Methoxychlor Reregistration Eligibility Decision (RED)

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This document serves as and explains the U.S. Environmental Protection Agency's (hereafter referred to as EPA or the Agency) reregistration eligibility decision (RED) for methoxychlor (CAS Number 72-43-5). The Agency has determined that methoxychlor is not eligible for reregistration. Kincaid Enterprises was the source for all technical product for methoxychlor and its last product was canceled in 2003 for non-payment of the annual registration fee. Three registrants hold the remaining end-use product registrations, all of which are suspended. Of these registrants, two with suspended end-use registrations have submitted voluntary cancellation requests, and another registrant's methoxychlor products are being canceled for non-payment of the annual registration maintenance fee. EPA will be publishing notice of these voluntary cancellation requests in the Federal Register pursuant to the provisions of Section 6(f) of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA).

The following provides background information on the pesticide registration and reregistration status of methoxychlor, and a summary of the terms of its cancellation. Because of the incomplete data base and the cancellation of the technical product, EPA did not complete its risk assessment for methoxychlor.

Introduction

In 1988, FIFRA was amended to accelerate the reregistration of products with active ingredients registered prior to November 1, 1984. There are five phases to the reregistration process. The first four phases of the process focus on identification of data requirements to support the reregistration of an active ingredient and the generation and submission of data to fulfill the requirements. The fifth phase is a review by the Agency of all data submitted to support reregistration.

FIFRA Section 4(g)(2)(A) states that in Phase 5 "the Administrator shall determine whether pesticides containing such active ingredient are eligible for reregistration" before calling in data on products and either reregistering products or taking "other appropriate regulatory action." Thus, reregistration involves a thorough review of the scientific data underlying a pesticide's registration. The purpose of the Agency's review is to reassess the potential hazards arising from the currently registered uses of the pesticide; to determine the need for additional data on effects and environmental fate; and to determine whether the pesticide meets the "no unreasonable adverse effects" criterion of FIFRA.

On August 3, 1996, the Food Quality Protection Act of 1996 (FQPA) (Public Law 104-170) was signed into law. FQPA amends both the Federal Food, Drug, and Cosmetic Act (FFDCA), 21 U.S.C. 301 *et seq.*, and the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), 7 U.S.C.136 *et seq*. The

FQPA amendments went into effect immediately. This document presents the Agency's decision regarding the reregistration eligibility of the registered uses of methoxychlor.

Background

Methoxychlor is a member of the organochlorine class of pesticides. Other members of this class include DDT, chlorobenzilate, dicofol, and ethylan. Less closely related members of the class include lindane, dieldrin, endrin, chlordane, heptachlor, aldrin, endosulfan, depone, and toxaphene (Ref. 6). Methoxychlor was developed as a replacement for DDT and is a structural analog of DDT. Methoxychlor is an insecticide/miticide and was first registered as a pesticide in 1948 as a replacement for DDT. It has been used to control various nuisance species including cockroaches, mosquitoes, flies and chiggers, as well as various arthropods that attack field crops, vegetables, fruits, ornamentals, stored grain, livestock, and domestic pets. Methoxychlor has been formulated as wettable powders, dusts, emulsifiable concentrates, ready-to-use products (liquids), and pressurized liquids.

The Agency has determined that it is not necessary to assess the risks of methoxychlor pesticide products because there are no tolerances for methoxychlor and all remaining products have been suspended since 2000 and are in the process of voluntary cancellation through the FIFRA Section 6(f) cancellation process. This reregistration finding is based on the substantive data gaps, the absence of necessary tolerances, and the absence of a registered source of methoxychlor manufacturing use product. The Agency finds that methoxychlor does not meet the statutory requirements of reregistration.

Although human health and environmental risk assessments have not been done as a result of the incomplete data for methoxychlor, the Agency has significant concerns about the effects of methoxychlor on human health and the environment, including concerns about its endocrine disruption effects and persistent, bioaccumulative toxicity.

Methoxychlor is listed as a persistent, bioaccumulative, and toxic (PBT) chemical by the EPA Toxics Release Inventory (TRI) program. The reporting threshold for the manufacture of methoxychlor was lowered from 1000 pounds to 100 pounds in a 1999 rulemaking. PBT chemicals are of particular concern not only because they are toxic but also because they remain in the environment for long periods of time, are not readily destroyed, and build up or accumulate in body tissue. EPA's Office of Solid Waste and Emergency Response has identified methoxychlor as one of thirty waste minimization priority chemicals, in order to focus efforts on reducing or eliminating the generation of hazardous wastes containing these chemicals.

