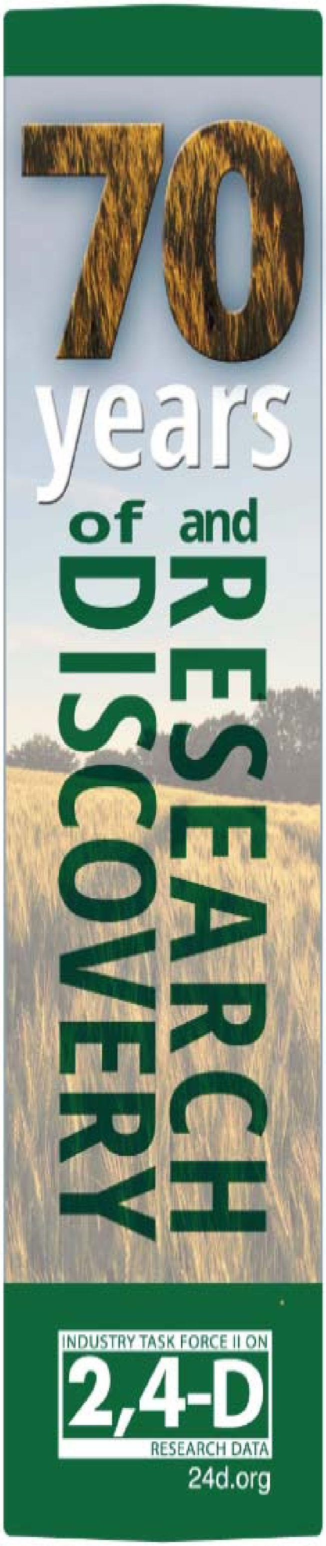


Environmental Toxicology of 2,4-D

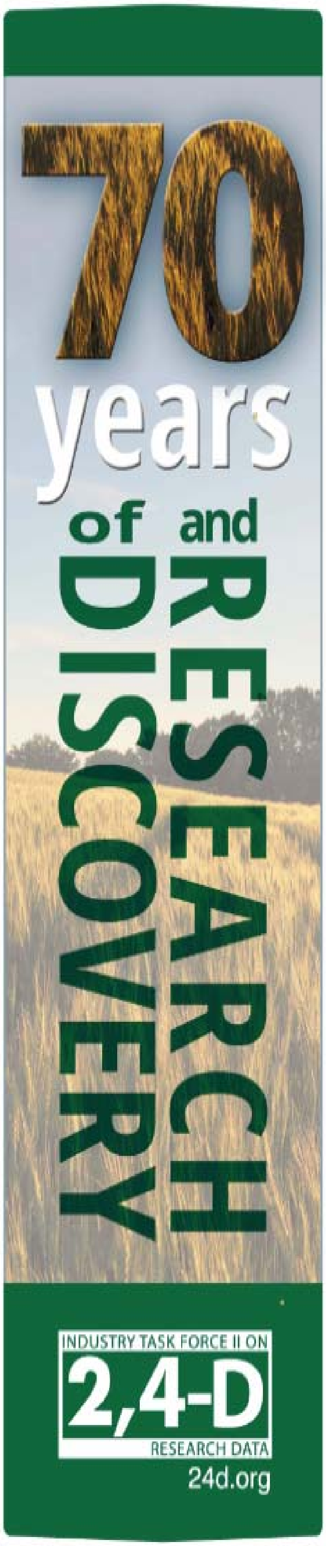
Environmental toxicology includes terrestrial wildlife and plants, and aquatic wildlife and plants. Exposures of wildlife to 2,4-D, whether from direct spraying or consumption of treated vegetation, is of low toxicological significance. Indeed, the greatest effect of 2,4-D on wildlife is likely to be the presentation of an enhanced habitat following spraying, which allows the infiltration of lower-growing, fruit-bearing plants. As documented in one long-term study[1], many common game species occupied the wildlife habitat created by a sprayed utility right-of-way out of an apparent preference and prospered there over a period of more than two decades.

