

2,4-D Re-evaluation Update and Label Improvement Program

The purpose of this document is to update developments since publication of the last Note to CAPCO on 2,4-D in February, 1989. Specifically, it is intended to:

- (a) summarize progress achieved to date under the ongoing re-evaluation of 2,4-D in Canada;
- (b) highlight the findings of recently published epidemiology and exposure studies;
- (c) outline the current status of 2,4-D in the U.S.; and
- (d) announce a Canadian label improvement program (LIP) for 2,4-D intended to reduce operator and public exposure, and upgrade label quality, consistency and accuracy.

This document is published under the authority of the Interdepartmental Executive Committee on Pest Management which represents the departments of Agriculture and Agri-Food, Health, Environment, and Natural Resources.

(publié aussi en français)

November 23, 1994

This document is published by the Submission Management and Information Division, Pest Management Regulatory Agency. For further information, please contact:

Publications Coordinator
Pest Management Regulatory Agency
Health Canada
2250 Riverside Drive
A.L. 6606D1
Ottawa, Ontario
K1A 0K9

Telephone: (613) 736-3592
Facsimile: (613) 736-3798
Information Service: 1-800-267-6315
(In Canada only)
Internet: pmra_publications@hc-sc.gc.ca
www.hc-sc.gc.ca



Background

The herbicide 2,4-dichlorophenoxyacetic acid (2,4-D) was first registered in Canada in 1946. It is still extensively used for broadleaf weed control in agriculture, forestry, along rights-of-way, and on turf. Commercial formulations may contain 2,4-D in the form of amine salts or low volatile esters and also may be formulated as mixtures with other herbicides such as dicamba, mecoprop, dichlorprop, bromacil, atrazine, picloram, triclopyr, MCPA, fenoxaprop-P-ethyl or glyphosate. The strength of the commercial formulations is expressed in terms of the acid equivalent content of the parent acid, which is the biologically active form.

The predominant use of 2,4-D products in Canada is in cereal crop production, where it is typically tank mixed with other herbicides. This practice reduces the total cost of the treatment, increases the spectrum of weed control and helps prevent the development of weed resistance—a growing problem with many of the newer herbicides that have a narrower mode of action compared to 2,4-D.

In forestry, 2,4-D products are used as management tools to suppress unwanted hardwood trees and brush which compete with conifers, or to prepare sites for the regeneration of new conifer stands. 2,4-D products are also used on grazing lands to control unpalatable and noxious weeds and to suppress brush in pastures and ranges. Industrial uses include control of brush on utility and transportation rights-of-way.

Urban uses include control of dandelions, plantain and other broadleaf weeds in turf and suppression of ragweed, poison ivy and other weeds of nuisance or threat to public health.

The re-evaluation of 2,4-D was announced in October 1980 under the authority of Section 19 of the *Pest Control Products (PCP) Act*. Re-evaluation was undertaken in view of the herbicide's broad range of applications and long history of use.

Re-evaluation Milestones

- October 1980 Announcement of re-evaluation and proposal for use pattern changes.
- December 1981 Agriculture and Agri-Food Canada, having discovered the presence of certain dioxins in 2,4-D products, set a limit on dioxin levels and required that technical grade 2,4-D be registered under the *PCP Act*.
- April 1982 Agriculture and Agri-Food Canada announced that 2,4-D products containing high volatile esters were being discontinued. As well, obsolete uses were deleted from the acceptable use pattern and a more precise definition of dosage ranges was developed.
- February 1989 New health and environmental data developed since 1980 under the auspices of Industry Task Forces (I&II) on 2,4-D Research Data were reviewed and summarized in *Note to CAPCO 89-01*. This document also contained the summary of a benefits study commissioned by Agriculture and Agri-Food Canada. No changes to the regulatory status of 2,4-D products were considered necessary as a result of this review.
- 1989 to present The Industry Task Force II has continued to develop and submit health and environmental data on 2,4-acid, 2,4-D dimethylamine and 2,4-D 2-ethylhexyl ester (isooctyl ester). Data submitted since 1991 have been scanned by CORE advisors, but have not been scheduled for review pending completion of the pivotal rat and mouse oncogenicity studies. Advisors have, however, commented on study protocols, whenever there was an opportunity, and have identified data gaps. The Health Protection Branch of Health Canada published a Fact Sheet, one of a series of Issues, on 2,4-D in May 1993.

