

2,4-D Formulants and their toxicology - Background document

By Paule Hjertaas, B.Sc; March 22. 2005

Most pesticide products are not used alone, but in conjunction with formulants (called 'inerts' in the U.S.) which are added to the active ingredient to make the pesticide more potent or easier to use. (1)

Relevant History of Formulants in Canada

Until the January 2004 formulants list (8) was published, the PMRA had no idea of what formulants were used in Canadian products. A previous list obtained by the Sierra Club (1997) was deemed not to be accurate by the acting director of the PMRA in summer 2001. (11)

In contrast, list of approved formulants in pesticide products have been available and regularly updated on the U.S. EPA web site for many years. (1, 11)

As is still the case in Canada under our new Pesticide Act, formulants used in individual pesticide products were also secret in the U.S. However, in 1996, the U.S. environmental groups North West Coalition for Alternatives to Pesticides (NCAP) and the National Coalition Against the Misuse of Pesticides (NCAMP, now renamed Beyond Pesticides- BP) successfully sued the EPA to force disclosure of the chemicals. (1) The process of obtaining formulants information remains cumbersome, but NCAP has published lists for some pesticide products, including 2,4-D. (6)

Likely Formulants in Canadian 2,4-D products

The following list is presented as a table.

Column 1 shows the formulants listed in the U.S. for 2,4-D. Several of the products have some health effects listed. (6, 7)

Column 2 lists the CAS # of each formulant. In order to check if known U.S. 2,4-D formulants were registered in Canada, I looked up each formulant's CAS #s and checked it against the Canadian list. CAS numbers are important because there are several systems to classify chemical compounds, which produces several synonyms for each. That is why the PMRA did not previously know what formulants were used in Canada. To sort it all out, an international numeric classification of chemicals was established (CAS). The Canadian formulants are now only listed by CAS numbers, so one has to know the number first in order to find any product on the list.

Column 3 shows where each formulant is listed in Canada.

List 1 are known toxins (identified as being of significant concern), **list 2 (potentially toxic), list 3 formulants that do not meet the criteria of any other list, 4A (minimum risk), 4B some may be toxic but no sufficient data.** List 1 formulants had to be identified on Canadian labels since Dec 31. 2001 only, and were to be phased out of all control products by Dec 31, 2004. List 2 formulants were to have been subject to disclosure labeling by December 2001(3), however they will only be disclosed by January 9, 2006.(5) Known allergens should also be listed such as peanuts in bait for instance. Seven of the listed formulants are on list 2, and two on list 4B. The numbers are in bold for easy identification.

Column 4: Californians for Pesticide Reform (CPR) published *Toxic Secrets* in 1998, about inert ingredients of pesticides. (1) The report points out that the EPA does not know how many pounds of formulants/year are used, but estimates that formulants make up on average 32 % of pesticide formulations. (1) The PMRA does not know anything about, or show interest in the issue. (5) Because domestic products are usually less concentrated, formulants make up a larger % of the formulation. Most U.S and Canadian formulants are listed as of unknown toxicity (list 3), but *Toxic Secrets* (1) identified over ¼ of all US listed formulants as known toxins by already being listed as carcinogens (C), toxic chemicals under the Toxic Release Inventory (TRI), occupational hazards (O), hazardous under US Clean Air Act, Clean Water Act, or the Safe Drinking Water Act (A), or active ingredients in the past or present (AI).

Table 1
LIST AND TOXICOLOGY OF FORMULANTS IN 2,4-D PRODUCTS (list copied from 6, 7)

Information about the identity of many formulants is not publicly available. The following 30 formulants are all registered in Canada. We do not now in what product they occur. While we don't know if these formulants are actually used in 2,4-D formulations in Canada, it is likely that they are. Hazards of the ingredients whose identity is available include the following:

<u>Formulant name (6, 7)</u>	<u>CAS #</u>	<u>Canada LIST (8)</u>	<u>CPR toxic (1)</u>
<ul style="list-style-type: none"> • Diethanolamine causes skin and lung irritation and severe eye irritation. (47) It can also cause nausea, headache, and wheezing. (48) It damages the liver, kidney, and blood. (47) 	CAS 111-42-2	2	TRI, A
<ul style="list-style-type: none"> • Dimethylamine is highly flammable. It can cause severe skin burns as well as wheezing and shortness of breath. (49) 	CAS 124-40-3	3	TRI, A, O
<ul style="list-style-type: none"> • Ethanolamine is corrosive. It burns skin and can permanently damage eyes. It can cause liver and kidney damage, as well as damage to developing fetuses. (50) 	CAS 141-43-5	3	O, AI
<ul style="list-style-type: none"> • Ethylenediamine tetraacetic acid has stunted fetal growth and caused birth defects and fetal death in laboratory tests. It also causes genetic damage. (51) 	CAS 60-00-4	3	A, AI
<ul style="list-style-type: none"> • Ethylene glycol can cause birth defects, 52 reduce fertility, and damage nerves and the kidney. Symptoms of exposure include nausea and headaches. (53) 	CAS 107-21-1	2	TRI, AI
<ul style="list-style-type: none"> • Ethylene glycol monobutyl ether (butoxyethanol) causes severe eye irritation and damages blood, nerves, and the also reduces fertility. (54) (synonyms: n-butoxyethanol, butyl cellosolve) 	CAS 111-76-2	2	A, O, AI kidney. It
<ul style="list-style-type: none"> • 2-Ethyl-1-hexanol causes birth defects (55) and severe eye irritation. It also damages the liver and kidney. (56) 	CAS 104-76-7	3	AI
<ul style="list-style-type: none"> • F.D.&C. Blue No.1 may cause irritation and is a possible carcinogen. (57) 	CAS 3844-45-9	3	-
<ul style="list-style-type: none"> • Glutaraldehyde is extremely destructive to eyes, skin, and the respiratory tract. It causes wheezing, headache, and nausea. In laboratory tests it has caused genetic damage and fetal toxicity. (58) 	CAS 111-30-8	3	AI
<ul style="list-style-type: none"> • 3-Iodo-2-propynyl butylcarbamate is severely irritating to eyes, damaging to the thyroid, and causes skeletal abnormalities in developing fetuses. (59) 	CAS 55406-53-6	3	AI, TRI
<ul style="list-style-type: none"> • Kerosene burns skin and eyes; irritates the nose, throat, and lungs; and may damage the kidney. (60) 	CAS 8008-20-6	3	AI
<ul style="list-style-type: none"> • Methyl alcohol has caused fetal toxicity, birth defects, and genetic damage in laboratory tests. It may cause kidney damage, dizziness, nausea, vomiting, and blindness. (61) 	CAS 67-56-1 for methanol	3	A, TRI, O
<ul style="list-style-type: none"> • Methyl pyrrolidinone causes eye irritation. 62 In laboratory tests, it has caused fetal death and reduced fetal weight. (63) 	CAS 872-50-4	3	TRI

<ul style="list-style-type: none"> • Naphthalene can cause anemia, liver damage, cataracts, and skin allergies. In laboratory tests it has caused birth defects and genetic damage.(64) 	CAS 91-20-3	3	A, TRI, O
<ul style="list-style-type: none"> • Silica (crystalline) has been classified as “carcinogenic to humans” by the International Agency for Research on Cancer. It has also caused genetic damage in some laboratory tests.(66) 	CAS14808-60-7	2	C
<ul style="list-style-type: none"> • Silica (amorphous) causes eye irritation and has caused lung damage, diarrhea, and tumors in laboratory tests.(67) 	CAS 7631-86-9	4A	-
<ul style="list-style-type: none"> • Sodium ligninsulfonate may cause eye, skin, and respiratory tract irritation. It has caused drowsiness and weakness in laboratory tests.(68) 	CAS 68512-34-5	3	-
<ul style="list-style-type: none"> • Triisopropanolamine causes severe eye irritation and may cause skin irritation or nausea. Inhalation can be fatal.(70) 	CAS 122-20-3	3	AI
<ul style="list-style-type: none"> • 1,2,4-Trimethylbenzene damages the central nervous system and is irritating to eyes, skin, and the upper respiratory tract.(71) 	CAS 95-63-6	3	-
<ul style="list-style-type: none"> • Xylenes cause eye and skin irritation, headaches, nausea, and confusion. In laboratory tests they have caused kidney damage and fetal death.(72) 	CAS 1330-20-7	2	A, TRI, O, AI

Other U.S 2,4-D formulants (7) listed in Canada:

Petroleum distillates	CAS 8002-05-9	2	-
Polyoxyethylene alkylamide (POEA)	CAS 61791-26-2	3	-
Potassium hydroxide	CAS 1310-58-3	4B	A, AI
Diethylene glycol	CAS 111-46-6	3	A
Diacetone alcohol	CAS 123-42-2	3	A, O, AI
Isobutane	CAS 75-28-5	3	A
Isopropanol	CAS 67-63-0	4B	TRI, O, AI
Alkyl phenol glycol ether	CAS 69029-39-6	3	-
Emulsified silicone oil	CAS 63148-62-9	3	-
Hydrogenated aliphatic solvent	CAS 64742-47-8	2	-

The following 1996 registered US formulants are not currently unlisted in Canada * are the following:

poly(dimethylsiloxane) (6)	CAS # 107-46-0
tetrakis(trimethylsilyloxy)silane (6)	CAS # 3555-47-3
nonylphenol (7)	CAS 25154-52-3
petroleum solvent (7)	CAS 64742-94-5

* The Canadian formulants list released to the Sierra Club in 1997 contained 17-20 nonylphenols, as well as poly(dimethylsiloxane), and petroleum solvent.

Discussion

The major reason for insisting on disclosure requirements of formulants is to ensure the use of least toxic ingredients in pesticide formulations. In the US, disclosure requirements clearly encouraged this trend. "The use of inerts classified by EPA as 'of toxicological concern', for which labeling is required, fell 86 %, from 57 chemicals in 1987 to eight in 1997. Similarly, the number of products in which they were used fell 97 %, from 1300 products in 1987 to 40 today." (1)

While we don't know if these formulants are actually used in 2,4-D formulations in Canada, it is likely that they are because of harmonization of the lists and the regulatory processes between the US and Canada (3, 8).

Of these 30 secret formulants (we don't know which is used where), 20% (7/30) are listed by the PMRA (or government of Canada) as potentially toxic (List 2) and 6.6 % (2/30) as "may be toxic but insufficient data" (list 4B). One only is a minimum risk product (list 4A), and 66% (20/30) are on List 3. (8)

As can be seen by column 4, many class 3 formulants have recognized toxicity outside of the pesticide legislation. In the US, 70% (21/30) of these same formulants are already recognized as chemically, biologically, or toxicologically active. These chemicals are able to cause cancer, reproductive and nervous system harm, and other health and environmental problems. 43 % (13/30) are or have been used as pesticide active ingredients in the US. (1)

Several such as *antifreeze*, *wood alcohol (methanol)* and *xylene* can be readily absorbed through the skin or by breathing them in, as well as by ingestion. *Glutaraldehyde* is very toxic when breathed in or ingested. (9)

The pesticide industry is biased towards considering only their own experimental data in regards to the safety of pesticide products. Let's remember that these experiments are only performed with one pesticide active ingredient at a time, not with the formulations we are currently exposed to. Nonetheless, many of these studies show various negative health consequences for the test animals, which are then processed through mathematical formulas to estimate their relevance to human health. Furthermore, many of the studies involve feeding a pesticide to animals, at high doses, both factors being irrelevant to common public exposures, which are more likely to occur through breathing in a smaller quantity of pesticide and get it on our skin and clothes. None of the studies industry currently submits include formulants. Furthermore, the discovery that many chemicals have endocrine effects at low dose indicates that the appropriate testing should be conducted, but they are not.

The pesticide industry would like to see epidemiological evidence discounted because, as they see it, there may be other factors or chemicals that would have contributed to occurrences of negative side effects of pesticide products. However, epidemiological studies look at the effects of the full pesticide formulations in the quantities and exposures currently relevant to human and environmental health. What the pesticide industry never mentions is that one of the reasons why it may be difficult to draw definite conclusions on toxicity may be the various secret chemicals (formulants) they themselves add to these pesticide active ingredients to make them easier to use or increase their toxicity. There is currently no understanding of the potential effects of such mixtures, or much effort to unravel them. (12)

Conclusion

Formulants are regularly added to a pesticide active ingredient to make it more potent or easier to use. The average pesticide formulation is made of 2/3 formulants, and domestic formulations (sold without requiring a license) are up to 99 % formulants.

While they remain secret in Canada, fully 70 % of the US commonly used 2,4-D formulants have serious toxicity of their own. Most of these are likely used in Canadian 2,4-D formulations. Much still remains unknown about formulants as most of them remain poorly tested or untested, even by themselves.