For the past 60 years, the herbicide 2,4-dichlorophenoxyacetic acid (2,4-D) has been widely used for broadleaf weed control in farming, forestry, non-crop areas, pasture, residential turf, and aquatics. The 2005 EPA Reregistration Eligibility Decision (EPA RED 2005)[2] granted continued registration of 2,4-D to include aquatic applications on ditch bank, surface and subsurface. 2,4-D is one of only six herbicides registered in the U.S. for use in aquatic environments.

2,4-D is an ideal compound when dealing with the problems caused by invasive, non-native freshwater plants. Both the liquid amine forms and the granular butoxyethyl ester form are labeled for aquatic use and are effective for control of Eurasian watermilfoil and water hyacinth. The target 2,4-D concentration for submerged invasive plants is up to 4 ppm; however, typical applications are 1 to 2 ppm. In Southern U.S. water hyacinth can easily be controlled by surface application of 2,4-D using 2 to 4 lbs. a.e./acre. An important label statement: "Except as stated [24 hr. waiting period after ester use], there are no restrictions on using water from treated areas for swimming, fishing, watering livestock or domestic purposes."[3]

Aquatic Invasive Plant Control

Aquatic vegetation plays an important role in the health of the aquatic ecosystem. Aquatic plants affect water movement, sedimentation, and water quality. However, a dilemma in the aquatic environment is in the form of invasive vegetation that is causing significant ecological and economic impact on precious aquatic, wetlands, and riparian systems. Although aquatic vegetation comes in several forms, including both submerged and emerged plants, today's greatest challenges involve the management of exotic plants that degrade water quality, human health, fisheries, water-bird habitat recreation, aesthetics and property values. 2,4-D is particularly useful because it is inexpensive and highly selective for Eurasian watermilfoil and water hyacinth when used at the labeled rate, leaving native aquatic species relatively unaffected.



Aquatic dissipation

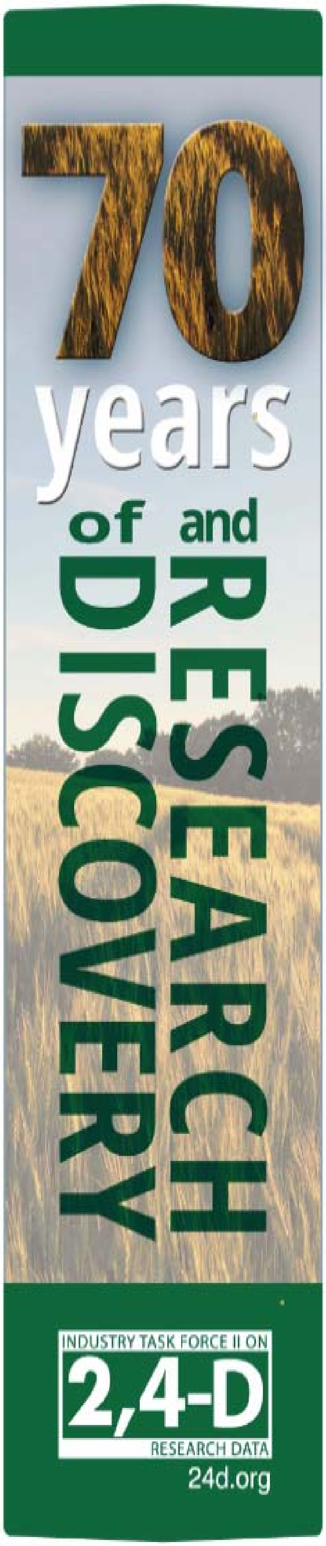
Aquatic dissipation studies show that 2,4-D had an apparent half-life in natural water of one to two weeks, although in areas such as a treated rice paddy, the half-life was as short as one day (See Table 1). The main route of degradation is by microorganisms. 2,4-D amine salts and 2,4-D esters are not persistent under most environmental conditions, water or soil. 2,4-D amine salt dissociation is expected to be instantaneous (<3 minutes) under most environmental conditions. 2,4-D ester hydrolyzes rapidly to the acid in normal agriculture soil and natural water conditions (<2.9 days). Under these conditions, the environmental exposure from 2,4-D esters and 2,4-D amines is expected to be minimal in both terrestrial and aquatic environments. The acid form of 2,4-D, as well as the amine and ester chemical groups, metabolized to compounds of non-toxicological significance and ultimately to forms of carbon. Thus, 2,4-D is considered a biodegradable compound. Under normal conditions, 2,4-D residues are not persistent in soil, water, or vegetation.