Studies Completed or in Progress	Number of Studies
Chemistry	
Physical properties-product specific	5-15 per formulation
Environmental Toxicology	
Avian	8
Aquatic Organism	33
Toxicology	
Acute Toxicology	16
Subchronic Toxicology	21
Chronic Toxicology	3
Mutagenicity	9
Acute Neurotoxicity	1
Chronic Neurotoxicity	1
General Metabolism	2
(limited)	
Environmental Fate	
Nontarget Phytotoxicity	14
Degradation Studies - Lab	4
Metabolism Studies - Lab	6
Mobility Studies	3
Dissipation Studies	34
Accumulation Studies	3
Moiety Studies	5
Spray Drift*	-
Residue Chemistry	
Plant & Animal Metabolism	7
Field Residue Studies	<u>28</u>
Total	<u>198</u>
* involves numerous studies coordinated by the Spray Drift Task Force which represents 34 companies	

Highlights of Recent Studies

Epidemiology Studies

2,4-D is undoubtedly the most thoroughly researched of any herbicide. It has been the subject of more than 90 epidemiological studies (Page, 1994), several of which have been published since the last Note to CAPCO was issued in February, 1989. Summary excerpts of these studies are presented here by way of update. For further details, please consult the list of references provided. The new epidemiology studies are still being assessed as part of the ongoing 2,4-D re-evaluation process, and definitive conclusions cannot yet be drawn.

1. Bond et. al. (1989) who assessed the relationship between phenoxy herbicides and cancer reported that:

“The total weight of evidence currently available does not support a conclusion that any of the phenoxy herbicides present a carcinogenic hazard to man.”

2. A panel of scientists was assembled by Harvard School of Public Health (1990) to evaluate the evidence on whether 2,4-D was a human carcinogen. In assessing all of the available data, the panelists reported that:

“While a cause-effect relationship is far from being established, the epidemiological evidence for an association between use of 2,4-D and Non-Hodgkin’s Lymphoma (NHL) is suggestive and requires further investigation. There is very little evidence of an association between use of 2,4-D and Soft-Tissue Sarcomas (STS) or Hodgkin’s disease, and no association between 2,4-D use and any other form of cancer.”

3. Mullison and Bond (1991) conducted what was, in substance, a review of 2,4-D toxicology studies published since the 1970’s. They concluded that:

- 2,4-D is not a carcinogen, or at worst, it is a very weak one. It does not have the general characteristics of carcinogenic compounds. 2,4-D and its metabolites are not considered to be genotoxic or capable of damaging DNA;
- recently completed studies support the conclusions of earlier studies that 2,4-D may be used without undue risk to humans, wildlife or the environment; and
- this opinion is shared by most scientific experts who have carefully examined all the data.

4. A case-control study of dogs was conducted by Hayes et. al. (1991) at National Cancer Institute to investigate canine malignant lymphoma and its relationship to chemical exposure including 2,4-D. The authors used a questionnaire to obtain information from dog owners on demographics, lifestyle and lawn chemical exposure. They concluded that:
 - owners in households with dogs that developed malignant lymphoma applied 2,4-D to their lawn and/or employed lawn care companies to treat their lawn significantly more frequently than control owners (odds ratio = 1.3);
 - risk rose to a two-fold excess with four or more yearly, owner-applied 2,4-D applications; and
 - the authors acknowledged the fact that the findings of such case-control interview studies may be biased because of differential recall of cases and references.

5. Bond and Rossbacher (1993) who conducted a review of the potential human carcinogenicity of MCPA, MCPP and 2,4-DP concluded that:

“These compounds have not produced tumors in animal studies under current test guidelines, giving no reason to predict that they would be carcinogenic in humans. Epidemiological studies have been conducted on three continents; greater emphasis is placed on the studies reported from western Europe, however, as this has been the area of more use. Although several of these studies provide suggestive evidence of associations between exposure to chlorophenoxy compounds and increased risks for some uncommon cancers, it is inconsistent and far from conclusive. None of the evidence specifically implicate MCPA, MCPP, or 2,4-DP as a human carcinogen.”

