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**United Nations Environment Programme**

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**Rotterdam Convention on the Prior Informed Consent Procedure for Certain Hazardous Chemicals and Pesticides in International Trade**
**Chemical Review Committee**
Second meeting
Geneva, 13–17 February 2006
Item 5 (b) of the provisional agenda*

**Listing of chemicals in Annex III of the Rotterdam Convention: Review of notifications of final regulatory action to ban or severely restrict a chemical: Alachlor**

# Alachlor

## Note by the Secretariat

1. Under article 5 of the Rotterdam Convention on the Prior Informed Consent Procedure for Certain Hazardous Chemicals and Pesticides in International Trade, when the Secretariat has received at least one notification from each of two prior informed consent (PIC) regions that contain the information required in Annex I to the Convention, it shall forward the notifications and accompanying documentation to the members of the Chemical Review Committee. The Committee shall review the documentation provided in such notifications and, in accordance with the criteria set out in Annex II, recommend to the Conference of the Parties whether the chemical in question should be included in Annex III and a decision guidance document drafted.

2. The Secretariat has received two notifications from two PIC regions relating to Alachlor which meet the information requirements of Annex I (Europe – the Netherlands and North America – Canada). Summaries of those notifications were included in PIC Circular XIV of December 2001 and PIC Circular XXII of December 2005 respectively. The notifications as they were received from the notifying countries are annexed to the present note.

3. The supporting documentation provided by Canada and the Netherlands, where available, may be found in documents UNEP/FAO/RC/CRC.2/10/Add 1 and Add 2 respectively.

* UNEP/FAO/RC/CRC.2/1.

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# Annex

*Secretariat for the Rotterdam Convention on the Prior Informed Consent Procedure for Certain Hazardous Chemicals and Pesticides in International Trade*

UNEP

# FORM FOR NOTIFICATION OF FINAL REGULATORY ACTION TO BAN OR SEVERELY RESTRICT A CHEMICAL

IMPORTANT: See instructions before filling in the form

**COUNTRY:** CANADA

## PART I: PROPERTIES, IDENTIFICATION AND USES

| 1. | IDENTITY OF CHEMICAL | |
|---|---|---|
| 1.1 | **Common name** | alachlor |
| 1.2 | **Chemical name according to an internationally recognized nomenclature (e.g. IUPAC), where such nomenclature exists** | IUPAC: 2-chloro-2',6'-diethyl-N-methoxy-methylacetanilide<br>C.A.:2-chloro-N-(2,6-diethylphenyl)-N-(methoxymethyl)acetamide |
| 1.3 | **Trade names and names of preparations** | - Lasso 4 Weed Killer Emulsifiable Concentrate<br>- Lasso 10 Granular Herbicide<br>- Lasso Emulsifiable Concentrate Weed Killer<br>- Lasso Emulsifiable Herbicide<br>- Lasso II Granule |
| 1.4 | **Code numbers** | |
| 1.4.1 | **CAS number** | 15972-60-8 |
| 1.4.2 | **Harmonized System customs code** | 380830 |
| 1.4.3 | **Other numbers (specify the numbering system)** | EINECS # 240-110-8<br>RTECS # AE1225000 |

| 1.5 | **Indication regarding previous notification on this chemical, if any** |
|---|---|
| 1.5.1 | ☐ This is a first time notification of final regulatory action on this chemical. |

## PLEASE RETURN THE COMPLETED FORM TO:


**Secretariat for the Rotterdam Convention**
**Plant Protection Service**
**Plant Production and Protection Division, FAO**
Viale delle Terme di Caracalla
00100 Rome, Italy

Tel: (+39 06) 5705 3441
Fax: (+39 06) 5705 6347
E-mail: pic@fao.org

**OR**

**Secretariat for the Rotterdam Convention**
**UNEP Chemicals**
11-13, Chemin des Anémones
CH – 1219 Châtelaine, Geneva, Switzerland

Tel: (+41 22) 917 8183
Fax: (+41 22) 797 3460
E-mail: pic@unep.ch

| | |
|---|---|
| 1.5.2 | ☐ This is a modification of a previous notification of final regulatory action on this chemical.<br>The sections modified are: _____<br>☒ This notification replaces all previously submitted notifications on this chemical. |
| | Date of issue of the previous notification: May 1, 1996 |

| 1.6 | **Information on hazard classification where the chemical is subject to classification requirements** |
|---|---|
| **International classification systems** | **Hazard class** |
| WHO | 1a - extremely hazardous |
| | |
| **Other classification systems** | **Hazard class** |
| EU | Xn - Harmful |
| | |

| 1.7 | **Use or uses of the chemical** |
|---|---|
| 1.7.1 | ☒ **Pesticide** |
| | **Describe the uses of the chemical as a pesticide in your country:** |
| | Herbicide for control of annual grasses and broadleaf weeds in corn and soybeans |
| 1.7.2 | ☐ **Industrial** |
| | **Describe the industrial uses of the chemical in your country:** |

| 1.8 | **Properties** |
|---|---|
| 1.8.1 | **Description of physico-chemical properties of the chemical** |

Form: yellow to white to wine red, odourless solid @ room temp;
yellow to red liquid @> 40°C;
Melting Point: 40.5-41.5 °C;
Boiling Point: 100 °C/0.0026kPa;
Vapour Pressure: 2.1 mPa (25°C);
Solubility: water 242 mg/l:
soluble in diethyl ether, acetone, benzene, chloroform, ethanol and ethyl acetate
slightly soluble in heptane;
Kow logP: 3.09.