Wildlife

Current studies show that 2,4-D is practically nontoxic to fish, amphibians (frogs), only slightly toxic to aquatic invertebrates and practically nontoxic to honeybees and earthworms[4] (See Table 2 Environmental Toxicology Profile).

Fish: The available acute toxicity data on 2,4-D indicate that the acid and amine salts are practically non-toxic to freshwater or estuarine/marine fish. The esters are highly to slightly toxic to marine or freshwater fish; however, 2,4-D butoxyethyl ester, applied as granules, degrades rapidly in aquatic field dissipation to the practically non-toxic acid form under alkaline conditions. The risk from the freshwater chronic exposure was well below the levels of concern, and the chronic risk for estuarine/marine aquatic species would be expected to be low. In studies by Environment Canada using juvenile salmonids and 2,4-D, results obtained were comparable to the low risks found in guideline studies.[5]

Invertebrates: The daphnia is small aquatic invertebrate animal used as an indicator species for toxicity studies. If the lower end of the food chain is unaffected, the higher end is unlikely to be impacted. Daphnia was slightly toxic to 2,4-D acid and practically non-toxic to other 2,4-D forms.



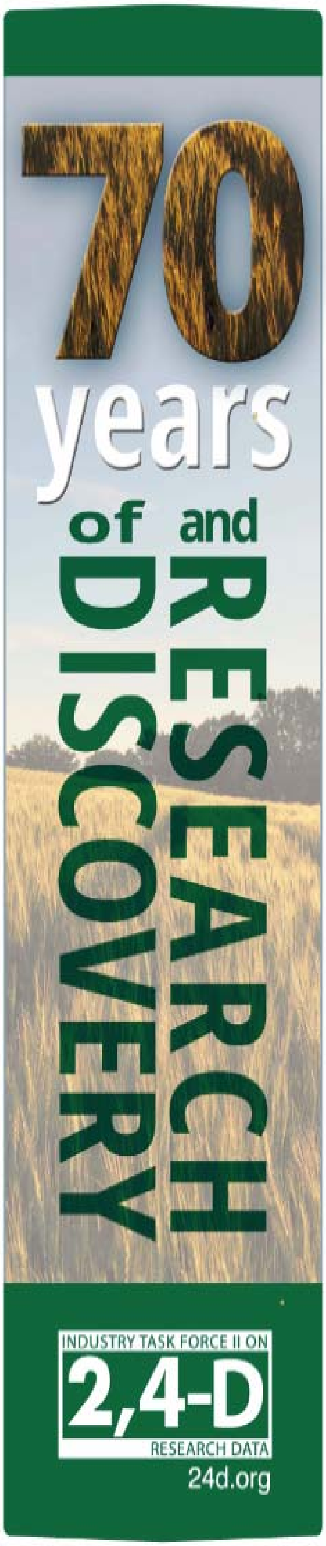
Frogs: Studies with frogs are not a required test species, but the industry desired to have modern, high quality data on an amphibian species. 2,4-D was practically non-toxic according to criteria used for a number of aquatic animals. These 2,4-D ester and amine screening studies showed low toxicity, 359 mg/L. Overspray contamination of surface waters from aerial application, also poses no risk to amphibians. There has never been a reported incidence of amphibian kill attributed to the application of 2,4-D salts or esters, which is consistent with the low risk values determined above.[6]