6. EPA Science Advisory Board (SAB)/Scientific Advisory Panel (SAP) Joint Committee (1993). The committee’s report “Assessment of Potential 2,4-D Carcinogenicity” stated:

“...our conclusion at this time is that while there is some evidence that NHL may occur in excess in populations which are likely to be exposed to 2,4-D, the data are not sufficient to conclude that there is a cause and effects relationship between exposure to 2,4-D and NHL. The data are however, sufficient to require continued examination of the issue through further studies.” (See also the section entitled “Status of 2,4-D in the United States”)

Exposure Studies

As an update to the previous Note to CAPCO, the highlights of several studies that have appeared in the scientific literature since 1989 are presented here. For further details, please refer to the original studies referenced.

1. Harris et. al. (1992) used biological monitoring to assess home owner and bystander exposure to 2,4-D during application of liquid or granular formulations to residential turf. They concluded that:
 - exposure was highest for home owners applying liquid formulations who did not receive instructions on use and wore their normal clothing. Exposures were directly related to spills of liquid concentrate on the bare hands or forearms, or excessive contact with the dilute liquid; and
 - 2,4-D was not detected in urine of bystanders potentially exposed during application to domestic turf.
2. Harris and Solomon (1992) used biological monitoring to assess exposure to adults following one-hour of controlled activities (walking, sitting, laying) on turf sprayed 1 or 24 hours previously. They concluded that:
 - individuals (wearing long pants, T-shirt, socks and covered footwear) exposed to turf sprayed either 1 or 24 hours previously had no detectable exposure to 2,4-D;
 - three of 10 individuals (wearing shorts, T-shirts, no socks or footwear) exposed to turf sprayed 1 hour previously had detectable levels of urinary 2,4-D. Individuals wearing the same clothing, but exposed to turf sprayed 24 hours previously did not have detectable levels of 2,4-D in their urine; and
 - dislodgeable 2,4-D residues were detectable on turf 1 and 24 hours after application. Residues were lower at 24 hours.
3. Solomon et. al. (1993) used biological monitoring to assess exposure to lawn care technicians carrying out their regular job functions over a 14-day period. Quantitative estimates of exposure cannot be drawn from the results due to limitations in study design.
4. In assessing the extent to which there is scientific support for the hypothesis that 2,4-D exposure is associated with any increased risk of human cancer, Munro et al (1992)

concluded that:

- the case-control epidemiological studies are inconclusive. These studies considered together provide, at best, only weak evidence of an association between 2,4-D and the risk of cancer;
- the structure of 2,4-D does not resemble a carcinogen. It is a simple organic acid that is largely excreted unaltered and there is no evidence that it is metabolized to critically reactive metabolites or has potential for bioaccumulation; and
- 2,4-D has no known mammalian hormonal activity and does not induce proliferative changes in any tissue or organ.

Status of 2,4-D in the United States

EPA Special Joint Committee

The U.S. Environmental Protection Agency (EPA) announced a Special Review (Data Call In) in September 1988. The EPA later requested that all available epidemiological and toxicological data be reviewed by a panel of experts. The Special Joint Committee of the Science Advisory Board (SAB) and Scientific Advisory Panel (SAP) was subsequently formed and first met on April 1-2, 1993, in Arlington, Virginia.

The Final Report of the Committee was submitted to EPA on March 22, 1994. Highlights of the report are as follows:

- Epidemiologic cohort studies which have tried to identify a hazard from exposure to 2,4-D have generally shown no increased risk of cancer. The Committee noted, however, that all of the populations for which specific exposure to the herbicide have been identified were small, and the follow-up period usually short. Some case-control studies have shown a risk of NHL in association with the occupation of farming, but many of these studies did not indicate whether this relationship was due to a specific exposure to 2,4-D, or to other agents. The Committee concluded that the studies conducted to-date cannot distinguish whether observed risks reported are due to the use of 2,4-D or some other aspect of farming as an occupation.
- The single extant canine epidemiologic study suggests that pet dogs may be at risk from exposure to 2,4-D or to areas treated by commercial lawn care services. Although this study is supportive of a finding of carcinogenicity, there are questions about its applicability to human carcinogenicity since the cancers may not be similar in dogs and humans, and exposures to 2,4-D were not clearly established. To substantiate these

results, the study should be replicated with improvement in the exposure measures and verification of the comparability of the cancers in canine and humans.