REF: Tomlin, CDS, 1997, The Pesticide Manual 11th Addition, British Crop Protection Council, U.K. p 22-23

| 1.8.2 | **Description of toxicological properties of the chemical** |
|---|---|

The following toxicity values have been reported:

| Study Type | Value |
|---|---|
| Oral rats $LD_{50}$ | 930-1350 mg/kg; |
| Dermal rat $LD_{50}$ | >2000mg/kg; |
| percutaneous rabbits $LD_{50}$ | 13 300 mg/kg; |
| inhalation (4h), rats | 1.04 mg/l air |

| | |
|---|---|
| | NOEL, rats (2y) ≤ 2.5 mg/kg b.w./day;<br>dog (1y) ≤ 1 mg/kg b.w./day<br><br>Oncogenic in rats but not mice;<br><br>Non-irritating to skin or eyes; contact sensitisation in guinea pigs<br><br>REF: Tomlin, CDS, 1997, The Pesticide Manual 11th Addition, British Crop Protection Council, U.K. p 22-23<br><br>Considered a potential human carcinogen by Agriculture Canada and Health & Welfare Canada (see Note to CAPCO C88-04) |
| **1.8.3** | **Description of ecotoxicological properties of the chemical**<br>The following toxicity values have been reported:<br><br>Study Type — Value<br>oral $LD_{50}$s:<br>bobwhite quail 1536 mg/kg<br>bee 32 mg/bee<br>$LC_{50}$: bobwhite quail and mallard duck (5d) >5620 mg/kg diet<br>$LC_{50}$ (96h):<br>Rainbow trout 1.8 mg/L<br>Bluegill sunfish 2.8 mg/L<br>fathead minnow 5.0 mg/L<br>channel catfish 2.1 mg/L<br>$LC_{50}$ earthworms (14d) 387mg/kg dry soil<br>$EC_{50}$ (48h):<br>Crayfish >320 mg/L<br>daphnia 10 mg/L<br>$TL_{50}$ *Selenastrum capricornutum* (72h) 12 µg/L<br><br>REF: Tomlin, CDS, 1997, The Pesticide Manual 11th Addition, British Crop Protection Council, U.K. p 22-23 |

## PART II: FINAL REGULATORY ACTION

| | |
|---|---|
| **2.** | **FINAL REGULATORY ACTION** |
| **2.1** | **The chemical is:** ☒ **banned** **OR** ❑ **severely restricted** |
| **2.2** | **Information specific to the final regulatory action** |
| **2.2.1** | **Summary of the final regulatory action**<br>• all uses banned Dec 31, 1985; low import tolerances set for corn, soybean, drybeans, meat and milk (1).<br>• all product registrations cancelled due to carcinogenic potential, and existence of a lower risk alternative product, metolachlor (2).<br>• manufacturer (Monsanto) requested review of regulatory action, as allowed by section 23 of PCPA. Alachlor Review Board formed Nov 13, 1985 (2).<br>• final report (October 1987), Board recommended restoration of alachlor registrations, believing that the relative safety of the alternative product metalochlor did not support cancellation of alachlor registrations. (2).<br>• the Minister maintained metolachlor safer than alachlor and ban upheld (3) |

| | | |
|---|---|---|
| 2.2.2 | **Reference to the regulatory document** | |
| | (1) Minister's announcement of February 5, 1985;<br>(2) The Report of the Alachlor Review Board, October 1987;<br>(3) Note to Capco C88-04 | |
| 2.2.3 | **Date of entry into force of the final regulatory action** | |
| | December 31, 1985 | |

| | | | |
|---|---|---|---|
| 2.3 | **Was the final regulatory action based on a risk or hazard evaluation?** | ☒ Yes | ☐ No |
| | **If yes, give information on such evaluation**<br>• Determined to be animal carcinogen from review of feeding studies in rats and mice; deemed to have potential as human carcinogen<br>• Primary concern was occupational exposure but presence of alachlor in ground water, with further potential of contamination, increased concerns of non-occupational exposure<br>• Determined that use of alachlor represents an unacceptable risk of harm to public health | | |
| | **Reference to the relevant documentation**<br>(1) Note to Capco C88-04<br>(2) The Report of the Alachlor Review Board, Government of Canada Publication, 1987 | | |

