105001
SHAUGHNESSEY NO.

17
REVIEW NO.

EEB BRANCH REVIEW

DATE: IN 10-20-83 OUT 11-28-83

FILE OR REG. NO. 241-238, 241-241

PETITION OR EXP. PERMIT NO.

DATE OF SUBMISSION 9-27-83

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TYPE PRODUCT(S): I, D, H, F, N, R, S Insecticide/Nematicide

DATA ACCESSION NO(S).

PRODUCT MANAGER NO. W. Miller (16)

PRODUCT NAME(S) Terbufos

COMPANY NAME American Cyanamid Company

SUBMISSION PURPOSE Registrant response to registration standard

SHAUGHNESSEY NO.	CHEMICAL, & FORMULATION	% A.I.
105001	Terbufos	N/A

4 pp.
and
6 pp. attachment

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

2 DEC 1983

MEMORANDUM

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

TO: William Miller (PM 16)
Registration Division, TS-767c

THRU: Dave Coppage
Head, Sec. 3
Ecological Effects Branch
Hazard Evaluation Division, TS-769c

THRU: Clayton Bushong
Branch Chief
Ecological Effects Branch
Hazard Evaluation Division, TS-769c

SUBJECT: Response to American Cyanamid's comments on the Terbufos Registration Standard

EEB has received American Cyanamid's comments on the Terbufos Registration Standard and the requested data. American Cyanamid's comments on the Ecological Effects Section are shown below and are followed by EEB's response.

71-4 "The Agency's Reregistration Standard stated that 'All pen-by-pen data must be provided to enable full statistical evaluation of the results' of Cyanamid's Avian Reproduction Studies (MIRDs 00085177 and 00097892). Individual pen data were utilized within each experimental group and subjected to a thorough statistical analysis sufficient to evaluate the effects of terbufos."

EEB Response

The use of "group" data cannot adequately evaluate the potential avian reproductive effects of a particular compound. EEB's statistical validation of the group data from the Fink & Reno (1973) reproductive studies (MIRD's 00085177 and 00097892) is not in full agreement with the investigator's conclusions concerning the statistical significance. EEB's validation record indicates overall reproductive impairment as compared to controls ($p < 0.05$) as well as a reduction in relative numbers of viable embryos as compared to eggs set at 2 ppm. Hence, the registration standard, indicating less than full confidence in the investigator's conclusions, requested the pen-by-pen data. EEB will use these data (which are now routinely submitted with avian reproduction studies) to more precisely evaluate the results and our concerns.

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The Registrant responded that "individual pen data were utilized within each experimental group....". This response begs the question of validating the statistical significance of the pen-by-pen data. We know they used "invidual pen data" in tabulating the "group" data. We are interested in validating the analysis of the pen data, not just an analysis of the group data derived from them. While we now do this routinely, this is especially necessary when a potential conflict exists between the author's reported results and the reviewer's evaluation.

71-5 "We recognize the concern of the Agency for the conduct of an actual wildlife monitoring study and suggest integrating this into the field monitoring study discussed under Environmental Fate (165)."

EEB Response

Although the suggestion seems reasonable, without having a protocol to review we cannot agree to integrate the wildlife monitoring study with the environmental fate study required by the Exposure Assessment Branch. At this point there is no reason to oppose the suggestion, however it should be noted that EEB sees no particular connection between the wildlife monitoring (which is a "terrestrial" study) and the fate monitoring, which appears to address potential runoff concerns.

We must emphasize that, should the company decide to integrate the two studies, compromises of the wildlife study design, controls or execution, made to "accomodate" constraints imposed by the fate study (e.g. - location, timing, or plain "bad luck") may not be acceptable. Careful planning, a thorough pre-test census, proper test execution and controls will be necessary to avoid a wasted field effort and provide meaningful results. We strongly urge that no field test commence without our concurrence on the protocol.

72-3 "Cyanamid has not registered nor has plans to register COUNTER® for crops or use patterns that potentially threaten estuarine or marine organisms. Further, the acute toxicity of COUNTER® to aquatic organisms is well known. (MIRDs 0037483, 00085176, 00087718 and 00101495; GS0109002, GS0109003, GS0109004) Thus, Cyanamid sees no justification for the conduct of the requested work."

EEB Response

The corn and sorghum registrations of Counter® encompass a significant potential for estuarine exposure through runoff, drift, or accidental applications in coastal counties of the U.S.. These registrations, combined with freshwater aquatic toxicity information and preliminary runoff estimates, triggered the requests for estuarine organism testing.