The technical pesticide product registration for methoxychlor was transferred from DuPont to Kincaid Enterprises in 1982. The Agency issued a data call in notice for methoxychlor to Kincaid Enterprises on May 23, 1984 for chronic toxicological data.

On December 9, 1988, EPA issued the Guidance for the Reregistration of Pesticide Products Containing Methoxychlor as the Active Ingredient (i.e., the Methoxychlor Registration Standard). The Registration Standard included a Data Call-In Notice (DCI) issued pursuant to FIFRA section 3(c)(2)(B), which required registrants of products containing methoxychlor used as the active ingredient to develop and submit additional data on product chemistry, residue chemistry, ecological effects, environmental fate, human toxicology and plant protection data. The Agency had determined these data to be necessary to support continued registration of pesticide products containing methoxychlor as the active ingredient. Failure to comply with the requirements of a Data Call-In Notice is a basis for suspension under section 3(c)(2)(B) of FIFRA.

Kincaid Enterprises Inc. (Kincaid) was the sole registrant who committed to produce the generic data for methoxychlor. All other registrants of end-use products requested a Generic Data Exemption (GDE) in response to the DCI. These GDE requests were granted which allowed the end-use registrants to rely on Kincaid's data. Some data requirements were subsequently waived in response to Kincaid Enterprises' request, provided that Kincaid amend its labels and cancel all uses except home garden/orchard, livestock, seed treatment, and ornamental applications. Kincaid submitted amended labels deleting unsupported uses in 1994, and these were later deleted by other registrants in response to EPA's request.

On April 7, 1998, the Agency issued a Notice of Intent to Suspend to Kincaid because of its failure to submit certain data required by the 1988 DCI. On May 13, 1998, Kincaid requested a hearing by filing a hearing request with the Agency. On September 3, 1998, Kincaid and the Agency entered into a settlement agreement that specified the outstanding data requirements from the 1988 DCI and set forth a new schedule for their submission. The Settlement Agreement stated that if Kincaid failed to comply with any of the terms and conditions relating to any of the requirements for data generation and submission, the Agency would request that the Administrative Law Judge (ALJ) issue an order suspending the registrations of Kincaid's affected products without any opportunity for a hearing. On September 14, 1998, the ALJ issued an accelerated decision and order incorporating the Settlement Agreement. The Judge's accelerated decision and order incorporating the Settlement Agreement was entered into the public docket for the matter.

On December 3, 1999, Kincaid failed to satisfy certain data requirements as required by the DCI and the ALJ's Order/Settlement Agreement. The Agency requested that the ALJ enter a suspension order and a suspension order was entered for all methoxychlor pesticide product registrations held by Kincaid. The suspension became effective on January 14, 2000. Subsequently, Kincaid missed a second deadline of March 3, 2000, for a number of other studies. The Agency filed a request with the ALJ asking to amend the January 14, 2000 suspension order to include these studies, and on April 12, 2000, the ALJ amended the January 14, 2000 suspension order to include the additional overdue studies as bases for suspension.

Because Kincaid failed to submit the data, in violation of the 1988 DCI and the accelerated decision and order incorporating the Settlement Agreement, and was no longer in compliance with the DCI, registrants of methoxychlor end-use products, who were previously eligible for the GDE, were also considered to be in noncompliance with the 1988 DCI requirements as amended by the accelerated decision and order incorporating the Settlement Agreement. Letters were mailed to all end-use registrants on April 14, 2000, notifying them that their GDEs for products containing methoxychlor were revoked. The letters explained that if these data requirements were not satisfied within 30 days, registrants who had received the DCI would be subject to a Notice of Intent to Suspend and those whose registrations had been granted subsequent to issuance of the DCI would be subject to a Notice of Intent to Cancel. No data were received. Notices of Intent to Suspend were issued on June 26, 2000. No Notices of Intent to Cancel were necessary because all products registered after the issuance of the DCI had already been voluntarily canceled. No hearings were requested, and therefore, pursuant to FIFRA Sections 3(c)(2)(B)(iv) and 6(e)(2), the proposed suspensions became final.

On April 4, 2002, the Agency published a proposed rule to revoke 79 tolerances for residues of methoxychlor (ref. Federal Register: April 4, 2002, Volume 67, Number 65, Pages 16073-16078). Since there were data gaps for all of the major studies, the Agency was not able to make a finding that existing tolerances for methoxychlor were safe for any population, especially for infants and children. Based on available information, the Agency had significant concerns with the effects of methyoxychlor on human health and the environment. Furthermore, as of June 2000, all product registrations of methoxychlor were either suspended due to registrants' noncompliance with a Data Call-In notice issued under FIFRA section 3(c)(2)(B) or canceled pursuant to registrants voluntary cancellation request under FIFRA section 6(f). EPA believed that all existing stocks of pesticide products labeled for the uses associated with the tolerances proposed for revocation had already been exhausted.

