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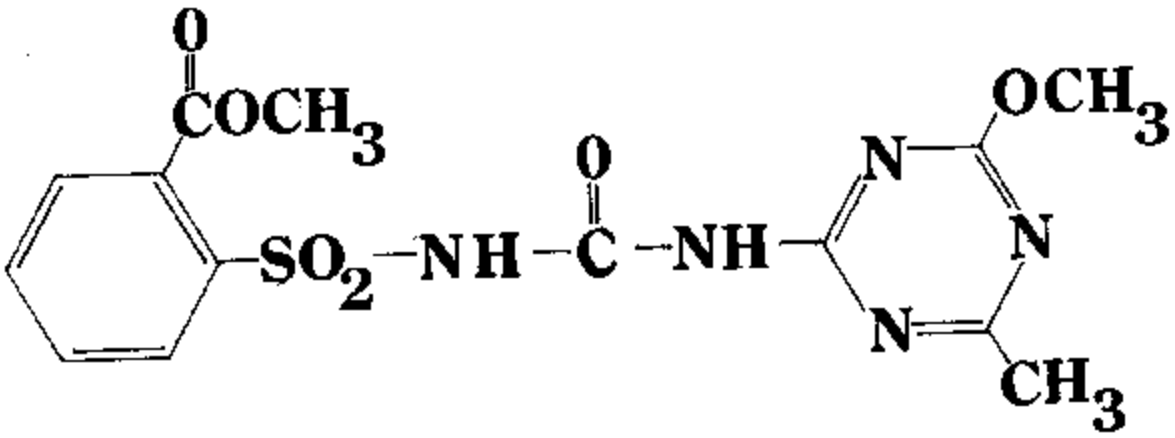
Food Production and Inspection Branch
Direction générale, Production et inspection des aliments

Plant Industry Directorate
Direction de l'industrie des produits végétaux

Discussion Document D87-04

METSULFURON-METHYL



Herbicide

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FOREWORD

METSULFURON-METHYL

As part of the ongoing efforts to provide a summary of the data received and outline the regulatory action of the active ingredient, metsulfuron-methyl, a discussion document has been prepared. This document reflects input from specialists within Agriculture Canada and with key interdepartmental advisors. Based on the reviews of all available information and in consideration of its economic benefits to Canadian farmers, a regulatory decision has been made to grant a temporary registration for metsulfuronmethyl and the end-use product Ally.

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METSULFURON-METHYL (ALLY) HERBICIDE

1. SUMMARY

The purpose of this document is to provide a summary of the data reviewed and outline the regulatory action on the active ingredient metsulfuron-methyl.

Agriculture Canada, with the assistance of advisors from Environment Canada, Fisheries and Oceans Canada and Health and Welfare Canada, has completed a review of the available data supporting metsulfuron-methyl. The data base is modern and reasonably complete. Additional information is required, however, to address concerns about potential detrimental modification of waterfowl and other wildlife habitat due to off-site movement of metsulfuron-methyl, and subsequent impact on nontarget vegetation and associated food resources.

No safety and health concerns have been raised on this chemical. The data indicate that the product is safe to use from the points of view of occupational hazard and dietary exposure.

With respect to environmental impact, metsulfuron-methyl has very low toxicity to fish and aquatic invertebrates, and is practically non-toxic to wildlife. However, it is relatively persistent and mobile and has a very high toxicity to a variety of broadleaf plants. The key environmental concern, therefore, is the movement of this chemical into adjacent wetlands and its subsequent impacts on wildlife from detrimental modification of wetland vegetation and associated food resources.

In assessing the risk to nontarget plants, on the use experience with chlorsulfuron (Glean), which is similar to metsulfuron-methyl in chemistry, mobility, persistence and activity was taken into consideration. Chlorsulfuron has been widely used in Saskatchewan and Alberta for five years without any reported incident of off-site plant damage (terrestrial or aquatic).

Metsulfuron-methyl is a broad spectrum broadleaf herbicide for use on cereal crops. It is effective at a very low rate of 4.5 g/hectare. It is more cost-effective than most herbicides registered for similar uses.