Birds and mammals: The compound is considered practically nontoxic to the mallard duck and bobwhite quail in 8-day dietary studies and only slightly toxic to birds in acute oral testing. Toxicity ranges for birds do not show distinct differences between the acid, salts, amine salts, and esters. Vertebrates are likely to be exposed to 2,4-D from either grazing treated/ contaminated vegetation or consuming contaminated insects.

The EPA conservative Tier I risk assessment would suggest (based on acute oral toxicity) risk to small mammals and birds following some applications of 2,4-D. Importantly the estimation of risk is greatly reduced for birds when short term dietary data (a more realistic route of exposure) are evaluated. Furthermore, for this risk assessment the estimation of residues on food items represent the maximum value determined for various pesticides immediately after application and does not take in consideration the degradation of 2,4-D in the environment (which is rapid) and added, the assumption is made that all food consumed has the maximum residue levels. The weight of the evidence (i.e. the lack of incidence reports and the conservative nature of the risk methodology) indicates that the risk to birds from 2,4-D is low. (Mammal toxicological evaluation, see the Toxicology Backgrounder).

Avian reproduction: In the avian reproduction study (quail), evaluations were recorded on avian health, body weight, feed consumption, number of eggs laid, fertility, embryo viability, hatchability, offspring survival, eggshell thickness. The no effect concentration (NOEC) was greater than 1000 ppm, practically non-toxic for all measurements – including no cracked eggs. Note that within a day of 2,4-D application at 2 lbs. a.e./acre, grass contains about 135 ppm and rapidly declines thereafter. There is an acceptable margin of safety to wildlife.

Bees: Risk to non-target insects do not exceed the Agency's level of concern. Honey bees may be exposed to 2,4-D by foraging flowering weeds present in treated crops. Studies performed according to OECD and EPA guidelines on 2,4-D dimethylamine and 2-ethylhexyl ester resulted in 72 hr LD50 values of > 100 µg a.e./bee for both acute contact and acute oral studies (practically non-toxic). Additionally, the main use of 2,4-D is not on flowering crops; therefore, the only likely exposure is from bees foraging on patches of flowering weeds within the crop. Thus, due to this restricted exposure pattern and low toxicity, the risk to pollinators and other beneficial insects is predicted to be minimal.



Earthworms: The acute risk to earthworms from the use of 2,4-D is low. Earthworms may be exposed from either single or multiple applications of 2,4-D to wide variety of crops but in particular from its use on pasture and turf. A laboratory toxicity study using the dimethylamine salt of 2,4-D on Eisenia foetida reported a 14 day LC50 of 350 mg/kg soil. This test was conducted by mixing a concentration of test substance in soil.

Non-target plants - aquatic and terrestrial: A variety of non-target terrestrial plant and growth stages were evaluated. Understandably, herbicides cause effects on at least some aquatic and terrestrial broadleaf plants. There may be concern about the risk to non-target terrestrial and aquatic plants from drift or run-off from a 2,4-D application. To address that concern, the Agency is implementing spray drift controls that will decrease the risk from 2,4-D drift onto non-target plants.

Bioaccumulation - bioconcentration: Environmental fate and animal data show that 2,4-D is relatively short-lived. Animal metabolism studies demonstrate that the herbicides are rapidly eliminated. Low potential for bioaccumulation or bioconcentration. A Canadian study spanning several decades showed no accumulative effect in soil.[7]

About the Task Force

The Industry Task Force II on 2,4-D Research Data is organized to provide funding for the on-going Good Laboratory Practice (GLP) research studies required to respond to the US EPA registration review and PMRA pesticide re-evaluation programs. The 2,4-D Task Force is comprised of those companies holding technical 2,4-D registrations: Dow AgroSciences (U.S.), Nufarm, Ltd. (Australia) and Agro-Gor Corp., a U.S. corporation jointly owned by Albaugh, LLC. (U.S.) and PBI-Gordon Corp. (U.S.).