On July 17, 2002, EPA announced the revocation of all tolerances for residues of methoxychlor (Federal Register: July 17, 2002, Volume 67, Number 137, Pages 46906-46909). Without a tolerance or exemption from the requirements for a tolerance, food containing pesticide residues is considered to be unsafe and therefore adulterated under the Federal Food, Drug and Cosmetic Act (FFDCA), and such food may not be distributed in interstate commerce.

Uses

Methoxychlor has been used to control various nuisance species including cockroaches, mosquitoes, flies and chiggers, as well as various arthropods that attack field crops, vegetables, fruits, ornamentals, stored grain, livestock, and domestic pets. Methoxychlor has been formulated as wettable powders, dusts, emulsifiable concentrates, ready-to-use products (liquids), and pressurized liquids.

Health Effects

Although a human health risk assessment has not been done as a result of the incomplete data base for methoxychlor, the Agency has significant concerns about the effects of methoxychlor on human health and the environment. Methoxychlor was used by the U.S. and the Organization for Economic Cooperation and Development (OECD) as one of the key chemicals in validating components of the Endocrine Disruption Screening Program. Methoxychlor has been discussed extensively in the public literature in connection with its effects on endocrine-mediated processes and disruption of the hypothalmic-pituitary-gonadal axis. Kupfer and Bulger[(1)] found that both methoxychlor and its metabolites have estrogen-like activity with several metabolites having proestrogen activity.

Gray et al.[(2)] investigated the effects of methoxychlor on the pubertal development and reproductive function in the male and female rat (Long-Evans hooded) by dosing rats exposed to methoxychlor from gestation, weaning, lactation, through puberty. In females they found precocious vaginal opening, abnormal estrus cycle, inhibition of luteal function and a blockage of implantation. In males they found an inhibition of somatic growth and accessory gland weight, elevated pituitary and serum prolactin levels, and a suppression of testicular Leydig cell function. Some of these effects occurred at levels as low as 25 milligrams/kilogram/day (mg/kg/day). These observations are consistent with the earlier reports that methoxychlor mimics estrogen both in vivo and in vitro.

Goldman et al.[(3)] investigated the subchronic effects of methoxychlor on the rat (Long-Evans hooded) reproductive system by dosing for 8 weeks with 25 mg/kg or 50 mg/kg of methoxychlor by oral gavage. Pituitary prolactin levels were increased at both treatment levels, and gonadotropin-releasing hormone (GnRH) levels increased in the mediobasal hypothalamus at the high-dose level. The authors determined that the reproductive effects of methoxychlor are mediated in part by an increase in prolactin which in turn increased hypothalamic GnRH.

Cummings and Gray[(4)] of the U.S. EPA Health Effects Research Laboratory found that methoxychlor affects the decidual cell response of the rat uterus, suggesting a direct effect of the compound on the uterus. In a 3-generation rat reproduction study, methoxychlor reduced fertility and increased fetotoxicity. Methoxychlor at 1,000 parts per million (ppm) reduced fertility, litter size, and viability.

Khera et al.[(5)]

(Ref. 4) on the teratogenicity of methoxychlor found that treatment of pregnant rats with methoxychlor produced maternal toxicity in the form of reduced body weight gain at all doses tested (50 to 300 mg/kg/day). Developmental toxicity was noted as fetotoxicity at doses of 200 and 400 mg/kg/day and as a dose-related increase of bone deformities (wavy ribs) at 100, 200, and 400 mg/kg/day.

Environmental Effects

Based on available data, methoxychlor is classified as very highly toxic (LC_{50} < 0.1 mg/L) to aquatic animals (fish and invertebrates) on an acute exposure basis. Toxicity estimates were as low as 0.0005 mg/L (MRID 400946-02) for freshwater invertebrates. However, methoxychlor is practically nontoxic to birds on both an acute oral (LD_{50} >2000 mg/kg) and a subacute dietary (LC_{50}>5000 mg/kg/day) exposure basis.

