Fluoroacetamide (Compound 1081)
Position Document 2

Special Pesticide Review Division
Office of Pesticide Programs
U.S. Environmental Protection Agency

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I. Introduction

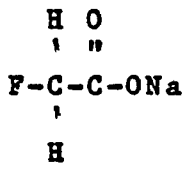
The Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) as amended, September 30, 1978, and its regulations require the Environmental Protection Agency (EPA) to review the risks and benefits of the uses of registered pesticides. This review process is set forth in 40 CFR 162.11. These regulations describe various risk criteria and provide that a Rebuttable Presumption Against Registration (RPAR) or continued registration shall arise if the Agency determines that any of these criteria have been met. Once a rebuttable presumption has arisen, registrants, applicants, and interested persons may submit evidence in rebuttal or in support of the presumption. These people may also submit evidence on the economic, social, and environmental benefits of any use of the pesticide. The Agency then determines whether the pesticide may be regulated so as to achieve a balance between risks and benefits.

The Agency formally initiated this review for all products containing fluoroacetamide (Compound 1081) by publishing an RPAR notice in the Federal Register [41 FR (232): 52792-809, December 1, 1976]. This document presents the Agency's analysis of information submitted by concerned individuals on the risks from the continued use of Compound 1081 and presents a discussion of label amendments proposed by the sole-remaining registrant.

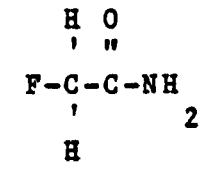
With these new use restrictions on the label, Compound 1081 does not meet or exceed any of the risk criteria set forth in 40 CFR 162.11. Therefore, the Agency has determined that the presumption against Compound 1081 has been rebutted and the registration of Compound 1081 should be continued.

A. Background

Sodium fluoroacetate (Compound 1080) was first used as a rodenticide in the 1940's. Fluoroacetamide, or Compound 1081, was developed in the early 1950's. Although Compound 1080 and Compound 1081 are different compounds, the chemical and pharmacological similarities of these two chemicals suggest that they would present similar hazards. Some of the Agency's conclusions about the hazards of Compound 1081 are based in part on data available for Compound 1080. The chemical formulas for Compound 1080 and Compound 1081 are:



Compound 1080



Compound 1081

Although both compounds are systemic insecticides, Compound 1080 and Compound 1081 are currently registered in the United States only as rodenticides. In other countries Compound 1081 has been used to control aphids on sugarbeets, beans, and strawberries.

B. Regulatory History

When Position Document 1 was issued, Compound 1081 was registered for use in two products. In 1978, the manufacturer of one, Fluorakil 100, requested a voluntary cancellation.

There is currently one Federally-registered Compound 1081 product, Fluorakil 90, which is used with cereal grain as bait to kill Norway rats and roof rats. It is manufactured by the ArCHEM Corporation and was originally registered on May 6, 1972 only for use against rats in sewers. The label specified that the product was effective against rats in sewers, but did not specifically restrict use of the product to a particular site. The registrant submitted to the Registration Division a proposed label with amendments which would clarify the use site restrictions and which would modify the use directions on the original label. This proposed label was approved by the Registration Division November 2, 1979.

C. Basis of Rebuttal Presumption

The rebuttable presumption of Compound 1081 was based on the Agency's determination that products containing Compound 1081 met or exceeded three risk criteria: lack of emergency treatment [40 CFR 162.11(a)(3)(iii)], acute toxicity to mammalian and avian species [40 CFR 162.11 (a)(3)(i)(B)(1) and (2)], and significant reduction of

populations of nontarget organisms and fatalities to members of endangered species [40 CFR 162.11(a)(3)(ii)(C)].

The following three sections explain each criterion further.

1. Lack of Emergency Treatment

The primary factors cited by the Agency as supporting an RPAR based on this risk criterion were:

- The Compound 1081 labels did not specifically prohibit use of the product around domestic dwellings where children are likely to be exposed to it.

- If ingested, symptoms of poisoning might not occur until after Compound 1081 has been absorbed into the bloodstream. Once a substantial dose of Compound 1081 is absorbed into the bloodstream, the victim inevitably dies despite emergency treatment attempts.

- Monoacetin, a potentially effective drug for treating Compound 1081 poisoning, is not generally available for medical use in the United States.