| | | | |
|---|---|---|---|
| 2.4 | **Reasons for the final regulatory action** | | |
| 2.4.1 | **Is the reason for the final regulatory action relevant to the human health?** | ☒ Yes | ☐ No |
| | **If yes, give summary of the known hazards and risks presented by the chemical to human health, including the health of consumers and workers**<br>• Two long-term dietary studies in the rat, indicated an increase in the incidence of adenomas and adenocarcinomas in the nasal turbinates, and of stomach tumours at a number of doses (2).<br>• A long-term dietary mouse study indicated a statistically significant number of lung tumours in females at the highest dose (2).<br>• Based on the above results alachlor was deemed an animal carcinogen with potential as a human carcinogen (2)<br>• The primary concern was occupational exposure but the presence of alachlor in ground water, with further potential of contamination, increased concerns of exposure (2)<br>• Determined that use of alachlor represents an unacceptable risk of harm to public health (1) | | |
| | **Reference to the relevant documentation**<br>(1) Note to CAPCO C88-04<br>(2) The Report of the Alachlor Review Board, Government of Canada Publication, 1987. | | |
| | **Expected effect of the final regulatory action**<br>• Elimination of herbicide use of alachlor in Canada, thus eliminating hazard due to occupational exposure and exposure through contaminated ground water.<br>• At the time, some costs to farmers were expected due to virtual monopoly for Ciba-Geigy and a decrease in performance in certain instances however due to the continued presence of metolachlor these effects are expected to be relatively minor.<br>• No further effect anticipated as action was taken several years ago | | |

| | | | |
|---|---|---|---|
| 2.4.2 | **Is the reason for the final regulatory action relevant to the environment?** | ☐ Yes | ☒ No |
| | **If yes, give summary of the known hazards and risks to the environment** | | |
| | **Reference to the relevant documentation** | | |

| | |
|---|---|
| | **Expected effect of the final regulatory action** |
| | |

| | | |
|---|---|---|
| **2.5** | **Category or categories where the final regulatory action has been taken** | |
| **2.5.1** | **Final regulatory action has been taken for the chemical category** | ❑ **Industrial** |
| | **Use or uses prohibited by the final regulatory action** | |
| | | |
| | **Use or uses that remain allowed** | |
| | | |

| | | |
|---|---|---|
| **2.5.2** | **Final regulatory action has been taken for the chemical category** | ☒ **Pesticide** |
| | **Formulation(s) and use or uses prohibited by the final regulatory action** | |
| | All uses and formulations are prohibited | |
| | **Formulation(s) and use or uses that remain allowed** | |
| | None | |

**2.5.3 Estimated quantity of the chemical produced, imported, exported and used, where available.**

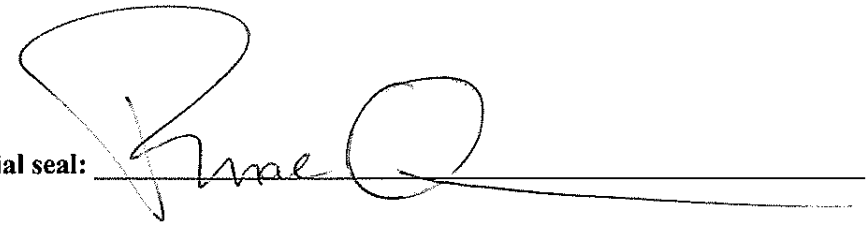
| | Quantity per year (MT) | Year |
|---|---|---|
| **Produced** | | |
| **Imported** | | |
| **Exported** | | |
| **Used** | | |

| | |
|---|---|
| **2.6** | **Indication, to the extent possible, of the likely relevance of the final regulatory action to other states and regions** |
| | • no further impact likely to take place as product was banned several years ago |

| | |
|---|---|
| **2.7** | **Other relevant information that may cover:** |
| **2.7.1** | **Assessment of socio-economic effects of the final regulatory action** |
| | • at the time, the two most widely used herbicides for control of annual grasses in corn and soybean were alachlor (Monsanto) and metolachlor (Ciba-Geigy). Keeping alachlor on the market would have provided the growers with choice thus insuring against monopolistic practices (e.g. price increases) (2).<br>• on average crop yields and weed control for metolachlor and alachlor were equal. However, there was some concern that in specific circumstances there are significant differences in performance. This led to concern that, even though the overall impact would be small, some individuals would be very hard hit by the removal of alachlor from the market place (2).<br><br>Ref:<br>(2) The Report of the Alachlor Review Board, Government of Canada Publication, 1987 |
| **2.7.2** | **Information on alternatives and their relative risks** |
| | |
| **2.7.3** | **Relevant additional information** |
| | |

## PART III : GOVERNMENT AUTHORITIES

| Ministry/Department and authority responsible for issuing/enforcing the final regulatory action | |
|---|---|
| **Institution** | Pest Management Regulatory Agency, Health Canada |
| **Address** | 2720 Riverside Drive<br>Ottawa, Ontario K1A 0K9<br>Canada |
| **Telephone** | +1 613-736-3660 |
| **Telefax** | +1 613-736-3659 |
| **E-mail address** | Trish_MacQuarrie@hc-sc.gc.ca |
| **Designated National Authority** | |
| **Institution** | Pest Management Regulatory Agency, Health Canada |
| **Address** | 2720 Riverside Drive<br>Ottawa, Ontario K1A 0K9<br>Canada |
| **Name of person in charge** | Trish MacQuarrie |
| **Position of person in charge** | Director, Alternative Strategies and Regulatory Affairs Division |
| **Telephone** | +1 613-736-3660 |
| **Telefax** | +1 613-736-3659 |
| **E-mail address** | Trish_MacQuarrie@hc-sc.gc.ca |

**Date, signature of DNA and official seal:** 

*Interim Secretariat for the Rotterdam Convention on the Prior Informed Consent Procedure for Certain Hazardous Chemicals and Pesticides in International Trade*