Based on a review of all available information and in consideration of its economic benefits to Canadian farmers, this herbicide has been granted a temporary registration under the following conditions and limitations:

a. The product is to be used for ground application only. Aerial application is prohibited.

b. A 15-meter setback zone from water bodies must be observed.

c. The registrant is to develop additional data to assess potential impact to wildlife habitat and aquatic life.

2. PRODUCT CHEMISTRY

2.1 Pesticide Name

Common name: metsulfuron-methyl
Chemical name: methyl 2-[3-(4-methoxy-6-methyl-1,3,5-triazine-2-yl)ureidosulphonyl]benzoate
Trade name: Ally

2.2 Physical and Chemical Properties

Chemical Abstracts Registry No: 74223-64-6
Empirical formula: $C_{14}H_{15}N_5O_6S$
Molecular weight: 381.4
Physical form: white to pale yellow solid
Melting point: 158°C
Vapor pressure: 5.8×10^{-5} mm Hg at 25°C
Ionization constant (pka): 3.5
Octanol/water partition coefficient (Kow): 0.018
Solubility: in water at 25°C

unbuffered,	pH 4.1	109 mg/L
buffered	pH 4.6	270 mg/L
buffered	pH 5.4	1750 mg/L
buffered	pH 6.7	9500 mg/L

in organic solvents at 20°C

n-hexane	0.79 mg/L
xylene	580 mg/L
ethanol	2300 mg/L
methanol	7300 mg/L
acetone	36000 mg/L
methylene chloride	121000 mg/L

Stability: stable in air to approximately 140°C
Hydrolysis: at 25°C, half-life 800 hr. at pH 5, and stable at pH 7 (no measurable hydrolysis for 1000 hr.)

3. DEVELOPMENT AND USE HISTORY

Metsulfuron-methyl is developed and manufactured by DuPont as a herbicide for selective weed control in cereal crops. It has been accepted for use by several countries including the United States.

This herbicide also has a potential for weed and brush control on pasture and rangeland, forest and non-cropland areas.

4. REGULATORY POSITION AND RATIONALE

Metsulfuron-methyl is a broadleaf herbicide for use on cereals. It controls a wide spectrum of weeds at a very low application rate (4.5 g/ha) and thus will be more cost-effective than most herbicides registered for similar uses, e.g. various combination products. This herbicide is currently registered for use in the U.S.A. Some Canadian farmers have expressed the view that without the product, they are in an unfavorable position vis-a-vis American competitors in both domestic and international grain markets.

This product has other advantages over most herbicides in that it has greater flexibility in application timing and it controls later germinating weeds. In addition, the low use rate, formulation and packaging facilitate great ease of mixing, handling, storage and container disposal.

Laboratory studies indicate that this herbicide has very low toxicity to mammals, birds, fish and aquatic inverterbrates. However, concerns have been raised about potential off-site movement and subsequent impact on nontarget aquatic plants and associated food resources, e.g., wildlife habitat around prairie sloughs. The available information on metsulfuron-methyl is considered inadequate for a full assessment of impact in this regard. The use experience with chlorsulfuron may, however, have some value. Chlorsulfuron is similar to metsulfuron-methyl in chemistry, mobility, persistence and activity. It has been widely used in the prairie provinces of Saskatchewan and Alberta for five years without any reported incident of off-site plant damage (terrestrial or aquatic). It is therefore unlikely that metsulfuron-methyl will have any significant impact on the aquatic environment when used by ground application and when a 15-meter buffer zone is observed.

Based on the above considerations, metsulfuron-methyl has been granted a temporary registration for 1987 under the following conditions and limitations:

a. The product is to be used by ground application only, and aerial application is prohibited.

b. A 15-meter buffer zone must be observed around water bodies.

c. The registrant is to develop additional data for assessment of the potential for movement of the chemical to aquatic sites and its possible adverse impact on fish and wildlife through modification of habitat from toxicity to nontarget plants.

5. TOXICOLOGY

A complete safety data base on metsulfuron-methyl is available and has been reviewed by Health and Welfare Canada. No health and safety concerns have been raised on the use of this product.

Insofar as dietary exposure is concerned, the data indicate that when metsulfuron-methyl is used as proposed on wheat and barley, residues are less than 0.1 ppm and would not pose a health hazard to consumers.

With regard to occupational hazards and the safety of this product to applicators and bystanders, it is considered that safety margins will be adequate providing safety precautions are observed by users.

