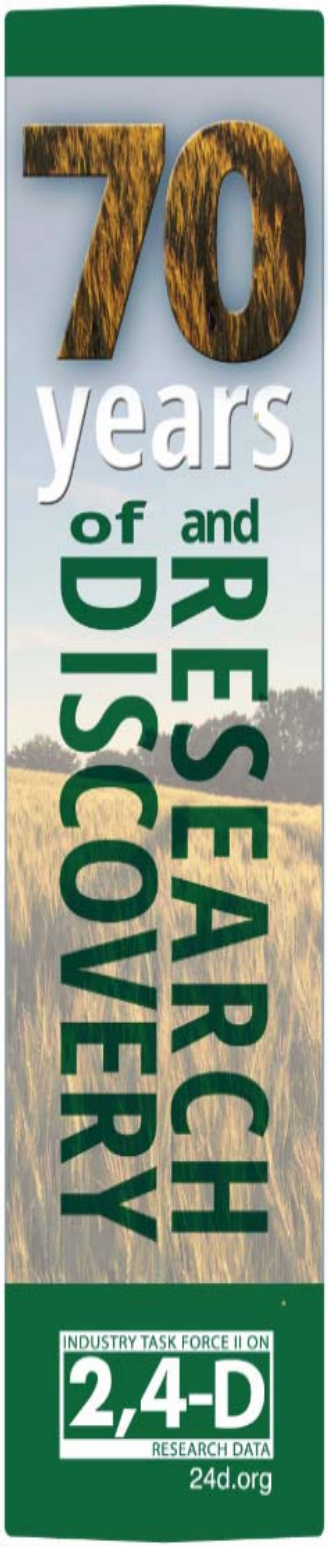


Summary of Regulatory and Expert Reviews of 2,4-D

2,4-D was one of the first selective herbicides developed (a selective herbicide controls weeds without harming the desirable plants), something which stimulated an enormous amount of research on 2,4-D all over the world. While it is not known what the total number of research studies currently is (in 1978 it was reported to be in excess of 40,000), it can be confirmed that the toxicology database alone exceeds 4,000 peer-reviewed, published studies, plus hundreds of unpublished Good Laboratory Practice (GLP) studies which the manufacturers must submit to various regulatory agencies around the world. Additionally, there are now more than 160 peer-reviewed, published epidemiologic studies relevant to 2,4-D.

As a result of this significant body of scientific evidence, the effects of 2,4-D are well understood – it does not present an unacceptable risk to human health or the environment when used according to product instructions. Most importantly, not one regulatory agency mandated with protecting public health classifies 2,4-D as a human carcinogen.

The following is a summary of recent expert panel reviews and regulatory decisions.

1. In 1996, the World Health Organization[1] concluded in its publication Pesticide Residues in Food – 1996 that ***"there was no evidence of carcinogenicity"*** in all animal feeding studies of 2,4-D. This determination was again confirmed in 2003.[2]

2. On October 2, 2001, the European Commission Health and Consumer Protection Directorate-General[3] re-registered 2,4-D for all uses within the European Union. In making this determination, the Directorate-General concluded:

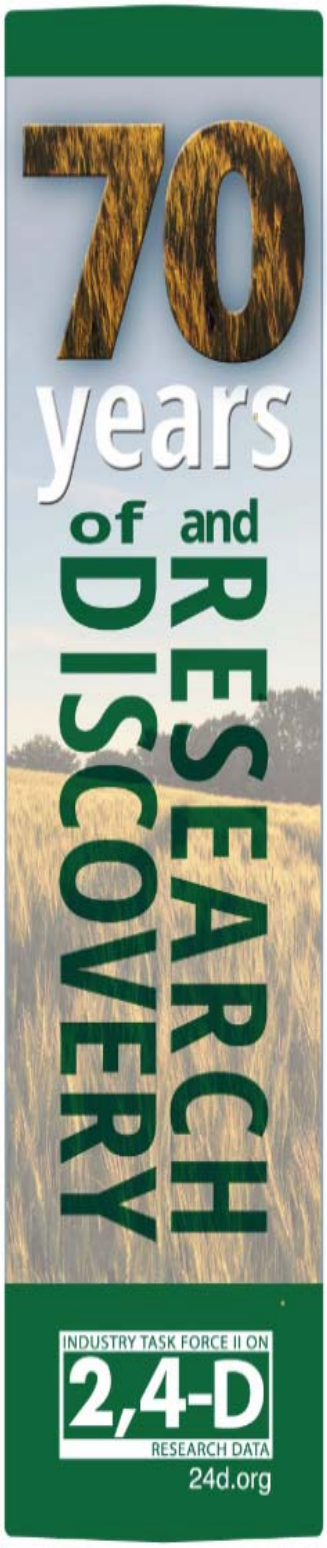
> ***"…no clear association between cancer development and exposure to phenoxy herbicides (including 2,4-D and 2,4-D 2- EHE) could be established from the available epidemiological studies."***