UNEP

# FORM FOR NOTIFICATION OF FINAL REGULATORY ACTION TO BAN OR SEVERELY RESTRICT A CHEMICAL

IMPORTANT: See instructions before filling in the form

COUNTRY: THE NETHERLANDS

## PART I: PROPERTIES, IDENTIFICATION AND USES

| 1. | IDENTITY OF CHEMICAL | |
|---|---|---|
| 1.1 | **Common name** | Alachlor |
| 1.2 | **Chemical name according to an internationally recognized nomenclature (e.g. IUPAC), where such nomenclature exists** | 2-Chloro-N-(2,6-diethylphenyl)-N-(methoxymethyl)acetamide; 2-Chloro-2',6'-diethyl-N-methoxymethylacetanilide; N-(methoxymethyl)-2,6-diethyl-2-chloroacetanilide; 2-Chloro-2',6'-diethyl-N-(methoxymethyl)acetanilide; alpha-chloro-2',6'-diethyl-N-(methoxymethyl)acetanilide |
| 1.3 | **Trade names and names of preparations** | CP-51144; Alanex; Anachlor, Alanox; Alochlor; Chimiclor; Lasagrin; LASSAGRIN; LASSO; LAZO; METACHLOR; METHACHLOR; Pilarzo; Pillarzo; Microtech |
| 1.4 | **Code numbers** | |
| 1.4.1 | **CAS number** | 15972-60-8 |
| 1.4.2 | **Harmonized System customs code** | 29242990 |
| 1.4.3 | **Other numbers (specify the numbering system)** | EINECS no. 240-110-8 |

| 1.5 | **Indication regarding previous notification on this chemical, if any** |
|---|---|
| 1.5.1 | θ This is a first time notification of final regulatory action on this chemical. |
| 1.5.2 | θ This is a modification of a previous notification of final regulatory action on this chemical.<br>The sections modified are: _____<br>X This notification replaces all previously submitted notifications on this chemical. |
| | Date of issue of the previous notification: ___before 1990_____ |

| 1.6 Information on hazard classification where the chemical is subject to classification requirements | |
|---|---|
| **International classification systems** | **Hazard class** |
| EU | Xn (harmful); R22, R40, R43; S2, S36/37/39 (DOSE) |
| WHO | Toxicity Class III (DOSE) |
| US EPA | Toxicity Class III (DOSE) |
| US EPA | B2 carcinogen (probable human carcinogen) (WHO/FAO) |
| | |
| **Other classification systems** | **Hazard class** |
| | |
| | |
| | |
| | |
| | |

| 1.7 Use or uses of the chemical | |
|---|---|
| 1.7.1 | X **Pesticide** |
| | **Describe the uses of the chemical as a pesticide in your country:** |
| | Prior to ban, alachlor was used as a selective pre- and post emergence herbicide for grasses and broadleaf weeds on e.g. corn, vegetables and forage crops. |
| 1.7.2 | θ **Industrial** |
| | **Describe the industrial uses of the chemical in your country:** |
| | Not relevant |

| 1.8 | Properties | |
|---|---|---|
| 1.8.1 | **Description of physico-chemical properties of the chemical** | |
| | Identity | colorless to yellow crystalline solid, odourless (HSDB) |
| | Formula | $C_{14} H_{20} Cl N O_2$ |
| | Molecular weight | 269.77 |
| | Solubility | 140 mg/l at 23 °C (HSDB)<br>18.07 mg/l at 25 °C (EPIWIN)<br>242 mg/l at 25 °C (DOSE) |
| | LogKow | 2.63; 3.53 (HSDB)<br>3.37 (est.); 3.53 (exp.) (EPIWIN) |
| | LogKoc | 2.08-2.28 (HSDB)<br>2.267 (EPIWIN) |
| | Vapour pressure | 2.2 E-5 mm Hg at 24 °C (HSDB; DOSE)<br>2.6 E-6 mm Hg at 25 °C (EPIWIN) |
| | Henry's Law constant | 3.2 E-8 to 1.2 E-10 atm-cu m/mole (HSDB)<br>2.23 E-8 atm-cu m/mole (EPIWIN) |
| | Melting point | 40-41 °C (HSDB; DOSE)<br>128.45 °C (EPIWIN) |
| | Boiling point | 100 °C at 0.02 mm Hg; 135 °C at 0.3 mm Hg (HSDB; DOSE)<br>378.17 °C (EPIWIN) |
| | BCF | 102.4 (EPIWIN) |

| 1.8.2 | **Description of toxicological properties of the chemical** |
|---|---|

1. Acute toxicity

| | |
|---|---|
| Oral: | LD50 rat 930-1360 mg/kg bw (WHO/FAO)<br>LD50 mouse1100 mg/kg bw (DOSE)<br>LD50 mouse 462-1040 mg/kg bw (IRPTC<br>LD50 rabbit 700 mg/kg bw (IRPTC) |
| Dermal: | LD50 rabbit 13300 mg/kg bw (WHO/FAO)<br>LD50 rat >2000 mg/kg bw (HSDB)<br>LD50 rat 13300 mg/kg bw (HSDB)<br>LD50 rabbit 3500 mg/kg bw (DOSE) |
| Inhalation: | 4-h LC50 rat 1.04 mg/l (DOSE) |
| Irritation: | slight irritant effects on rabbit skin and eye (WHO/FAO) |
| Sensitization: | strong dermal sensitization was seen in guinea pigs (WHO/FAO) |