Since there are no health concerns, details of the toxicology are not reported here.

6. ENVIRONMENTAL ASPECTS: ENVIRONMENT CANADA INPUT

6.1 Summary

The prominent modes of degradation of metsulfuron-methyl in soil, water and sediment are by microbial action under aerobic and anaerobic conditions and by chemical hydrolysis, the latter being significant only under acidic conditions. Photodegradation is insignificant.

Residues degrade faster in warm, moist soils of low pH. In prairie soils herbicidally-active residues persist for at least two growing seasons. High water solubility, poor soil adsorption and results of laboratory leaching experiments suggest metsulfuron-methyl has a significant potential for movement through leaching and run-off. Field studies with technical material in the prairies have provided variable results but, in general, indicate that leaching was limited and was related to amount of rainfall and soil type. Field studies with formulated material to assess movement through leaching and runoff are pending.

The requested use of metsulfuron-methyl is not expected to pose a hazard to wildlife from acute or dietary exposure or from food removal caused by low acute toxicity to invertebrates. However, the impact on wildlife habitat and associated food resources cannot be evaluated because minimal-effect-levels for nontarget plants have not been determined. The data submitted indicate that metsulfuron-methyl is likely to be toxic to aquatic plants at initial concentrations expected in prairie sloughs in the intended area of use. Algal toxicity tests and toxicity tests with plant species commonly associated with prairie sloughs are pending. These tests will 1) evaluate

potential impacts of metsulfuron-methyl on wildlife habitat and associated food resources in the intended area of use, and 2) determine if the current detection limits for metsulfuron-methyl in water and soil are adequate. In the interim, a 15-m buffer zone is suggested around sloughs and other wetlands to minimize possible off-site movement of metsulfuron-methyl and exposure of nontarget plants.

6.2 Environmental Chemistry and Fate

Metsulfuron-methyl is a weak acid (pKa = 3.5), the non-ionic form predominating at low pH.

Metsulfuron-methyl is highly water soluble (109 mg/L in distilled water at 25°C), particularly under buffered conditions and higher pH (270 mg/L at pH 5, 9500 mg/L at pH 7). Its higher water solubility is also reflected in its low octanol-water partition coefficient (Kow = 0.018).

Metsulfuron-methyl is moderately volatile with a vapour pressure of 5.8×10^{-5} mm Hg at 25°C.

The prominent modes of degradation of metsulfuron-methyl in soil, water and sediment are by microbial action under aerobic and anaerobic conditions. Chemical hydrolysis is also significant under acidic conditions. Photodegradation in soil or water is insignificant. In soil, the parent compound is degraded to saccharin and carbon dioxide by way of intermediate transformation products.

Metsulfuron-methyl is very persistent in cool, dry, alkaline soils. In a laboratory study with Canadian prairie soils, the half-life was 70 days in clay loam (pH 5.2), 102 days in sandy loam (pH 6.8) and 178 days in clay soil (pH 7.5). Field studies using radio-labelled metsulfuron-methyl in silt loam, silty clay loam and sandy loam soils (pH 6.1 to 8.2) in the northern U.S. and Canada (Alberta, Saskatchewan and Manitoba) indicated an average DT_{50} (50% decline time) of 2.5 months (range of 1 to 7 months). However, the parent compound persisted in the soils for at last two growing seasons. No data were available on the fate of transformation products. Differences in persistence between laboratory and field studies were a result of some combination of factors related to soil pH, moisture and temperature.

In prairie soils, herbicidally active residues persist for at least two growing seasons. A recropping interval of 22 months or more depending on the results of a preliminary field bioassay, may be necessary for crop rotation. Some tolerant crops may be grown after 10 months. Regular annual use of the product may lead to accumulation or buildup of residues although no data were available.

A laboratory anaerobic water/sediment study conducted at 25°C indicated that the approximate DT_{50} in natural water ranged from 5 weeks at pH 5.8 to 25 to 30 weeks at pH 6.9. Because the water in prairie sloughs is mainly alkaline (pH up to 9.7) and well buffered, metsulfuron-methyl is expected to persist in the water column for more than 30 weeks and thus potentially accumulate from regular annual use. Studies on persistence of metsulfuron-methyl in water and sediment have been suggested to address this concern.