2. Acute Toxicity to Mammalian and Avian Species

The Agency determined that lethal amounts of Compound 1081 bait may be consumed by mammals or birds and therefore

Compound 1081 is hazardous to nontarget species. In addition, the Agency determined that Compound 1081 poses a hazard to predators which feed on sick or dead animals that have consumed the poisoned bait. These determinations were based on LD_{50} data for Compound 1080.

3. Significant Reduction of Populations of Nontarget Organisms and Fatalities to Members of Endangered Species

The Agency concluded that the use of Compound 1081 reduces populations of nontarget organisms and kills members of endangered species because:

- Compound 1081 is extremely toxic to vertebrates.
- Baits treated with Compound 1081 might be applied over a fairly large geographic area and might be consumed by many types of animals.
- Poisoned bait might be applied in areas known to be inhabited by endangered species.

II. Rebuttal Analysis

After the Compound 1081 RPAR was issued, registrants and other interested people were invited to review the data upon which the RPAR was based and to submit information to

support or refute the Agency's findings; respondents could also submit information on the economic, social, and environmental benefits derived from the use of Compound 1081.

According to 40 CFR 162.11(a)(4)(i), and (ii), a presumption against registration may be rebutted either by proving that anticipated exposure to the pesticide, when considered with proposed restrictions and directions for use, is not likely to result in any significant acute effects in applicators, users, or non-target animals or is not likely to result in significant chronic adverse effects in humans or the environment.

Fourteen respondents, listed in Appendix II of this document, submitted information on Compound 1081. Eight respondents [#24, #5, #46, #32, #40, #36, #41, and #48 (30000/8)] expressed support for the continued registration or reregistration of Compound 1081 for commensal rodent control and attempted to rebut the risk criteria. Six respondents [#61, #50, #55, #57, #56, and #42 (30000/8)] stated that the registration of Compound 1081 should be cancelled because it poses a hazard to nontarget wildlife species, but they provided no new information in support of their position.

The Agency concluded that the eight respondents supporting continued registration or reregistration of Compound 1081 did not successfully rebut any of the risk criteria. Nevertheless,

the Agency determined that if certain restrictions on use and modifications of use directions on the label were agreed to by the registrant, anticipated exposure of humans and nontarget species of wildlife and domestic animals would be reduced to insignificant levels. Since the registrant voluntarily agreed to these label revisions, the Agency concludes that the presumption has been rebutted.

A discussion of the Agency's analysis of the rebuttals is given below according to risk criteria. Then the new restrictions on use and modification of use directions on the label will be described.

A. Risk Criterion: Lack of Emergency Treatment

Respondents did not show that commonly available medical treatment in the U.S. can prevent persons from dying after accidental ingestion of Compound 1081. Those rebuttal submissions which addressed this risk criterion will now be discussed.

1. Availability of Emergency Treatment

One respondent asserted that many persons who received prompt first aid treatment have recovered after ingesting supposedly lethal amounts of Compound 1080 [Fitzwater, 1977 (46:30000/8)]. This assertion warrants some consideration because it could indicate that people receiving prompt first aid treatment after ingesting lethal amounts of Compound 1081 might also recover, since Compound 1080 and

Compound 1081 are pharmacologically similar. However, in the recoveries cited, the doses were not documented, so the amounts of Compound 1080 ingested may have been sublethal, thus making successful treatment possible. In addition, not only have the majority of people who have ingested Compound 1080 died, but in the only documented incident of Compound 1081 poisoning, all three victims died. Therefore, while there have been some recoveries from Compound 1080 poisoning, the overall case history indicates that first aid treatment is not effective for Compound 1081 poisoning.

The same respondent suggested that monoacetin and acetamide may be effective emergency treatments for Compound 1081 poisoning. The Agency has recognized that monoacetin is potentially effective for treating Compound 1081 poisoning, but the respondent did not attempt to refute the Agency's finding that this treatment is not readily available in emergency situations. In addition, the respondent failed to demonstrate that acetamide is effective in treating human cases of Compound 1081 poisoning. One cited article (Phillips and Worden, 1957) demonstrated only that acetamide may be effective in treating Compound 1081 poisoning in rats. The respondent cited a second reference (Moore, 1950) to support the contention that acetamide has been effective in Japan for treating humans poisoned with Compound 1081. However, the reference contained no information which actually supported this contention.