2. Short-term exposure

- In a 90-days feeding study with rats and dogs a NOAEL of 200 mg/kg diet was found; at 2000 mg/kg diet some reductions in growth rate occurred (WHO/FAO, 1996)
- Six months dosing of dogs with capsules containing 0, 5, 25, 50 and 100 mg/kg bw/day (first 3 weeks) or 75 mg/kg bw/day (remainder of the study) resulted in liver weight increase beginning in males at 5 mg/kg bw/day and in females at 25 mg/kg bw/day and above. Histopathological findings included discolouration, fatty degeneration, elevated AP and LDH activity and biliary hyperplasia at 25 mg/kg bw/day and above. Dose-related mortality and emaciation was noted in both sexes at 25 mg/kg bw/day. A NOEL for systemic toxicity could not be established (WHO/FAO, 1996; IRIS).
- In an oral 1-year study with dogs and doses of 1, 3, 10 mg/kg bw, hemosiderosis was seen in kidney and spleen (3 mg/kg bw ) and liver (10 mg/kg bw) with hematologic findings (red cell destruction and replenishment) and increased liver weight (IRIS). The NOAEL was established to be 1 mg/kg bw (WHO).

3. Long-term exposure

- Rats exposed for 2 years to 14-126 mg/kg bw/day showed signs of toxicity at all dose levels with major lesions being a highly significant increase in ocular lesions (uveal degeneration) and dose-related hepatotoxicity as well as other gross and microscopic findings in thyroid, kidneys, brain, spleen, heart, prostate and ovaries. A NOEL for systemic toxicity could not be established (WHO/FAO, 1996; IRIS).
- A 2-year feeding study in rats and doses of 0, 0.5, 2.5 and 15 mg/kg bw/day resulted in a LOEL of 15 mg/kg bw/day for molting of retinal pigmentations, increased mortality rate in females and abnormal disseminated foci in the liver of males. The NOEL for systemic toxicity was 2.5 mg/kg bw/day (IRIS; WHO, 1996).

4. Reproductive toxicity, embryotoxicity and teratogenicity

- No teratogenic effects were observed in rats exposed by gavage to doses of 0, 50, 150 and 400 mg/kg bw/day during day 6 to 19 of gestation; the NOEL for maternal toxicity was 150 mg/kg bw/day; based on soft stools, red matter around nose and mouth, hair loss, anogenital staining and reduced weight gain at the higher dose (WHO/FAO). At 400 mg/kg bw/day decrease in fetal body weight and a slight increase in the number of resorptions and post-implantation loss was observed resulting in a slight decrease in the number of viable fetuses; the NOEL for embryotoxicity was 150 mg/kg bw/day (IRIS).
- In a 3-generation reproduction study in rats and doses of 0, 3, 10, and 30 mg/kg bw/day the NOEL for reproductive toxicity was found to be 30 mg/kg bw/day; the NOEL for systemic toxicity was found to be 10 mg/kg bw/day. At 30 mg/kg bw/day kidney toxicity (discolouration and weight increase ) was seen in adult F2 parents and F3 pups. (WHO/FAO). Lower ovary weights were noted in females of each generation and in F3 pups at 30 mg/kg bw/day (IRIS).
- Rabbits dosed with 0, 50, 100, and 150 mg/kg bw/day by intubation during day 7 to 19 of gestation showed maternal toxicity (reduced body weight gain) at 150 mg/kg bw/day. The NOEL for maternal toxicity was 100 mg/kg bw/day. No anomalies were noted in the fetuses (NOEL for developmental toxicity 150 mg/kg bw/day) (IRIS).
- Histological examination of the testes of rats given Lasso by gavage at up to 790 mg/kg bw for 75 days showed a dose-related reduction in spermatopoiesis, decreased number of spermatogonia and increased number of tubules without spermatozoa (HSDB).

*Conclusion: Alachlor is found to be not teratogenic and embryo/foetotoxic at doses showing maternal toxicity. Based on the available data it was proposed to classify Alachlor as "Repro category 3: Xn, R62 (draft RIVM/CSR).*

5. Mutagenicity

*In vitro*

- After incubation of cultured human lymphocytes at 2-40 mg/l a dose-related increase in aberrations was seen (WHO/FAO).
- Studies with *Escherichia coli* and several strains of *Salmonella typhimurium* showed negative results, both with and without metabolic activation (WHO/FAO).
- Commercial grade Alachlor was mutagenic without metabolic activation in *Saccharomyces cerevisae* D4, while technical Alachlor only showed mutagenic activity in this strain after activation by *Zea mays* extract (WHO/FAO).
- Alachlor increased DNA single stand breaks and alkali labile lesions of DNA in freshly isolated rat hepatocytes by forming numerous DNA damaging metabolites (DOSE).

*In vivo*

- Chromatid-type aberrations were observed in the bone-marrow of rats after a single i.p. injection of 2.5 mg/kg bw of Alachlor (unspecified source). In a second rat study with doses up to 1000 mg/kg bw technical Alachlor, no chromtid aberrations were detected (WHO/FAO).