Methoxychlor's effects on the hypothalmic-pituitary-gonadal axis along with the developmental effects previously described in the Health Effects section raise concern for the potential endocrine disrupting effects of methoxychlor on non-target animals. These concerns are underscored by the structural similarity of methoxychlor to DDT. The lack of avian reproduction data on methoxychlor is a major uncertainty given the recognized chronic reproductive risk associated with DDT through thinning eggshells. An ecological risk assessment has not been done as a result of the uncertainties associated with the incomplete data base for methoxychlor.

Insufficient data are available for EPA to develop an environmental fate assessment for methoxychlor. No environmental fate data requirements have been successfully fulfilled for this pesticide. Literature cited in the 1989 EPA publication *Guidance for Registration of Pesticide Products containing Methoxychlor as an Active Ingredient* provide preliminary data indicating that methoxychlor is persistent in the environment, which is predictable given this organochlorine compound's structural similarity to DDT.

Data Gaps

The following sets forth the substantive data gaps for methoxychlor. Products containing methoxychlor will be canceled pursuant to Section 6(f) of FIFRA and are not eligible for reregistration, therefore, no DCIs are issued with this document.

Toxicology

- Guideline 83-1 (a) Chronic toxicity - rodent
- Guideline 83-1 (b) Chronic toxicity - non-rodent
- Guideline 83-2 (a) Oncogenicity - rat
- Guideline 83-2 (b) Oncogenicity - mouse
- Guideline 83-3 (a) Teratogenicity - rat
- Guideline 83-3 (b) Teratogenicity - rabbit
- Guideline 83-4 Two-generation reproduction - rat
- Guideline 85-1 General metabolism

Residue Chemistry

- Guideline 171-4 (a) Nature of Residue - Plants
- Guideline 171-4 (b) Nature of Residue - Livestock
- Guideline 171-4 (e) Storage stability
- Guideline 171-4 (j) Magnitude of residue - meat, milk
- Guideline 171-4 (k) Crop field trials

Environmental Fate and Effects

- Guideline 161-1 Hydrolysis
- Guideline 161-2 Photodegradation - water
- Guideline 161-3 Photodegradation - soil
- Guideline 162-1 Aerobic soil metabolism
- Guideline 162-2 Anaerobic soil metabolism
- Guideline 162-3 Anaerobic aquatic metabolism
- Guideline 162-4 Aerobic aquatic metabolism
- Guideline 163-1 Leaching/adsorption/desorption
- Guideline 164-1 Soil field dissipation

Ecological Effects

- Guideline 71-4 (a) Avian reproduction - quail (upland game bird)
- Guideline 71-4 (b) Avian reproduction - duck (water fowl)

Tolerances

On July 17, 2002, EPA announced the revocation of all 79 tolerances for residues of methoxychlor (ref. Federal Register: July 17, 2002, Volume 67, Number 137, Pages 46906-46909).

Regulatory Conclusion

The Agency has completed its reregistration eligibility decision for the pesticide methoxychlor, and has determined that methoxychlor is not eligible for reregistration. All registered technical sources of methoxychlor were canceled in 2003, and all tolerances have been revoked. Voluntary cancellation of remaining products is in process. The products remain suspended until the voluntary cancellations are effective.

The Agency has determined that it is not necessary to assess the risks of methoxychlor products because there are no tolerances for methoxychlor and all of the remaining products have been suspended since 2000 and are in the process of voluntary cancellation through the FIFRA 6(f) cancellation process. This reregistration finding is based on the substantive data gaps, resulting in significant uncertainties regarding the environmental fate and effects of methoxychlor, the absence of necessary tolerances, and the absence of a registered source of methoxychlor manufacturing use product. The Agency finds that methoxychlor does not meet the statutory requirements of reregistration.

Sale and distribution of existing stocks or products already in the channels of trade labeled and used for non-food uses is permitted. However, the Agency does not expect that any such products remain following suspension of the technical product in 2000 and cancellation of all tolerances in 2002.

/s/ June 30, 2004
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2. Gray, L.E. Jr., J. Ostby, J. Ferrell et al. 1989. A dose- response analysis of methoxychlor-induced alterations of reproductive development and function in the rat. Fund. Appl. Toxicol. 12(1): 92- 108.

3. Goldman, J.M., R.L. Cooper, G.L. Rehnberg, J.F. Hein, W.K. McElroy, and L.E. Gray Jr. 1986. Effects of low subchronic doses of methoxychlor on the rat hypothalamic-pituitary reproductive axis. Toxicol. Appl. Pharmacol. 86(3): 474-483.

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5. Khera, K.S., C. Whalen, and G. Trivett. 1978. Teratogenicity studies on linuron, malathion, and methoxychlor in rats. Toxicol. Appl. Pharmacol. 45(2): 435-444.