In spite of the scientific acceptance of the reality of endocrine disruption and low dose effects, none of the studies mandated by the PMRA are designed to identify either effect in pesticide active ingredients. None have been submitted for formulants.

Many chemical mixtures studied have shown synergistic effects. It should be no big surprise that formulants can affect the toxicity of an active ingredient such as 2,4-D. Most epidemiological studies cannot account for formulants because they are secret. Different formulants likely affect the toxicity or absorbability of a particular active ingredient in different ways, therefore confusing the relationships between a particular illness and a particular pesticide active ingredient such as 2,4-D.

No buyer or user of any pesticide product knows all ingredients it contains. Even the PMRA cannot tell how much more dangerous or toxic a formulation is than the individual pesticide active ingredient tested. They are not yet looking. That is likely why claims of safety in advertising are illegal, because “they may be interpreted as relating to personal safety and, as a result, may cause some confusion.” (13). The PMRA should follow its own regulations and make no safety statements.

REFERENCES

1. Northwest Coalition for Alternatives to Pesticides; 1998; Toxic Secrets Inert Ingredients in Pesticides 1987-1997; report by Californians for Pesticide Reform

2. Vacco, Dennis C, Attorney General; revised 1994; The Secret Hazards of Pesticides: Inert Ingredients; New York State Dept of Law

label comparisons: the first 4 mixed amines on the list all contain less than .4% active ingredients (AI) total (that includes dicamba and mecoprop). The first 3 commercial products listed contain between 19.4 to 58.2 % AI. That is why the warnings are not so strong on domestic labels, because the PMRA still works exclusively with "the dose makes the poison"

3. PMRA PRO2000-04; <http://www.pmra-arla.gc.ca/english/pdf/pro/pro2000-04-e.pdf>

4. Pesticide Act - Canada

5. PMRA personal communication

PMRA correspondence.

Labelling of List 2 formulants and other questions

Date: Wed, 02 Mar 2005 16:32:36 -0500

From: PMRA INFOSERV <PMRA_INFOSERV@hc-sc.gc.ca>

To: Dale & Paule Hjertaas

Hello Ms. Hjertaas,

In response to your first question, please be advised that List 2 formulants must be listed on pest control product labels by January 9, 2006. Regarding your second and third questions, I am sorry to inform you that the PMRA does not have any statistics as to pesticide use or pesticide composition. You may wish to address these questions to Statistics Canada.

I trust this is satisfactory.

Robert Martin

Regulatory Information Officer / Agent d'information sur la réglementation
Pest Management Regulatory Agency/Agence de réglementation de la lutte
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613-736-3799
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www.eddenet.ca

From: Dale & Paule Hjertaas

To: PMRA INFOSERV <PMRA_INFOSERV@hc-sc.gc.ca>

Subject: when list 2 formulants on labels? + other questions

01/03/2005 04:42PM

Hi ,

1. I was checking REG 2004-1 and did not find in it whether list 2 formulants were currently identified on labels, and when it started. PRO2000-04 indicated they should be by Dec 31, 2001. Was it enforced as planned?

2. Do you know how many pounds/year of formulants (in general, for individual ones) are used ?

3. The US EPA estimates that formulants make up on average 32 % of pesticide formulations. Is it the same in Canada? If you have the information, it would be interesting to get an average composition (AI versus formulants) of domestic products versus commercial, and also Canadian sales of domestic products versus commercial.

Thank you,

Paule Hjertaas

6. Cox, Carolyn; summer 1999; 2,4-D: Toxicology, part 2; Journal of Pesticide Reform Vol 19, NO 2

7. Inert Ingredients in Commercial 2,4-D Products;(as of June 1999) <http://pesticide.org/24Dinerts.html>
(NCAP does not list it any more on their site, but I obtained it from them)

8. PMRA REG-2004-01

9. various MSDS sheets and serious sites on toxicity found on the Internet yesterday.(sorry I did not record the sites)

10. Coalition for a Healthy Ottawa fact sheet on 2.4-D review.

11. MITTELSTAEDT, Martin; Federal pesticide list outdated Roster of permitted inactive compounds found to be '85-to-90-per-cent incorrect'; The Globe and Mail; Tuesday, July 17, 2001 (Print Edition, Page A4)

"The federal list of inactive ingredients allowed in pesticides is a shambles, with sloppy record-keeping, a cancer-causing chemical added in error, and possibly thousands of compounds on the roster that an official says should not be there.