- Toxicology studies executed so far indicate that rats (but not other animal species tested) may develop astrocytomas from exposure to 2,4-D. However, this outcome has not been reported in the human studies. An ongoing rat study at higher doses will clarify whether this finding is treatment-related or not. Tests with 2,4-D have not shown any mutagenic changes under experimental situations.
- The Committee concluded that, at this time, the data are not sufficient to find that there is a cause and effect relationship between the exposure to 2,4-D and NHL. Because there is some evidence the NHL occurs in excess in populations that are likely to have been exposed to 2,4-D, there should be continued examination of the issue through further studies.

To help resolve the 2,4-D controversy, the Committee recommended the following steps:

- Completion of EPA-requested rodent studies;
- Animal carcinogenicity studies that test 2,4-D jointly with other substances that might reflect the human exposure situation;
- A replication of the dog epidemiology study;
- Additional case/control epidemiology studies, with careful attention to exposures, particularly multiple exposures;
- Human epidemiology studies, particularly cohort studies designed to assess both relative risk of NHL and comparative risk of all mortality (or all disease incidence, if possible);
- Additional follow-up and analysis of worker cohorts involved in production of 2,4-D.

EPA – Industry Task Force Agreement

The EPA announced on October 9, 1992, that the agency and the Industry Task Force representing the registrants of 2,4-D had reached an agreement to make label changes to

2,4-D products in order to reduce exposure. In addition, the Industry Task Force agreed to carry out a consumer education program highlighting the reasons for the exposure reduction measures. The Industry Task Force agreed to these exposure-mitigation measures as an alternative to EPA's suspension of their products for failure to meet deadlines for submitting certain toxicology studies. The label changes include the following:

- Mechanical transfer of 2,4-D from containers of five gallons or more;
- Protective clothing, including chemical resistant or rubber gloves, eyewear such as goggles, and coveralls or chemical resistant aprons, must be worn during open pouring of volumes over one gallon;
- Hygiene statements - washing hands and other exposed areas of the body and laundering of clothing before re-use;
- Reduced application rates;
- Use limited to two applications per year on turf;
- A restricted entry statement for turf.

The agreement is implemented through the amendment of registrations of technical and manufacturing-use products containing 2,4-D acid or any derivative of the acid.

Canadian Label Improvement Program (LIP) for 2,4-D

While 2,4-D is under re-evaluation, Agriculture and Agri-Food Canada's position remains one of continued but cautious use. As a prudent measure in the interest of public safety, and in line with gradual harmonization efforts with EPA, Agriculture and Agri-Food Canada has made a regulatory decision to implement a label improvement program aimed, primarily, at exposure reduction.

Label improvement program initiatives have been favourably received by registrants and product users. The Industry Task Force and the Crop Protection Institute are supportive of this initiative.

The Industry Task Force, in consultation with the Plant Industry Directorate, developed generic draft labels for the various use scenarios of 2,4-D. CORE advisors at Chemical Evaluation Division and Toxicological Evaluation Division of Health Canada's Food Directorate; the Commercial Chemicals Evaluation Branch of Environment Canada; and the

Forest Pest Management Institute of Natural Resources Canada were subsequently consulted. In addition to exposure mitigating measures, this label improvement program is also intended to upgrade label quality, consistency and accuracy.

Label Amendments

The 2,4-D end-use product labels will be amended with respect to the following:

1. Protective Clothing and Equipment

a. Commercial Class Products:

Handling the concentrate (mixing and loading): wear long-sleeved shirt, long pants, chemical-resistant gloves, socks and shoes, and protective eye wear (face shield or safety glasses). Rinse gloves before removal.

Coveralls or a chemical-resistant apron should also be worn when open pouring from containers greater than 5 L.

Handling the dilute spray solution (during application or repairing or cleaning equipment): wear a long-sleeved shirt, long pants, chemical-resistant gloves, socks and shoes. Rinse gloves before removal.

Gloves are not required during application when applicator is in an enclosed tractor or in an enclosed airplane cockpit.

b. Domestic Class Products:

Wear long-sleeved shirt, long pants, socks, shoes and chemical-resistant (e.g., rubber) gloves.

2. Operator Use Precautions

a. Commercial Class Products:

- Wear freshly laundered clothing and clean protective equipment daily.
- Rinse gloves before removal.