72-4 "Cyanamid agrees to conduct the early fish life cycle and aquatic invertebrate life cycle studies."

EEB Response

While we are in agreement on this point, EEB would like to clarify for the record the data requirements under 72-4 for Counter®. These are a "fish early life stage" study and an "aquatic invertebrate life cycle" study. The "fish life cycle" test referred to in Cyanamid's remarks is actually a "reserved" requirement under 72-5, the imposition of which is pending the results of studies under 72-3 and 72-4.

John Bascietto

John Bascietto
Wildlife Biologist
Ecological Effects Branch
Hazard Evaluation Division, TS-769c

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September 27, 1983

Mr. William Miller
Product Manager (16)
Registration Division (TS-767)
U.S. Environmental Protection Agency
Crystal Mall, Building #2
1921 Jefferson Davis Highway
Arlington, VA 22202

Re: Initiation of Reregistration Process for Manufacturing-Use Products and Certain End-Use Products Containing Terbufos as the Single Active Ingredient

Dear Mr. Miller:

Enclosed is American Cyanamid's submission of the FIFRA 3(c)(2)(B) Summary Sheet pertaining to the Reregistration Process for Terbufos. American Cyanamid takes issue with certain of the data requirements listed in the referenced document. We have listed those data requirements and our rationale for so doing in Exhibit 1. After the Agency reviews this attached submission, we will meet at your convenience to resolve these issues.

Very truly yours,

William A. Steller

William A. Steller, Manager
Plant Industry Registrations

WAS:sd
Enc.

Accn. # 251414

Rec'd EPA
10/3/83

EXHIBIT I

Cyanamid has reviewed the Reregistration Standard for COUNTER® (terbufos) issued by the EPA on June 30, 1983. Although Cyanamid recognizes and intends to fill data gaps where no information has been submitted to the Agency, we feel that some previously submitted studies are sufficient to assess the hazards of the product and that some new studies are adequate to eliminate the need for other EPA-requested studies. Due to the scope of the requests in the Standard it is necessary to discuss each test within the four (4) sections of the Testing Guidelines.

I. PRODUCT CHEMISTRY (158:120)

The EPA requests the following product chemistry data:

Reg No.	Product data
61-2	Statement of Composition
62-2	Certification of Limits
62-3	Analytical methods for enforcement of limits
63-6	Boiling point
63-8	Solubility
63-9	Vapor pressure
63-11	Octanol/water partition coefficient
63-12	pH
63-14	Oxidizing or reducing action
63-15	Flammability
63-16	Explodability
63-17	Storage stability
63-18	Viscosity
63-19	Miscibility
63-20	Corrosion

Cyanamid agrees to conduct studies to fill the above listed data gaps in as timely a manner as possible. Our resources are heavily taxed by current research and development activities and the conduct of this work will require reordering priorities. Cyanamid requests an extension for the completion of this work to the third quarter of 1984.

Rec'd EPA 10/3/83

II. TOXICOLOGY (158:135)

The EPA has requested the following new toxicology studies:

Reg. No.	Product
81-2	Dermal LD_{50} - Rat/Rabbit
81-3	Inhalation LC_{50} - Rat
83-1	24-Month Rat Study
83-1	12-month Dog study
83-2	18-Month Mouse Study
83-3	Teratology - Rat
83-3	Teratology - Rabbit
84-2	In vitro CHO/HGPRT
84-2	In vitro chromosome aberration
84-2	In vitro sister chromatid exchange
84-2	In vivo cytogenetics
84-2	In vivo unscheduled DNA synthesis
84-2	In vitro unscheduled DNA synthesis
84-2	Dominant lethal

81-2 Cyanamid agrees to conduct the additional dermal LD_{50} tests on
81-3 rabbits and rats and submit a rat inhalation LC_{50} study.

83-1 Cyanamid submitted a reevaluation of the "24-Month Oral Toxicity and Carcinogenicity Study of AC 92,100 in Rats" on September 9, 1983. This report was originally recieved by the EPA on May 29, 1975 (MIRD 00049236) in Pesticide Petition 4F1496, EPA accession No. 090808. It was upgraded to meet current testing guidelines resulting from an August 5, 1982 discussion between Cyanamid and the Agency. This discussion was preceded by correspondence from the Agency outlining the original study's deficiencies (Attachment I).

83-1 A 12-Month Dog Study seems unnecessary in light of Cyanamid's previously submitted 6-Month Dog Study (MIRD 00063209).