Studies with acid soils (pH 5.6-6.5) indicate that metsulfuron-methyl adsorbs poorly in soils. Soil column experiments with freshly treated acid soils (pH 5.6-6.7) showed that 85% to 100% of the applied radioactivity leached through the columns. A soil TLC study also indicated that metsulfuron-methyl was mobile in sandy loam and silt loam soils. In soils with a higher pH, the mobility of metsulfuron-methyl is expected to increase because of increased solubility, increased ionization of the chemical and decreased adsorption. Results from field studies in the prairies with radio-labelled technical material were variable, but in general indicate that leaching was limited and was related to amount of rainfall and soil type. There was very little leaching (1%) below 22 cm in the dark brown soil at Swift Current (silt loam, pH 6.1) and Saskatoon (silty clay loam, pH 6.2). However, in the black soil at Stettler, Alberta (sandy loam, pH 6.9), 12% of the applied activity had leached down to 22-35 cm soil depth after 1 month. There was no indication that leaching had stopped at 35 cm as soil from a greater depth had not been sampled. Field studies with formulated material to assess leaching in black and gray-wooded soils are pending.

Because of its high water solubility and poor soil adsorption characteristics, metsulfuron-methyl has a potential for movement in runoff water if there is rainfall soon after application of the herbicide. This could result in contamination of adjacent wetlands and subsequent damage to nontarget plants. Field runoff studies based on the use of indicator plants are pending. In the interim, a 15-meter buffer zone is suggested around sloughs and other wetlands to minimize contamination of nontarget habitats adjacent to use areas.

6.3 Environmental Toxicology

Wild Birds. Wild birds may be exposed to metsulfuron-methyl by direct overspray, spray drift, or by consumption of vegetation or prey sprayed with this herbicide. Exposure through these routes is not expected to result in adverse toxicological effects because of low application rates and residues, and the extremely low acute oral and dietary toxicity of the technical and formulated product to bird species tested. Technical

metsulfuron-methyl is practically non-toxic to 6-month old mallards (LD_{50} greater than 2510 mg/kg). Technical metsulfuron-methyl was not toxic to 14-day-old Mallard or Bobwhite Quail when administered in the diet for 5 days (both LC_{50}'s greater than 5620 ppm).

Wild Mammals. Wild mammals may be exposed to metsulfuron-methyl by direct overspray, spray drift or by consumption of vegetation or prey sprayed with this herbicide. Exposure through these routes is not expected to result in adverse effects because of (1) low application rates and residues, and (2) the extremely low toxicity of the technical and formulated product to laboratory mammals exposed by oral, dermal or respiratory routes.

No mortalities were observed in rats administered single oral doses of 5000 mg/kg of the active as technical grade or formulated product. Acute oral tests on single rats indicated 25000 mg/kg of technical material was not lethal. The approximate lethal oral dose in dogs was greater than 2500 mg/kg.

Orally administered metsulfuron-methyl is very rapidly cleared by rats and ruminants, predominantly in the urine.

When metsulfuron-methyl was administered orally to rats as ten repeated doses up to 3400 mg/kg over a two-week period, only slight weight losses were observed. Mice exposed to dietary doses as high as 5000 ppm for 90 days showed only decreases in body weight gain associated with decreased food consumption. Dietary concentrations as high as 5000 ppm were not toxic to rats fed continuously for two years. Dogs consuming a diet containing 5000 ppm for one year were also not affected.

In rabbits, the acute lethal dermal dose was greater than 2000 mg/kg of the active as technical grade or formulated product. Rabbits exposed dermally up to 2000 mg/kg of the technical material for 21 days showed no compound-related effects. Rats inhaling doses up to 5.3 mg/L of technical material were not adversly affected.
Metsulfuron-methyl had no embryopathic or teratogenic potential when orally administered to rats at concentrations as high as 1000 mg/kg or to rabbits at 700 mg/kg.

Amphibians and Reptiles. No data are available, however a hazard is not expected given the plant specific mode of action of metsulfuron-methyl and its low acute toxicity to aquatic invertebrates and fish (LC_{50}'s > 150 mg/L).