Published 2,4-D toxicology endpoint classification as:

> ***"No evidence of carcinogenicity."***

3. In 2001, the authors of the Handbook of Pesticide Toxicology Chapter 72, "Phenoxy Herbicides (2,4-D)"[4] concluded:

> ***"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 directions."***



4. A scientific literature review of the potential risks to workers using 2,4-D formulations published by the Government of British Columbia[5] states:

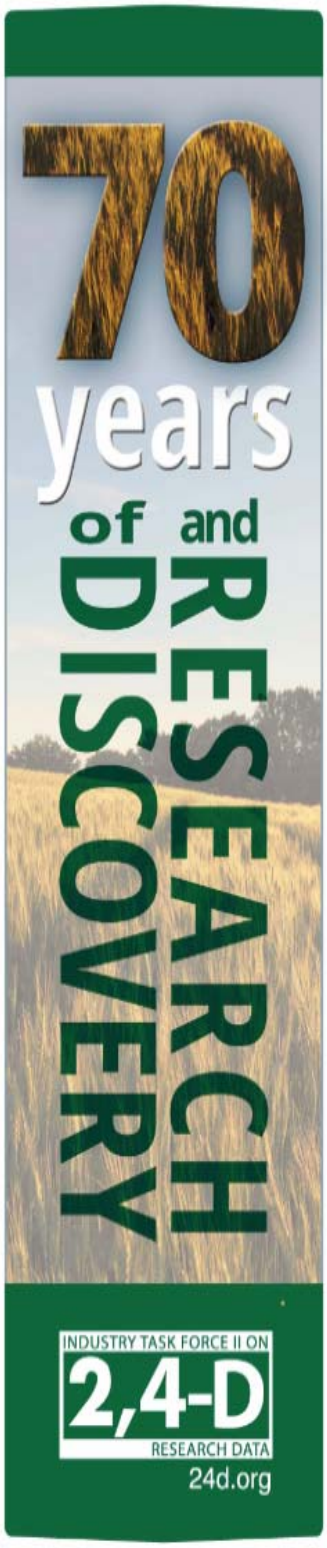
"2,4-D is possibly the most extensively researched of all pesticides, and the data have been examined by an unusual number of advisory committees and work groups. ... A conclusion that 2,4-D has little potential for carcinogenic effect is supported by the absence of effects in animal carcinogenicity 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."

5. On August 8, 2005, the United States Environmental Protection Agency (EPA) released a comprehensive environmental and health assessment of 2,4-D.[6] After examining the combined risk from exposure through food, drinking water and residential uses, with realistic assumptions, the EPA concluded that 2,4-D would "not exceed" the Agency's level of concern. The EPA also released a review of the epidemiology relevant to 2,4-D, stating:

"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 epidemiological evidence that would implicate 2,4-D as a cause of cancer. 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 Reregistration Eligibility Decision. 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."

6. In 2008 Health Canada's Pest Management Regulatory Agency (PMRA) conducted its re-evaluation of 2,4-D and determined "*that 2,4-D meets Canada's strict health and safety standards*."[7] PMRA continues to hold the position that:

"No other international regulatory body considers 2,4-D to be a human carcinogen. Based on all available and relevant data, Health Canada agrees with this position…Health Canada found that 2,4-D does not increase the risk of cancer and can be used safely by homeowners, provided label directions are followed"



7. In 2012, the EPA denied the petition by the Natural Resources Defence Council (NRDC) on the grounds that its claims were either without scientific merit, misinterpreted, or failed to state sufficient grounds for revocation.[8] The EPA noted that:

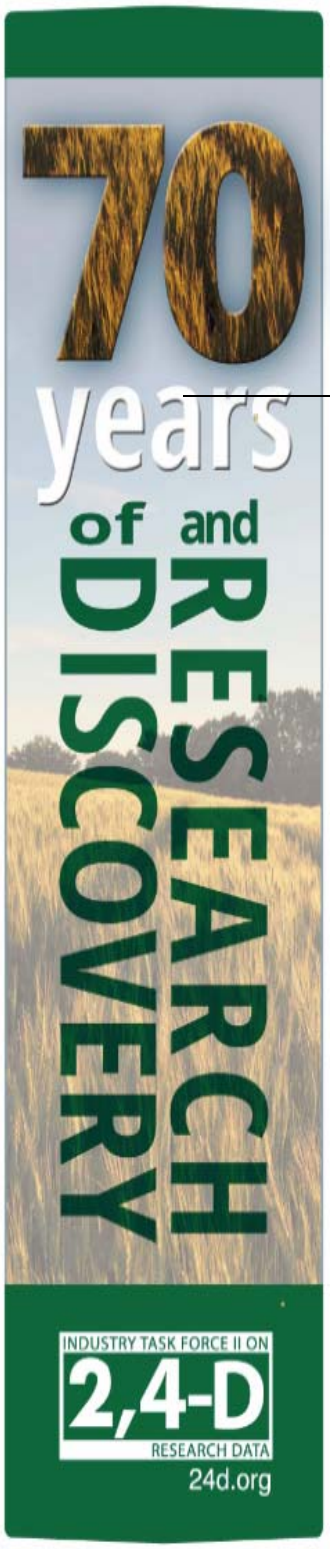
> *"NRDC's arguments regarding the reported oxidant effects of 2,4-D do not change the weight of evidence as to 2,4-D's cancer classification because the primary evidence on cancer—rodent carcinogenicity studies and human epidemiology data—do not support a positive cancer finding."*

8. In 2014, the conclusions of the European Food Safety Authority (EFSA) following the peer review of the initial risk assessments carried out by the competent authority of the Rapporteur Member State Greece, for the pesticide active substance 2,4-D were reported.[9] It concluded that "it was therefore agreed that 2,4-D, as currently manufactured, is unlikely to have a genotoxic potential or pose a carcinogenic risk to humans." The report goes on to conclude that:

> *"No conclusive association can be established between exposure to phenoxy-herbicides (including 2,4-D acid) and human carcinogenicity. No conclusive evidence in the open literature that 2,4-D may exhibit toxicological properties other than those concluded already based on the toxicity studies conducted with the technical active substance."*

9. On October 14, 2014, the U.S. EPA published a memorandum[10] in response to Public Comments received regarding an expanded use pattern in corn and soybeans. This response once again reiterated the EPA's extensive studies which have found no cause-and-effect relationship between the use of 2,4-D and cancer.

> *"The Agency determined, based on several reviews of epidemiological studies, in addition to the animal studies, that the existing data did not support a conclusion that links human cancer to 2,4-D exposure. …This classification was based on the lack of evidence of carcinogenicity in two well-designed and well-conducted animal studies of adequate power and dose in two species (mice and rats), and on the lack of epidemiological data supporting an association between 2,4-D exposure and cancer."*



10. In its 2015 evaluation[11], while voting to classify 2,4-D as **"possibly carcinogenic to humans"** (Group 2B), the IARC review panel concluded, **"there is inadequate evidence in humans for the carcinogenicity of 2,4-D"** as epidemiological studies did not find strong or consistent increases in risk of NHL or other cancers in relation to 2,4-D exposure and there was limited evidence in experimental animals for the carcinogenicity of 2,4-D due to methodological concerns regarding the positive studies.

References:

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

[2] World Health Organization. 2,4-D in Drinking-water, Background document for development of WHO Guidelines for Drinking-water Quality. 2003

[3] European Commission Health & Consumer Protection Directorate-General. Commission working document. Review Report for the Active Substance 2,4-D Re-evaluation. 7599/VI/97-final. 1 October 2001. (20011001.pdf)

[4] Kennepohl, E. and Munro, IC Chapter 72 Phenoxy Herbicides (2.4-D). Handbook of Pesticide Toxicology, Vol 2, Chapter 72.6. Agents and Toxic Actions:1623-1638, 2001.

[5] Toxicology and potential health risk of chemicals that may be encountered by workers using forest vegetation management options. Part III: Risk to workers using 2,4-D formulations. British Columbia. Forest Practices Branch. II. Title. RC965.F59D67 2003. https://www.for.gov.bc.ca/ftp/hfp/external/!publish/Dost_Papers/5-Dost-24D.pdf

[6] U.S. Environmental Protection Agency. Reregistration Eligibility Decision for 2,4-D. Docket # OPP-2004-0167, 2005. (/govtrev/opp2005.pdf)

[7] http://www.hc-sc.gc.ca/cps-spc/pest/part/protect-proteger/24d/index-eng.php

[8] U.S. Environmental Protection Agency. http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPP-2008-0877-0446

[9] http://www.efsa.europa.eu/en/efsajournal/doc/3812.pdf

[10] U.S. Environmental Protection Agency, October 14, 2014. "Response to Public Comments Received Regarding New Uses of Enlist Duo™ on Corn and Soybeans", pg 2.

[11] https://www.iarc.fr/en/media-centre/pr/2015/pdfs/pr236_E.pdf

March 17, 2016