- The results of a micronucleus test in mouse bone marrow were found to be negative (DOSE).
- No clastogenic effects were observed in rats following administration of 200 mg/kg diet for 280 days (WHO/FAO).
- In a *Drosophila melanogaster* wing spot test significant increases in both small and total spots were found at all 4 concentrations tested and in the frequency of twin spots at the highest dose of 10mM (DOSE). This test is considered to be a doubtful assay on mutagenicity (RIVM/CSR, 2001).

*Other*

- Chromosomal aberrations increased in *Tradescantia paludosa* after 18-24 h exposure to 0.8% Alachlor (DOSE).
- Alachlor demonstrated to induce mutations in the blue-green alga *Nostoc muscorum* (HSDB)

*Conclusion: The only valid and positive assay on mutagenicity was the assay with human lymphocytes, all other in vitro test were found to be negative. Since Alachlor was not mutagenic in most of the in vivo assays, RIVM proposed not to classify Alachlor as mutagenic. However, caution is needed because of its similarity in chemical structure with ramrod, an active mutagen on murine bone-marrow cells. Furthermore, positive mutagenicity data for 2,6-diethylaniline, a metabolite of Alachlor, are reported (RIVM/CSR, 2001).*

6. Carcinogenicity

- In a 18-months feeding study with mice and doses of 0, 26, 78 and 260 mg/kg bw/day an increased Incidence of bronchio-alveolar tumours was seen in females at 260 mg/kg bw. Because of the extremely low incidence of these tumours in control females compared to historical controls, the observed tumours were not considered to be treatment related (WHO/FAO).
- In a 2-years feeding study with rats and doses of 0, 14, 42, and 126 mg/kg bw/day a dose-related Increase in nasal turbinate adenomas and an increase in malignant stomach tumours at 126 mg/kg bw/day was observed in both sexes. In addition an increase in follicular cell tumours in the thyroid was noted in male rats at 126 mg/kg bw/day. In a second study with a complex dosing regime the same results were found (WHO/FAO).
- In a second 2-year feeding study in rats with doses of 0, 0.5, 2.5 and 15 mg/kg bw/day a statistically significant increase in nasal turbinate adenomas was noted at 15 mg/kg bw. Submucosal gland hyperplasia of the nasal turbinate was also observed (WHO, 1996). According to RIVM/CSR in the 2,5 mg/kg bw dose group one nasal tumour occurred. The NOAEL in this study was 0.5 mg/kg bw (RIVM/CSR, 1993).
- There has been some discussion on whether the nasal tumours in rats are relevant for humans. It was postulated that the nasal tumours in rats were caused by the metabolite 2,6-diethylaniline, which is specific to the rat, and is not formed in mice and apes and probably also not in humans (CTB, 1986).

*Conclusion: The available data from two rat studies clearly indicate that Alachlor is carcinogenic (WHO, 1996). Alachlor is not evaluated by IARC.*

Effects on human health

- Patch tests in volunteers with Lasso revealed sensitization in 5/21 volunteers (WHO/FAO)
- Alachlor has the potential to be absorbed from the gastrointestinal tract and from intact skin. No published data on the extent of absorption following inhalation in man or animals (WHO/FAO).
- The probable oral lethal dose in humans is 0.5-5 g/kg bw.

<u>Guideline value:</u>

- In view of the data on carcinogenicity, the WHO derived drinking-water guidelines by applying linearized multistage extrapolation on the evidence of nasal tumours in rats. This resulted in the following values; concentrations of 200, 20 and 2 µg/l in drinking-water are associated with excess lifetime cancer risks of $10^{-4}$, $10^{-5}$, and $10^{-6}$, respectively (WHO, 1996).
- Because Alachlor is not considered to be genotoxic by RIVM/CSR a guideline value was derived using a threshold approach. Based on the overall NOAEL of 0.5 mg/kg bw and using an uncertainty factor of 100 an ADI of 0.005 mg/kg bw was derived (RIVM/CSR, 1993). The 'College voor de Toelating van Bestrijdingsmiddelen'(CTB) in the Netherlands adopted this overall NOAEL in their evaluation of 1994 (CTB, 1994).

| 1.8.3 | **Description of ecotoxicological properties of the chemical** |
|---|---|

1. Aquatic organisms

| | |
|---|---|
| Algae: | 48 h EC50 growth rate 0.11 mg/l (RIVM/CSR) |
| Invertebrates: | 96-48 h EC50 *Daphnia magna* 0.05-10 mg/l (DOSE, WHO/FAO) |
| | 96 h LC50 *Procambarus acutus* 19.5 mg/l (DOSE) |
| | 24-96 h LC50 mud crab larvae 27-10 mg/l (saltwater)(DOSE) |
| Fish: | 96 h LC50 guppy, rainbow trout and bluegill sunfish 0.75-2.8 mg/l (DOSE, WHO/FAO) |
| | 48-96 h LC50 *Cyprinus carpio* 4.60-7.14 mg/l (HSDB) |

Other aquatic species: LC50 for *Bufo americanus* larvae is 3.3 mg/l (DOSE)