- Wash hands before eating, drinking, using tobacco or using the toilet.
- If herbicide penetrates clothing remove immediately; then wash thoroughly and put on clean clothing. Throw away clothing and other absorbent materials that have been drenched or heavily contaminated with this product's concentrate.
- After using this product, remove clothing and launder separately and promptly, and thoroughly wash hands and exposed skin with soap and water. Follow manufacturer's instructions for cleaning personal protective clothing and equipment. If no such instructions for washables are provided, use detergent and hot water. Keep and wash personal protective equipment separate from household laundry.
- After work, remove all clothing and shower using soap and water.

b. Domestic Class Products:

- Rinse gloves before removal.
- Wash hands before eating, drinking, using tobacco or using the toilet.
- If pesticide penetrates clothing, remove immediately; then wash thoroughly and put on clean clothing.
- Remove clothing and launder separately before reuse, and promptly and thoroughly wash hands and exposed skin with soap and water, then shower.
- Re-use gloves for pesticide application only.

3. Mechanical Transfer System

10 and 20 L containers: Manufactures are required to incorporate a built-in plastic spout on the containers, to minimize spillage and exposure.

Containers larger than 20 L: Use a transfer system that avoids open pouring when transferring the liquid concentrate from such containers into the spray tank.

4. Pre-harvest Intervals

As required by *Regulatory Directive Dir93-18*, labels should not be silent with respect to pre-harvest intervals prior to grazing, feeding to livestock and harvesting for hay.

Although data have been submitted to Health Canada by the Task Force on metabolism in wheat, poultry and lactating goats, there is presently a lactating cow metabolism study being performed. This study is most relevant to this issue but will not be available for evaluation until late 1994 or early 1995. Consequently, Health Canada can not provide any comments on grazing restrictions at this time.

However, instead of leaving the labels silent, the grazing restriction recommended by EPA for lactating animals can be used in the interim.

Wheat, barley, rye, fall rye, winter wheat:

- Do not permit lactating dairy animals to graze fields within 7 days after application.
- Do not harvest forage or cut hay within 30 days after application.
- Withdraw meat animals from treated fields at least 3 days before slaughter.

Field Corn:

- Do not permit lactating dairy animals to graze fields within 7 days after application.
- Do not harvest as forage within 30 days after application.
- Withdraw meat animals from treated fields at least 3 days before slaughter.

Stubble land, pastures, rangelands, road sides, uncropped land:

- Do not permit lactating dairy animals to graze fields within 7 days after application.
- Do not harvest forage or cut hay within 30 days after application.
- Withdraw meat animals from treated fields at least 3 days before slaughter.

5. Aerial Application

The issue of “silent labels” for pesticide products in general is being addressed by a task force representing regulatory agencies and the industry as announced in the *Regulatory Proposal Pro93-02 (Aerial Applications of Pesticides)*.

For products containing 2,4-D as an active, registrants of Commercial Class and Restricted Class products are required under the L.I.P. to state or contraindicate on the label applications by air to crops, pasture, rangeland, stubble, non-crop land, woodland and forestry sites. Silent labels are not acceptable.

While a complete assessment of the potential risk of spray drift of 2,4-D on non-target organisms by Environment Canada is awaiting submission of compound-specific data on vapour pressure, volatilization and environmental toxicology by Industry Task Force, the following precautionary statements are recommended in the interim:

- Avoid direct applications to any body of water. Do not contaminate water through spray drift or by cleaning of equipment or disposal of wastes.
- State the minimum volume per hectare, that can be safely used, depending on the type of application system and the target site. Use boom pressure of 235 kPa or less. Avoid placing nozzles where spray will enter wing tip vortices.
- Do not apply this product directly to, or otherwise permit it to come into direct contact with desirable crops or other desirable broadleaf plants or non-target species and do not permit spray mists to drift onto them.
- Coarse sprays are less likely to drift, use only nozzles or nozzle configuration which minimize the production of fine spray drops. Do not angle nozzles forward into the airstream and do not increase spray volume by increasing nozzle pressure. When spraying, avoid combination of pressure and nozzle type that will result in fine particles (mist) which are more likely to drift. A spray thickening agent or drift retardant may be used with this product to aid in reducing spray drift.
- Do not use human flaggers.
- Avoid Spray Drift: Apply only when there is little or no hazard from spray drift. Small quantities of the spray, which may not be visible, may seriously injure susceptible crops and damage sensitive non-target habitat. A method must be used to detect air movement, lapse conditions, or temperature inversions (stable air) such as the use of balloons or a continuous smoke column at or near the spray site or a smoke generator on the spray equipment. If the smoke develops into layers or indicates a potential for hazardous spray drift, do not spray.
- Buffer Zones: Appropriate buffer zones should be established between treatment areas and aquatic systems and treatment areas and significant wildlife habitat.