Terrestrial Invertebrates. Metsulfuron-methyl is nontoxic to honey bees, Apis mellifera (contact LD_{50} ¢ 25 g/bee), and earthworms (LC_{50} ¢ 1000 mg/kg). The requested use of metsulfuron-methyl is not expected to pose a hazard to terrestrial invertebrates from acute toxicity. However,

terrestrial invertebrates may be at risk from plant removal in nontarget habitats as a result of contamination by metsulfuron-methyl.

Aquatic Invertebrates. Metsulfuron-methyl was not acutely toxic to Daphnia magna at concentrations as high as 150 mg/L (v/v). Aquatic invertebrates should not be at risk from acute toxicity as a result of contamination by metsulfuron-methyl. However, aquatic invertebrates may be at risk from the loss of plants commonly associated with sloughs.

Soil Microbial Systems. Little information was available on the effect of metsulfuron-methyl on soil ^{14}C microorganisms. A laboratory study on ^{14}C-cellulose digestion showed that there was limited effect on anaerobic microorganisms in sediment.

Wildlife Habitat Considerations. The use of metsulfuron-methyl is not expected to pose a hazard to wildlife from food removal associated with acute toxicity to terrestrial or aquatic invertebrates (although data were limited). The impact on wildlife habitat and associated food resources from the use of metsulfuron-methyl cannot be evaluated because the minimal-effect-level for nontarget plants has not been determined.

Metsulfuron-methyl is absorbed by foliage and roots and is translocated. Metsulfuron-methyl inhibits cell division in the shoots or roots by blocking synthesis of the amino acids valine and isoleucine. Sensitivity of plant species is related to the rate of metabolic inactivation of metsulfuron-methyl.

No data were available for algae or other nontarget plants to determine minimal-effect-levels of metsulfuron-methyl. Some data on the effects of this herbicide on aquatic macrophytes were available for efficacy studies in the laboratory and in rice paddies in southeast Asia. Although these studies were not designed to determine minimal-effect-concentrations, they do indicate that this herbicide is phytotoxic to aquatic plants at very low concentrations in water.

The most sensitive aquatic plants reported were the submerged species, Potamogeton nodosus and P. pectinatus. Growth in shoot length was inhibited by 77-90% relative to the control 4 weeks after treatment at a nominal rate of 1 g/L prior to plant emergence from the soil. As 1 g/L was the lowest rate tested, the minimum-effective-concentration for growth inhibition is unknown. However, a concentration of 0.05 g/L or less is not unreasonable to assume based on the dose-growth response of submersed aquatic plants to other sulfonyl ureas or other herbicides.

Efficacy studies in rice paddies in southeast Asia indicated that metsulfuron-methyl provided 90-100% growth inhibition of submersed, floating and emergent broadleaf plants at treatment rates of 2-3 g a.i./ha. Little or no control of emergent grasses was reported at rates as high as 8 g a.i./ha.

Since the minimal-effect-level for nontarget plants has not been determined, the impact on wildlife habitat and associated food resources from the use of metsulfuron-methyl cannot be evaluated. However, the data submitted indicate that metsulfuron-methyl is likely to be toxic to aquatic macrophytes at initial concentrations expected in slough water from runoff. Exposure of floating, emergent and slough-margin vegetation to overspraying from ground application and spray drift into nontarget habitats adjacent to use areas is also potentially hazardous. In addition, as metsulfuron-methyl has a high degree of residual phytotoxicity in soil and in water/sediment, repeated use of metsulfuron-methyl could pose an additional hazard to plants in nontarget habitats from residue accumulation in soil or water.

Sloughs in the prairie pothole region of Canada support a substantial portion of North American waterfowl populations during the breeding season. Their reproductive and recruitment success depend on continued access to a variety of sloughs (e.g., temporary, semi-permanent, permanent). These sloughs provide a balance of protective cover and appropriate nesting vegetation as well as plant and aquatic invertebrate food resources for laying hens and young ducklings from mid-April to late September.

Algal toxicity tests and toxicity tests with plant species commonly associated with prairie sloughs are pending. These tests will evaluate potential impacts of metsulfuron-methyl on wildlife habitat and associated food resources in the intended area of use. They will also determine if the current detection limits for metsulfuron methyl of 0.1 g/L in water and 0.2 g/L in soil are adequate.