2. Terrestrial organisms

| | |
|---|---|
| Earthworms: | 14 d LC50= 387 mg/kg soil |
| Birds: | oral LD50 Bobwhite quail 1536 mg/kg bw (WHO/FAO) |
| | oral LD50 mallard duck >2000 mg/kg bw (DOSE) |
| | oral LD50 Gallus gallus 748 mg/kg bw (RIVM/CSR) |
| | 5-day LC50 mallard duck >=5000 mg/kg diet (WHO/FAO) |
| | 5-day LC50 bobwhite quail >=5000 mg/kg diet (WHO/FAO) |
| | 8-day LC50 pheasant >10000 mg/kg diet (HSDB) |
| | 8-day LC50 bobwhite quail >5000 mg/kg diet (HSDB) |
| Bees: | oral LD50 > 20 µg/bee (RIVM/CSR) |
| | contact LD50 > 16 µg/bee (RIVM/CSR) |

Other beneficial species: no data

3. Environmental fate

In soil, alachlor is transformed to its metabolites primarily by biodegradation. The half-life of alachlor disappearance from soil is about 15 days, although very little mineralisation has been observed. Alachlor is highly to moderately mobile in soil and the mobilisation decreases with an increase in organic carbon and clay content in soil. In water, both photolysis and biodegradation are important for the loss of alachlor, although the role of photolysis becomes important in shallow clean water (HSDB).

References

CTB (1986).Verslag Werkgroep L. 132e vergadering d.d. 28 augustus 1986. Agendabijlage L-132.9.2.1: Standpunt RIVM-DGA van den Tonkelaar, E.M. en C.L.Maas (in Dutch).

CTB (1994). College voor de Toelating van Bestrijdingsmiddelen. Verslag C-24.3.6. dd.d. 17 juni 1994 (in Dutch).

Environmental Endocrine Disruption: An Effects assessment and analysis document. Risk Assessment Forum U.S. Environmental Protection Agency Washington, D.C. 20460, Draft, April 1996.

IRIS, Integrated Risk Information System provided by US EPA.

IRPTC, Scientific Reviews of Soviet Literature on Toxicity and Hazards of Chemicals No. 84 Methalochlor (Lasso. United Nations Environment Programme, Moscow, 1985.

Miljøprojekt nr. 290 Male reproductive health and environmental chemicals with estrogenic effects. Danish Environmental Protection Agency, 1995.

DOSE (update 4/2000) The Dictionary of Substances and their Effects, the Royal Society of Chemistry.

EPIWIN, Estimation Programs Interface for Microsoft Windows 3.1. Syracuse Research Corp. North Syracuse, New Yersey, 1997.

HSDB Hazardous Substances Data Bank, National Library of Medicines.

RIVM/CSR (1993). Alachlor. Risico-evaluatie voor de consument en/of particuliere toepasser. RIVM National Institute for Public Health and Environment, Februari 1993. (in Dutch).

RIVM/CSR (2001). Alachlor. Discussion of the classification for health effects of the following pesticides on the DG VI priority list. RIVM. National Institute for Public Health and Environment.

RTECS, Registry of Toxic Effects of Chemical Substances, provided by NIOSH.

WHO/FAO (1996). Data sheets on pesticides No. 86 Alachlor, WHO/PCS/DS/96.86, November 1996.

WHO (1996). Guidelines for drinking-water quality. Second Edition. Volume 2. Health criteria and other supporting information. World Health Organization, Geneva.

## PART II: FINAL REGULATORY ACTION

| 2. | **FINAL REGULATORY ACTION** | | | |
|---|---|---|---|---|
| 2.1 | **The chemical is:** | **X banned** | **OR** | **θ severely restricted** |
| 2.2 | **Information specific to the final regulatory action** | | | |
| 2.2.1 | **Summary of the final regulatory action**<br>It is prohibited to sell, stock, store or use alachlor as pesticide.<br>The Pesticide Authorisation Board (In Dutch: College voor de Toelating van Bestrijdingsmiddelen (CTB)) decided to withdraw all applications of alachlor from 1.1.1987. In 1989, a request for re-authorisation of alachlor was submitted. This request is still under discussion. | | | |
| 2.2.2 | **Reference to the regulatory document**<br>Decree of Ministry of Agriculture and Fisheries, Ministerial Order of 30 October 1986. | | | |
| 2.2.3 | **Date of entry into force of the final regulatory action**<br>1.1.1987. | | | |

| 2.3 | **Was the final regulatory action based on a risk or hazard evaluation?** | **X Yes** | **θ No** |
|---|---|---|---|
| | **If yes, give information on such evaluation**<br>The final regulatory action was based on an evaluation of data regarding the hazard for leaching to groundwater in combination with the carcinogenic properties attributed to alachlor and/or its metabolites (CTB, 1986).<br>In the period 1989-1994, risk assessments for workers, consumers and the environment were made following a renewed request for authorisation of alachlor in 1989 (CTB, 1994; RIVM/CSR documentation). | | |
| | **Reference to the relevant documentation**<br>CTB (1986). Verslag Werkgroep L. 132e vergadering d.d. 28 augustus 1986 (in Dutch).<br>RIVM/CSR Documentation (confidential).<br>CTB (1994). Verslag C-24.3.6. d.d. 17 juni 1994 (in Dutch). | | |