Note: For Restricted Use (Forestry and Woodland Management), precautionary statements may be more specific with respect to wind speed, spray volume, pressure and nozzle type.

6. Re-entry Interval for Turf

Do not allow people (other than applicator) or pets on treatment area during application. Do not enter treated areas until spray has thoroughly dried (or dust has settled for dry product).

7. Delete Emergency Use on Oats

Because of marginal tolerance of oats to 2,4-D, and since several highly selective post-emergence herbicide products are now available for broadleaf weed control in this crop, reference to use on oats should be deleted from all 2,4-D amine products.

8. Maximum Application Frequency to Turf

In the U.S., several applications of 2,4-D per year to turf were common, but the EPA-Industry Task Force Agreement reduced the maximum number of applications in lawns, parks and golf courses to 2 per year.

In Canada, because of our shorter growing season, normally 2 applications are required for good turf management. The first application is made in early spring and the second application is made in late summer/early fall. This does not include spot treatments for control of perennial weeds.

Although the current lawn/turf management practices in Canada normally do not require more than 2 applications, alone or in combination with fertilizer blends, to safeguard against excessive use, the Commercial Class and Domestic Class product labels should bear the following statement:

- For good turf/lawn management, normally two applications per year per treatment site are adequate. This does not include spot treatments.

9. Maximum Application Rates

In accordance with the EPA-Industry Task Force Agreement, the maximum rate of application on product labels in the U.S. has been reduced as follows:

2.24 kg acid equivalent per hectare per application for pasture and rangelands (except for hard-to-kill woody species).

4.48 kg acid equivalent per hectare per application for forestry site preparation and conifer release.

2.24 kg acid equivalent per application for turf.

In Canada, the maximum application rates currently carried on product labels for each of the above use scenarios are comparable to those rates agreed to by EPA and the

Industry Task Force. The Plant Industry Directorate is currently working on revisions to a global Use Pattern for 2,4-D. Once completed, registrants will be required to ensure that all application rates are in full compliance.

Implementation of the Label Improvement Program (LIP)

The LIP requires that all end-use products and fertilizer-pesticide combinations containing 2,4-D acid or the following derivatives of 2,4-D acid as an active ingredient be amended:

- Dimethylamine Salt
- 2-Ethylhexyl (Isooctyl) Ester
- Diethanolamine Salt
- Sodium Salt
- Isopropylamine Salt
- Triisopropanolamine Salt
- 2-Butoxyethyl Ester
- Isopropyl Ester

Amendments 1 to 7 apply to all Commercial (Agricultural) Class and Restricted Class end-use products. Amendments 1, 2, 6 and 8 apply to Domestic Class end-use products. Amendments 1, 2, 3, 5, 6 and 8 apply to Commercial Class end use products that are intended for turf uses only.

Amendments 1 and 2 should appear both on the product label and the booklet, amendments 3, 4, 5, 6, 7 and 8 are required on the booklet of the product, if applicable.

Specimens of generic labels highlighting the new additions for Domestic Class 2,4-D products and Commercial Class 2,4-D Ester, 2,4-D Amine and 2,4-D Plus Mecoprop (for turf) products are available upon request. In order to maintain consistency, registrants are advised to incorporate the exact statements as referred to in this document and highlighted in the specimen labels when amending their labels. It is of crucial importance that statements be exact so that we can use an electronic label-proofing program to improve our efficiency when checking for compliance with the LIP. Exact wording will also avoid problems of inconsistent labelling which have been brought to our attention in the past.

Deadlines

All registrants of Domestic, Commercial and Restricted Class end-use products containing

2,4-D as an active, alone or in combination with other actives, are required by this Regulatory Document to submit completed applications for amendment of their labels by February 28, 1995. Applications received by the Plant Industry Directorate after this date may not be processed by December 31, 1995.