Another respondent indicated that antidotes are described in the literature [National Pest Control Association, Inc., 1977 (48:30000/8)]. A more recent edition of the clinical toxicology text cited in support of this statement (Clinical Toxicology of Commercial Products, 4th Edition) indicated that monoacetin has proved to be an effective antidote for Compound 1080 poisoning in monkeys, but stated that this treatment is not available for the pharmaceutical market (Gosselin et al., 1976). In addition, this reference indicated that while acetamide and ethyl alcohol may be of value in treating Compound 1080 poisonings, these treatments have not been clinically tested and no treatment protocol has been established for using these chemicals. In conclusion, no rebuttal submissions refuted the Agency's determination that emergency treatment for Compound 1081 poisoning was not readily available.

2. Time Factor

No respondent successfully refuted the Agency's determination that it is important to obtain emergency treatment immediately after ingestion of Compound 1081 and that a time delay could be fatal. The Agency indicated in Position Document-1 that time delays could be expected to cause fatalities because: first, Compound 1081 is rapidly absorbed from the gastrointestinal tract; second, once a lethal dose is absorbed into the bloodstream, treatment is invariably unsuccessful; and third, lack of symptoms prior to absorption of a fatal dose into the bloodstream may prevent the victim from obtaining treatment in time.

One respondent indicated that the time lag between ingesting the poison and the appearance of symptoms is greater for Compound 1081 than Compound 1080 [Fitzwater, 1977 (46:30000/8)]. The references cited verify this for laboratory animals (Phillips and Worden, 1957). They indicated that no information regarding the time lag in humans was available at the present time. However, even if the greater time lag were present in humans,this would not necessarily mean that Compound 1081 is absorbed more slowly from the gastrointestinal tract than Compound 1080. Phillips and Worden indicated that the slower action of Compound 1081 is due to a slower biochemical conversion to a physiologically poisonous intermediate product rather than a delay in its absorption into the bloodstream. Since no effective antidote is readily available, the Compound 1081 must be flushed from the gastrointestinal tract before absorption into the bloodstream or the victim will die. Because symptoms do not appear immediately, a victim may delay seeking treatment until a fatal dose has already been absorbed into the bloodstream. Therefore, no rebuttal submission refuted the presumption regarding the time factor involved in seeking emergency treatment.

3. Dose Likely to Be Consumed in an Accident

No respondent attempted to rebut the Agency's determination that a typical dose of Compound 1081 which could be accidentally ingested would be fatal.

4. Likelihood of Exposure to Compound 1081

Two respondents maintained that accidental exposure to Compound 1081 has been very rare [Fitzwater, 1977 (46:30000/8); Spear, 1977 (48:30000/8)]. They pointed out that during the last 22 years only one incident resulting in death is known to have occurred in the United States; in 1976 three children died after eating Compound 1081-treated cookies, which they obtained from the unlocked truck of a pest control operator. Nevertheless, the Agency is concerned about even very infrequent human exposure to this pesticide because it is so highly toxic and because an effective emergency treatment is not available. Non-applicators, especially children, could come into contact with Compound 1081 if the pesticide were stored, transported, or applied negligently. Applicators could also be exposed if storage, mixing, or application was not performed according to appropriate safeguards.

In its rebuttal submission, the National Pest Control Association indicated that any risk of exposure posed by use of Compound 1081 was due to the fact that the Agency had not restricted the pesticide to use by Certified Commercial Applicators only, and that the Agency had not specifically limited the use of the pesticide for sewer rat control [Spear, 1977 (48:30000/8)]. The Agency subsequently classified Compound 1081 for restricted use by Certified Commercial Applicators [43 FR (28):5782-91, Feb. 9, 1978]. In addition, Compound 1081 is in fact registered only for control

of rats in sewers. However, the Agency agrees that the original label for Compound 1081 was unduly vague about the permissible site and pest.

At the time the Agency reviewed these rebuttal submissions, the Agency concluded that the possibility of exposure to Compound 1081 was still cause for concern unless additional use restrictions and directions were prescribed.