A list of the approximately 4,600 ingredients Health Canada allowed in pesticides at the end of 1997 -- an 86-page document -- has been obtained by The Globe and Mail, but the official said it is "probably 85-to-90-per-cent incorrect today" because of the number of errors in the list and frequent changes in manufacturers' products.

The official, Diana Somers, acting director of the health-evaluation division of Health Canada's Pest Management Regulatory Agency, said the number of inactive compounds in the most recent, secret government list is about 5,000.

She said the agency is trying to verify what is in the 8,000 to 10,000 pesticide products sold in Canada, going over each product to eliminate errors, but the work is difficult because of the complex chemical names used. Some ingredients go by more than one name.

Although Canada is having difficulty with this task, the U.S. Environmental Protection Agency updates its list regularly and makes it available on its Web site. The EPA has about 2,500 inactive ingredients licensed for use, half the number on the Canadian list. A pesticide critic says Health Canada's inability to keep an accurate record of what is in pest-control products calls the department's competence into question. "I think that's really scary, if they can't even keep a list up to date," Janet May of the Toronto Environmental Alliance said. "It doesn't give you a lot of faith in the regulatory agency."

Almost all pesticides contain two different types of compounds, the active ingredients that actually do the work of killing bugs, weeds and other pests, and the inactives. These, known as formulants, do such jobs as making the active ingredients easier to apply or more adherent.

Manufacturers are required to list on the package the active ingredients they use, but most formulants are kept confidential as trade secrets. They make up 90 per cent and even more of many commonly sold pesticides. Many formulants are themselves toxic, or are known or suspected carcinogens. The 1997 formulant list, for instance, included dozens of dangerous items, such as asbestos fibres, which can cause lung disease and cancer, and lead, a toxic heavy metal, along with benign products such as peanut butter.

Ms. Somers said she doubts pesticide manufacturers are selling products in Canada containing formulants not registered for use in the United States because the industry is integrated across North America. She said the Canadian list could shrink to the size of the U.S. one when the agency's review is completed and all errors are purged. "I suspect it would be very similar to the U.S. because all our formulants come from there," Ms. Somers said.

Ms. May contended that Health Canada's sloppy-record keeping has made Canada vulnerable to obsolete products not allowed in the United States, where pesticide registration is more thorough. Ms. Somers, asked if unregistered U.S. formulants were ending up in Canada, said: "I doubt that. . . . I think that's conjecture."

Health Minister Allan Rock said last month, after The Globe and Mail published an article on the items on the 1997 formulant list, that he would introduce legislation this fall requiring manufacturers either to remove toxic inactive ingredients or to list them on the label. Ms. Somers said the government will not release its revised list of inactive ingredients until the new legislation is adopted. The 1997 list includes vinyl chloride, a carcinogen. Ms. Somers said the agency was alarmed at the discovery of this compound, ordered a review, and found staff had added the chemical in error.

Susan Sang, a toxicologist at the World Wildlife Fund, identified dozens of chemicals on the list that are hormone disruptors, suspected of causing birth defects, or are carcinogens or suspected carcinogens."

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Diana Somers, Acting Director, Bus: (613) 736-3510, Fax: (613) 736-3505, E-mail: diana_somers@hc-sc.gc.ca
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12. COMPLEX CHEMICAL MIXTURES

FY 2000 Science to Achieve Results (STAR) Program
NATIONAL CENTER FOR ENVIRONMENTAL RESEARCH
U.S. Environmental Protection Agency
National Institute for Occupational Safety and Health
National Institute of Environmental Health Sciences

Opening Date: April 10, 2000

Closing Date: July 10, 2000

Location of quote:

Under "Research Goals and Scope," then find "Exposure Assessment."

The EPA states clearly there are **no methods for assessing the toxicity of mixtures of chemicals**. "A major, long-term challenge for regulatory agencies is to develop defensible means of combining exposure assessments in a manner that provides meaningful ways of determining potential health risks from total exposures to many chemicals. Lacking are methods to characterize potential toxicological risk."

13. PMRA Regulatory Directive DIR 96-02 and Pest Control Products Regulations

Paule Hjertaas is a biologist, herbalist, environmental health consultant and free-lance writer living in Regina. She has been researching the issue of pesticides and health for over 18 years.