and concluded: "...there is inadequate evidence of a causal relationship between exposure to chlorophenoxy herbicides and the development of non Hodgkin's Lymphoma (NHL) and other cancers in humans at this time, and the available data could not be interpreted as showing the presence or absence of a carcinogenic effect."

Expert Reviews of 2,4-D

Jan.
2004

BC Ministry of Forests expert review by Prof. Frank Dost, Oregon State University:

"A conclusion that **2,4-D has little potential for carcinogenic effect** is supported by the absence of effects in animal carcinogenicity assays, the absence of genetic effects of 2,4-D, the behaviour of the herbicide in the body and the biologically inconsistent and ambiguous results of epidemiology studies."

Jun.
2004

United States Environmental Protection Agency:

After examining the combined risk from exposure through food, drinking water and residential uses, the EPA concluded that 2,4-D would "**not exceed**" the Agency's level of concern. As well, the Agency concluded that short-term margins of exposure for homeowner applications of 2,4-D to lawns were "**not of concern.**" The EPA also released a review of the recent epidemiology pertinent to 2,4-D: "**Based on the above reviews of the above studies, HED [Health Effects Division] concludes there is no additional evidence that would implicate 2,4-D as a cause of cancer.**"

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."

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."
- EPA's decision document, RED, lists all studies considered by the agency. This bibliography of 988 studies and 145 published papers and references identifies all the information evaluated. The decision is based on an expert review of all applicable science.

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

United States 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.”

Acceptable for use according to label directions

- 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.