B. Risk Criteria: Acute Toxicity to Mammalian and Avian Species; Significant Reduction of Nontarget Populations and Fatalities to Members of Endangered Species

Respondents did not submit any data to show that Compound 1081 is not acutely toxic to mammalian and avian species. However, three respondents maintained that Compound 1081 does not pose a substantial hazard to nontarget organisms, including members of endangered species, when used to control rats in sewers [Arbaugh, 1976 (24:30000/8); Fitzwater, 1977 (46:30000/8); and Spear, 1977 (48:30000/8)]. However, because the labels for Compound 1081 products which were in effect when the RPAR was issued did not clearly describe the registered use, it was possible that these products could have been used at sites other than sewers under the false impression that such use was permissible. Such use could pose a risk to nontarget or endangered species. In addition, even if Compound 1081 were used only in sewers, exposed rat carcasses could pose some hazard to

domestic cats and dogs. Therefore, the Agency concluded that this risk criterion was not rebutted, unless additional use restrictions and directions were prescribed.

C. Amendment of the Label

After completion of its review of the rebuttals, the Agency determined that the presumption against Compound 1081 had not been rebutted even though the pesticide had been classified for restricted use by Certified Commercial Applicators. The Agency concluded, however, that if the registrant agreed to certain use restrictions and modified use directions on the label, the presumption would be rebutted because the likelihood of exposure to humans, nontarget mammals and birds, and endangered species would then be very remote. The rationale for the label restrictions is discussed in Section III of this document.

The use restrictions and modified use directions are:

1. Site Clarification

The labels should be modified so that it is clear that Compound 1081 may only be used in sewers to control roof rats and Norway rats. The label should also indicate that the location of application inside the sewers should be selected such that entry by unauthorized personnel is unlikely.

2. Other Restrictions

a. Use by Certified Commercial Applicators

The label should be amended to indicate that Compound 1081 may not be made available to or used by anyone other than Certified Commercial Applicators or persons under the supervision and in the physical presence of a Certified Commercial Applicator.

b. Preparation, Storage, and Disposal

The label should indicate that baits must be prepared and mixed at the facility of the applicator and that baits must not take the form of any food normally consumed by humans. (Baits were previously in the form of wafers or cookies.) Persons preparing the formulation from the dry concentrate must wear gloves and a respirator. Equipment used to handle and mix Compound 1081 must be identified and used only for this purpose.

All Compound 1081 baits and containers must be clearly labeled and kept locked during storage and transport. Sewer exits in the treatment area must be inspected daily, and dead animals collected and disposed of by the Certified Applicator. Control efforts must cease if there is evidence of unauthorized use of the sewer. At the end of operations, all unused baits and containers must be picked up and disposed of by the Certified Applicator. All containers (which must be triple-rinsed and empty), solutions, baits,

and poisoned animals must be disposed of in a landfill which has been approved by the appropriate local Health or Environmental Department.

The Agency concluded that these specific label restriction would make exposure of humans and of nontarget mammalian or avain species including endangered species very remote.

III. Discussion: Rationale for Label Amendments

A. Site Clarification

Position Document 1 implied that the labels in effect at that time permitted Compound 1081 to be used against rodents in locations other than sewers. The Agency reevaluated the scope of permissible uses of Compound 1081 and concluded that the pesticide was registered only for use against rats in sewers, since this was the only pest and site indicated on the labels and proposed in the original applications from both registrants. However, the Agency determined that much confusion would be eliminated if the label were amended to state clearly that the product could be used only for rat control in sewers. The Agency determined that this restriction would significantly reduce the risks to nontarget organisms and endangered species, since these animals, not generally being found in sewers, would have little or no exposure to it. Although raccoons and opossums do frequent sewers, no significant impact on their population at large would be

expected. Human exposure would be unlikely, since use around domestic dwellings or barns would be specifically prohibited.

B. Other Restrictions

The Agency also concluded that the risk of secondary poisoning to nontarget species, including domestic dogs and cats, would be significantly reduced by the label amendment requiring that dead animals be collected daily and disposed of by the Certified Applicator. Secondary poisoning could occur by chance if a poisoned rat moved outside a sewer before dying and if the carcass was not found by the Certified Applicator. However, the Agency concluded that this situation is unlikely to happen often enough to be of concern. The risk of accidental human exposure would also be reduced by the label amendment restricting the use of Compound 1081 to Certified Applicators.