| 2.4 | **Reasons for the final regulatory action** | |
|---|---|---|
| 2.4.1 | **Is the reason for the final regulatory action relevant to the human health?** | X Yes θ No |
| | **If yes, give summary of the known hazards and risks presented by the chemical to human health, including the health of consumers and workers** | |
| | In 1987, the Pesticide Authorisation Board (CTB) decided to withdraw all applications of alachlor on the basis of carcinogenic properties attributed to alachlor and/or its metabolites. Two chronic studies in rats clearly showed that Alachlor is carcinogenic to rats. It is noted that there has been discussion whether the nasal tumours in rats are relevant for humans. It was postulated that the nasal tumours in rats were caused by the metabolite 2,6-diethylaniline, which is specific to the rat, and is not formed in mice and apes and probably also not in humans. In view of the serious effects, it was, however, decided to prohibit Alachlor, until further evidence was submitted to prove that the nasal tumours were indeed rat-specific (CTB, 1986).<br>In view of the supposed carcinogenic effects, leaching to groundwater would be an unacceptable risk to the general population. In the Netherlands groundwater can be used for drinking water and therefore groundwater must remain free from pesticides (precaution principle). Leaching of alachlor and/or its metabolites from soil to groundwater amounts to 40% of the applied dose. In soils, containing a very low organic carbon amount (< 3%), leaching can be even higher (up to 92%). Metabolites include 2,6-diethyl-N-methoxymethyl-acetanilide and 2,6-diethyl-N-methoxymethyl-2-methyl-sulfonyl-acetanilide (CvF, 1980). | |
| | **Reference to the relevant documentation** | |
| | VROM (1987) Persbericht. Verbod van het bestrijdingsmiddel Alachloor. Ministerie van Volkshuisvesting, Ruimtelijke Ordening and Milieuhygiene d.d. 4 maart 1987. Agendabijlage L 136.3.3.<br>CTB (1986).Verslag Werkgroep L. 132e vergadering d.d. 28 augustus 1986. Agendabijlage L-132.9.2.1: Standpunt RIVM-DGA van den Tonkelaar, E.M. en C.L.Maas (in Dutch).<br>CvF (1980). Verslag Werkgroep voor Fytofarmacie – Subgroep L dd 18-3-1980. Agendabijlage L-94.6.2.1. | |
| | **Expected effect of the final regulatory action** | |
| | Prevention of carcinogenic effects and of contamination of drinking water derived from groundwater. The final regulatory action led to a complete risk reduction. | |

| 2.4.2 | **Is the reason for the final regulatory action relevant to the environment?** | **Yes** X **No** |
|---|---|---|
| | **If yes, give summary of the known hazards and risks to the environment** | |
| | | |
| | **Reference to the relevant documentation** | |
| | | |
| | **Expected effect of the final regulatory action** | |
| | | |

| 2.5 | Category or categories where the final regulatory action has been taken | |
|---|---|---|
| 2.5.1 | **Final regulatory action has been taken for the chemical category** | θ **Industrial** |
| | **Use or uses prohibited by the final regulatory action** | |
| | Not relevant. | |
| | **Use or uses that remain allowed** | |
| | | |

| 2.5.2 | **Final regulatory action has been taken for the chemical category** | X **Pesticide** |
|---|---|---|
| | **Formulation(s) and use or uses prohibited by the final regulatory action** | |
| | All applications are prohibited. | |
| | **Formulation(s) and use or uses that remain allowed** | |
| | None. | |

| 2.5.3 Estimated quantity of the chemical produced, imported, exported and used, where available. | | |
|---|---|---|
| | **Quantity per year (MT)** | **Year** |
| **Produced** | | |
| **Imported** | | |
| **Exported** | | |
| **Used** | | |

| 2.6 | Indication, to the extent possible, of the likely relevance of the final regulatory action to other states and regions |
|---|---|
| | |

| 2.7 | Other relevant information that may cover: |
|---|---|
| 2.7.1 | Assessment of socio-economic effects of the final regulatory action |
| | |

| 2.7.2 | Information on alternatives and their relative risks |
|---|---|
| | |
| 2.7.3 | Relevant additional information |
| | |

## PART III : GOVERNMENT AUTHORITIES

| Ministry/Department and authority responsible for issuing/enforcing the final regulatory action | |
|---|---|
| **Institution** | Ministry of Housing, Spatial Planning and the Environment<br>Ministry of Agriculture |
| **Address** | P.O. Box 30945<br>2500 GX The Hague<br>The Netherlands |
| **Telephone** | +31 70 339 3939 |
| **Telefax** | +31 70 339 1297 |
| **E-mail address** | |
| **Designated National Authority** | |
| **Institution** | Ministry of Housing, Spatial Planning and the Environment |
| **Address** | P.O. Box 30945<br>2500 GX The Hague<br>The Netherlands |
| **Name of person in charge** | drs. K.A. Gijsbertsen |
| **Position of person in charge** | Designated national authority |
| **Telephone** | +31 70 339 4744 |
| **Telefax** | +31 70 339 1297 |
| **E-mail address** | karel.gijsbertsen@minvrom.nl |

**Date, signature of DNA and official seal:** The Hague, 11 September 2001