All registrants are required to comply with the LIP by December 31, 1995. Product labels that do not show the new exposure reduction measures will not be renewed after that date. If label improvement of your product is not completed by this date, product registration will lapse.

Registrants that have products with Master Product status should apply first to amend their labels before registrants that have products with Master Copy status. Once submissions for the Master Products have passed through the review stage, applications for amendment of Master Copy products can be submitted.

There will be no fee charged for the LIP. However, if the draft label submitted under this program incorporates other changes, then the appropriate fee will be charged. Inclusion of amendments other than LIP amendments under the same submission number may delay the processing of the submission beyond the deadline of December 31, 1995 and delay renewal.

With the implementation of the LIP and maintenance of rigorous product quality standards, exposure of user groups such as farmers, forestry workers, commercial applicators and lawn owners to 2,4-D will be significantly lower than that sustained prior to re-evaluation. With new improvements underway in formulation technology such as solventless formulations and soluble packets, further reductions in operator exposure and container disposal are anticipated.

Please direct any inquiries regarding this Note to CAPCO to:

Dr. Najib Malik
Herbicide and Plant Growth Regulators Section
Pest Management Regulatory Agency
Health Canada
2250 Riverside Drive
A.L. 6606E1
Ottawa, Ontario
K1A 0K9
Telephone: (613) 736-3626

Distribution

Canadian Association of Pesticide Control Officials

Public Interest Groups

User Groups

Crop Protection Institute

Industry Task Force II on 2,4-D Research Data

Registrants of 2,4-D Products

References

A. Scientific Journal Publications

1. Bond, G.G., Rossbacher, R. (1993) A review of potential human carcinogenicity of the chlorophenoxy herbicides MCPA, MCPP, and 2,4-DP. *Br. J. Ind. Med.* 50(4):340-348.
2. Bond, G., Bodner, K.M. and Cook, R.R. (1989) Phenoxy herbicides and cancer: Insufficient epidemiological evidence for a causal relationship. *Fund. App. Tox.* 12:162-188.
3. Harris, S.A. and K.R. Solomon. 1992. Human Exposure to 2,4-D following controlled activities on recently sprayed turf. *J. Environ. Sci. Health*, B27(1)9-22.
4. Harris, S.A., K.R. Solomon and G.R. Stephenson. 1992. Exposure of Home owners and Bystanders to 2,4-D. *J. Environ. Sci. Health*, B27(1) 23-38.
5. Hayes, M.H., R.E. Taron, K.P. Cantor, C.R. Jessen, D.M. McCurrin, and R.C. Richardson. 1991. Case-Control Study of Canine Malignant Lymphoma: Positive Association with Dog Owner's Use of 2,4-D Herbicides. *J. Natl Cancer Inst.* 8:1226-1231.
6. Mullison, R.W. and G.G. Bond. 1991. Epidemiology and Toxicology of 2,4-D. *Weed Technol.* 5:898-906.
7. Munro, C.I., G.L. Carlo, J.C. Orr, K.G. Sund, R.M. Wilson, E. Kennepohl, B.S. Lynch, M. Jablinske and N.L. Lee. 1992. A Comprehensive, Integrated Review and Evaluation of the Scientific Evidence Relating to the Safety of the Herbicide 2,4-D. *J. Amer. College of Toxicol.* 11:559-664.
8. Solomon, K.R., Harris, S.A. and G.R. Stephenson 1993. Applicator and Bystander Exposure to Home Garden and Landscape Pesticides, pp 262-274 in K.D. Racke and A.R. Leslie, Editors, ACS Symposium Series 522, Pesticides in Urban Environments, Chapter 22.

B. Miscellaneous Reports

1. Donald L. Page, March 1994, Industry Task Force II on 2,4-D Research Data. Agricultural Aviation.
2. Harvard School of Public Health. 1990. The Weight of Evidence of the Human Carcinogenicity of 2,4-D. Final Report.
3. Health Protection Branch, Health and Welfare Canada. Fact Sheet, May 1993
4. US EPA SAB/SAP Final Report. March 22, 1994.
5. U.S. EPA Press Advisory. October 9, 1992.