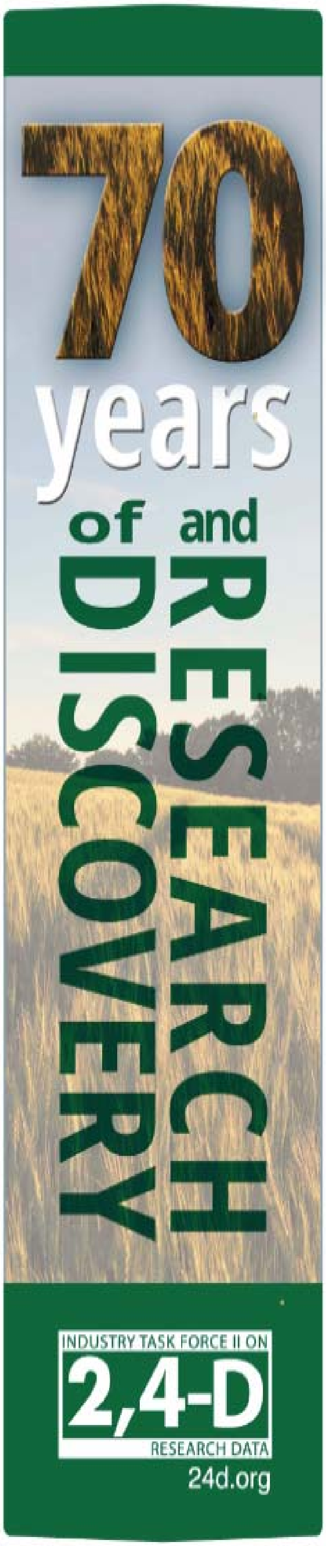


Table 1: 2,4-D Aquatic Test Results

Location	Rate a.e.	Concentration ppb	Half-life days	<70 ppb Days*
Green Lake MN	10.8 lbs/A foot subsurface	3987	3.2	21
Lake Woodruff, FL	3.8 lbs/A Surface	---	2.3	4
Rice in LA	1.5 lbs/A Surface	1372	1.1	13 ppb at 3 days
St. Johns River, FL	3.8 lbs/A Surface	348	0.7	27 ppb at 1 day
St. Johns Insitu M1 to M3	3.8 lbs/A Surface	459 - 526	~ 1	5 - 8
ND Pond	41.8 + 41.8 lbs @ 31 days	4780	1st = 13.9 2nd = 6.5	---
NC Pond	41 + 45 lbs @ 30 days	2210	1st = 19.7 2nd = 2.7	7

** In the application area*

Table 2: Environmental Toxicology Profile:

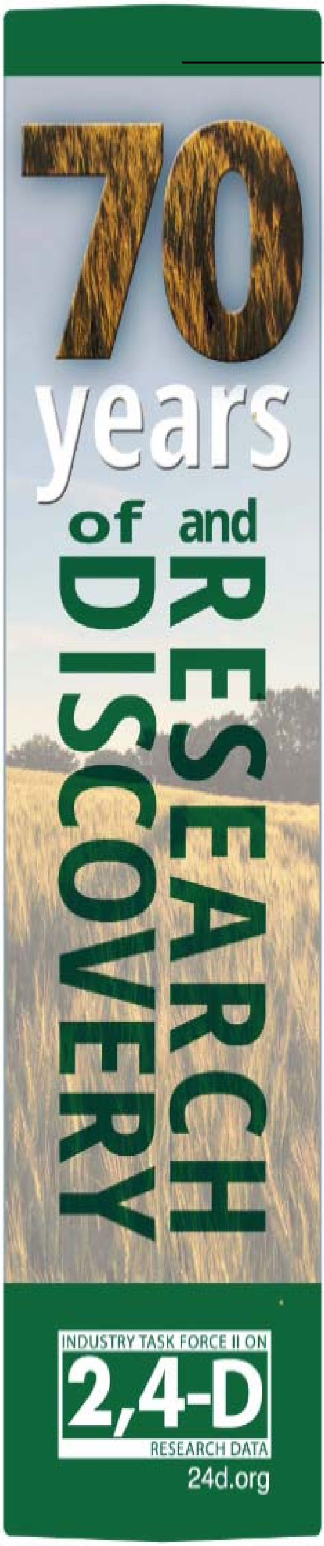
EPA Guideline Requirement	Exposure Value	EPA Toxicity Category
Acute oral LD_{50} [a] – Bobwhite Quail	668 mg/kg	Slightly toxic
Acute oral LD_{50} – Mallard duck	>2000 mg/kg	Slightly toxic
8-day dietary LC_{50} [b] – Mallard duck	>5620 ppm	Practically non-toxic
8-day dietary LC_{50} – Bobwhite quail	>5620 ppm	Practically non-toxic
Avian reproduction NOEC	>1000 ppm	Practically non-toxic
96 h LC_{50} – Bluegill sunfish	263 mg/L[c]	Practically non-toxic
96 h LC_{50} – Rainbow trout	358 mg/L	Practically non-toxic
96 h LC_{50} – Fathead minnow	320 mg/L	Practically non-toxic
96 h LC_{50} – Freshwater juvenile salmonids	299-744 mg/L	Practically non-toxic
96 h LC_{50} – Tidewater Silverside	175 mg/L	Practically non-toxic
96 h LC_{50} – Shrimp	467 mg/L	Practically non-toxic
96 h EC_{50} – Oyster	57 mg/L	Slightly toxic
48 h EC_{50} – Daphnia	>25 mg/L	Slightly toxic
Frogs 96 hr. exposure LC_{50}	359 mg/L	Practically non-toxic
Honeybee contact LD_{50}	>100 µg/bee[d]	Practically non-toxic
Honeybee topical LD_{50}	>100 µg/bee	Practically non-toxic
Earthworm 14 day LC_{50}	>350 mg/kg soil	Practically non-toxic

a. The LD50 value indicates the lethal dose of an active ingredient which is expected to cause death to 50% of the test animals treated. The higher the LD50 the lower the acute toxicity of the compound.

b. The LC50 value indicates the lethal concentration of an active ingredient which is expected to cause death to 50% of the test animals treated. The higher the LC50 the lower the acute toxicity of the compound.

c. For aquatic organisms, values greater than 100 mg/L is considered practically non-toxic.

d. For bees, values greater than 11 µg/bee is considered practically non-toxic.



References:

[1] Bramble, W.C., and W.R. Burns. A long-term ecological study of game food and cover on a sprayed utility right-of-way. Purdue University. 1974. Bulletin No. 918:16.

[2] US EPA Reregistration Eligibility Decision for 2,4-D. 2005. Docket # OPP-2004-0167

[3] See 2,4-D Master Label at: http://www.24d.org/masterlabel/aquatic.aspx

[4] Industry Task Force II on 2,4-D Research Data. Unpublished results of over 60 toxicology and 54 environmental toxicology studies with 2,4-D submitted to the U.S. EPA to support the reregistration of 2,4-D. 1989 - 1995.

[5] Wan, MT; RG Watts and DJ Moul; Environment Canada. 1991.

[6] WHO Pesticide Residues in Food - 1997. Part II - Toxicological and Environmental. WHO/PCS/98.6: 255-346.

[7] Smith, A.E. et al. Degradation, Fate, and Persistence of Phenoxyalkanoic acid Herbicides in Soil. Review of Weed Science. Vol. 4:1-24. 1989.

March 17, 2016