Restrictions on preparing the formulation and storing and disposing of baits and poisoned animals would also contribute to reducing the risk of human exposure to an insignificant level. The acute toxicity of the chemical would be the same, but the likelihood of accidental human exposure would be very low.

IV. CONCLUSIONS

A presumption against registration may be rebutted by proving that anticipated exposure to a pesticide, when considered with proposed restrictions and directions

for use, is not likely to result in any significant acute or chronic effects in humans, nontarget animals, or the environment, [40 CFR 162.11(a)(4).]

The registrant for Fluorakil 90 voluntarily proposed that the restrictions and modified directions for use be incorporated in the labels of new stocks of the product. The proposed label was approved November 2, 1979. With these new use restrictions and modified directions for use, the presumption concerning the lack of emergency treatment is rebutted, since the risk of accidental human poisonings is now very remote and therefore insignificant. The presumptions concerning acute toxicity to nontarget avian and mammalian species, significant reduction in populations of nontarget species, and fatalities to members of endangered species are also rebutted because the risk of exposure to nontarget species, including endangered species, is now very unlikely. Therefore, the Agency concludes that the presumption against the registration of Compound 1081 has been rebutted.

If, in the future, other people submit applications to register a product containing Compound 1081, they will be required to comply with these new restrictions.

Appendix I. REFERENCES

1. Federal Register, December 1, 1976. Notice of presumption against registration and continued registration of pesticide products containing Compound 1080 and Compound 1081; 41(232):52792-52809.

2. Federal Register, February 9, 1978. Optional Procedures for Classification of Pesticide Uses by Regulation; Pesticide Use Restrictions; 43(28):5782-91.

3. Gosselin, R.E. et al., 1976. Clinical Toxicology of Commercial Products, 4th Edition. The William and Wilkins Co., Baltimore, MD.

4. Markley, Merle H., (CED), 1977. EPA memo of November 14, 1977 to William Coniglio (SPRD); Analysis of Adequacy of 1081 Rebuttal.

5. Moore, R., 1950. Summary of "1080" accidents. Rodent Control Conference, Dallas, Texas. January 31 - February 2; 4 p.

6. Phillips M.A. and Alastair N. Worden, 1957. The Mammalian Oral Toxicity of Fluoroacetamide. J. Sci. Food Agric., 8:653-657.

7. Tippens, T.W., September 29, 1978. Letter to Wm. Miller; Cancellation of registration.

Appendix II. REBUTTAL SUBMISSIONS COMPOUND 1081

1. Arbaugh, Howard, December 31, 1976; ArChem Corporation, Portsmouth, Ohio; (24:30000/8).

2. Deck, Errett, March 7, 1977; U.S. Department of Agriculture, Washington, D.C.; (5A:30000/8).

3. Deck, Errett, March 9,, 1977; U.S. Department of Agriculture, Washington, D.C.; (5B:30000/8).

4. Edmiston, Beula, March 3, 1977; Committee for the Preservation of the Tule Elk, Los Angeles, California; (61:30000/8).

5. Fitzwater, William D., March 2, 1977; BioLOGIC Consultants, Albuquerque, New Mexico; (46:30000/8).

6. Grant, Allan, December 28, 1976; American Farm Bureau Federation, Park Ridge, Illinois; (32:30000/8).

7. Harkness, Bernard J., December, 31, 1976; Montana Farm Bureau Federation, Bozeman, Montana; (40:30000/8).

8. Hinkle, Maureen K., March 7, 1977; Environmental Defense Fund, Washington, D.C.; (50:30000/8).

9. Kopecky, Edward F., March 1, 1977; Cedar Rapids, Iowa; (55:30000/8).

10. Lavigne, J.H., January 4, 1977; Fike Chemicals, Incorporated, Nitro, West Virginia; (36:30000/8).

11. Randall, Dick, March 7, 1977; Defenders of Wildlife, Washington, D.C.; (57:30000/8).

12. Senske, William M., February 8, 1977; Senske Weed and Pest Control, Spokane, Washington; (41:30000/8).

13. Smerdon, Glenn E., March 10, 1977; State Department of Agriculture, Olymphia, Washington; (56:30000/8).

14. Spear, Philip J., March 4, 1977; National Pest Control Association, Vienna, Virginia; (48:30000/8).

15. Weber, William J., February 9, 1977; Leesburg, Florida, (42:30000/8).