7. FISH AND FISH HABITAT:
FISHERIES AND OCEANS CANADA INPUT

7.1 Environmental Chemistry and Fate

The main decomposition products, saccharin, 2-(aminosulphonyl)benzoate and carbon dioxide, seem to pose little threat to aquatic environments given the scale and manner of usage of the active ingredient.

7.2 Mobility

Regarding movement in soils: one study demonstrated little vertical movement in soils whereas another shows quite significant movement, at least to the 35 cm level, within a period of one year. Thus, movement of the active ingredient from treated soils to aquatic habitats could be through runoff water and its associated sediments or by means of ground water under certain circumstances.

7.3 Dissipation

Regarding persistence in soils: half-lives reported ranged from one to ten months. There were differences due to climate and soil types, but by far the most common observation was one to two months. One study involved both U.S. and Canadian soils and, in the case of the U.S. soils, it also explored the issue of spring versus fall (brush control) applications. In the majority of cases the halflives did not change materially with time of application. No Canadian stations received fall applications, but this ommission is not as important as it may seem in that the registration for the product is being requested for crops, not brush control. Were an application made for registration for brush control, the availability of such Canadian data would become crucial.

Regarding persistence in aquatic environments: the only data presented were for one laboratory study conducted under anaerobic conditions. Five to 20-week half-lives were reported.

No field data were reported.

7.4 Effect on Aquatic Vertebrates

Acute toxicity tests of the active ingredient on rainbow trout, and bluegill sunfish showed no mortalities after 96-hour exposure to 150 ppm of the material. Bioaccumultation factors approached unity.

7.5 Effect on Aquatic Invertebrates

Acute toxicity data for Daphnia magna were the same as for fish.

7.6 Effect on Phytoplankton

Nothing reported.

7.7 Effect on Aquatic Macrophytes

A key issue is potential damage to fish food organisms and the plants that support their communities. The proponent tried to address the aquatic macrophyte issue by utilizing

data obtained from studies they had conducted. These studies were done to support the product registrations for use in rice paddies plus the sensitivities or suspected sensitivities of plant species related to those designated important by the Canadian Wildlife Service. The critical levels of exposure ranged from 1 to 20 ppb. This review of existing "data" is suspect, as the proponent states. Although the Department of Fisheries and Oceans (D.F.O.) finds this well intentioned data to be inadequate, they point out that metsulfuron-methyl in water is toxic to aquatic plants at very low concentrations.

7.8 Advisory Statement

Given the acute toxicity data cited above, the application rate of 4.5 g/ha and the water solubility of 109 mg/L, contaminated runoff or groundwater sources do not seem to pose a threat to the fish and invertebrate tested. However, this assumption is based upon solubility in distilled water. Any increased solubility in natural waters would have to be taken into account in future decision making.

Aquatic field studies, such as those conducted for soils were not attempted. Such studies should consider not only analyses of residues, but also long-term effects on aquatic macrophytes, phytoplankton, zooplankton and other fish food organisms.

The basic concern for the safety of the aquatic environment and wetlands is certainly reflected in the wording of the label which prohibits aerial application and contamination of any water, including irrigation water. Specific buffer zones around wetlands and any body of water are not mentioned on the draft label. D.F.O. recommends that a 15-meter buffer zone should be required until field trials can provide information on the adequacy of this distance.

The major reservations of D.F.O. relate not only to the provision of discrete buffer zones, but also to the provision of:

a. studies that would document movement of metsulfuron-methyl (or lack of it) under Canadian conditions from various, treated soils to aquatic habitats.

b. studies that would determine persistence of transported material in water and sediments under Canadian conditions.

c. field studies that would determine effects of transported material on aquatic macrophytes, phytoplankton (and its primary productivity),

zooplankton and other representative fish food organisms.

d. laboratory studies on the effects of the active ingredient or its formulation on specific aquatic macrophytes. Advice from Environment Canada should be sought with regard to plant species and the tests required.

In general, either Canadian or U.S. E.P.A. guidelines exist for such studies, but the proponent should consult the appropriate Canadian government agency during the planning phase.

Please direct all inquiries regarding metsulfuron-methyl to Dr. Fa-Yan Chang, Herbicide and Plant Growth Regulator Section.

October 15, 1987