83-2 Cyanamid sees no reason for repeating "An 18-Month Carcinogenicity Study of AC 92,100 in Mice" (MIRD 00085170) for the following reasons: 1) the study was considered "State of the art" at the time of its original submission; 2) the study showed no oncogenic effects at any dose level tested (up to 8 ppm); and 3) the 24-month rat study was negative.

83-3 The EPA has recently received correspondence from Canadian regulatory authorities as to the validity of the "Teratogenic Study of AC 92,100 in Albino Rats" (Attachment II), thus, fulfilling a portion of regulation 83-3. This study was originally submitted on December 11, 1972 in Pesticide Petition 3G1340). A rabbit teratology study is in progress.

84-2 Cyanamid will submit three mutagenicity studies to the Agency in the near future; 1) DNA Repair test, 2) Chromosome Aberration Study and 3) Mammalian Cell Point Mutation Study. An Ames test was previously submitted (MIRD 00063209) and was negative. The necessity of doing further testing should not be considered before completion of the review of these new studies.

III. ENVIRONMENTAL FATE (158:130)

The following environmental fate studies have been requested:

Reg. No.	Product data
161-2	Photodegradation in water
163-2	Volatility (Lab)
165-2	Rotational crop (field) Monitoring studies (soil, water, sediment, fish)

161-2 Cyanamid originally submitted a photodegradation study of terbufos in water to the Agency on April 30, 1974 (MIRD 00087694) in Pesticide Petition 4F1496, EPA accession no. 091452. Our scientists have recently reviewed this study and are aware of its shortcomings. However, the study does answer the major questions embodied in the objectives, clearly showing that photolysis is a major contributing route to the degradation of terbufos in water and that hydrolysis is a major competing reaction.

163-2 A volatility study of COUNTER© is unwarranted. COUNTER© is formulated [redacted] and sold as a dry granular product. Cyanamid performed a farm worker exposure study in 1982 that included inhalation data and showed no significant risk of acute toxicity to users and submitted this to the EPA for review on June 27, 1983 (Attachment III). The Agency has yet to acknowledge receipt of this document. COUNTER© does not "Pose a potentially significant inhalation exposure to workers" (Subdivision O: 163-2(c)(2)) according to this study and EPA's Pesticide Information Monitoring System.

165-2 Based upon current and proposed crop registrations, common crop rotations and rates of application, conduct of rotational crop studies is not necessary. Our rationale is discussed below:

Corn (registered use) is most commonly followed by a small grain or legume (Attachment IV-A) and in the Corn Belt, corn-soybean rotations are very common. Soybeans(proposed use) are usually followed by a Graminaceous crop (Attachment IV-B). Current Testing Guidelines (Subdivision O) are concerned with rotational crops "When significant C14 pesticide residues of concern to the Agency are detected in the test crop analyzed in the confined accumulation study" (165-1(d)(1)) or "When a subsequent crop is treated with the same active ingredient as the initial crop" (165-1(d)(2)). No terbufos, or its related metabolites, in

excess of the negligible tolerance of 0.05 ppm were detected in the confined corn-soybean rotation study (MIRD 00087692) and no residues in excess of this tolerance were detected in corn (Attachment IV-C) or soybeans (Attachment IV-D)even when applied far in excess of the recommended rate in the same season. Further, wheat, being a representative small grain, does not accumulate terbufos or its toxic metabolites in the grain when COUNTER® is applied at a rate of 0.53 lbs. active ingredient per acre (Attachment IV-E). Based on soil residue studies (Attachments IV-F and IV-G), neither terbufos nor its toxic metabolites would be expected to carry through the winter at more than a fraction of a part per million.

Sugar beet (registered use) rotations most commonly involve a legume, small grain, potatoes, corn, or beans (Attachment IV-H). Neither labeled or excessive rates of COUNTER® applied to sugar beets would be expected to result in residues significant enough (Attachment III-G) to accumulate in any of these potential rotational crops. In addition, sugar beets would not be expected to accumulate residues in excess of the currently approved tolerance (0.05 ppm) even if subjected to excessive rates (Attachment IV-I).

Grain sorghum rotations include, almost exclusively, a fallow period and/or small grain or corn (Attachment IV-J), thus, precluding the need for further study. In addition, highest labeled rates applied to grain sorghum at planting do not result in detectable residues in the grain (Attachment IV-K). This reinforces the fact that COUNTER® and its toxic metabolites do not accumulate in the grain of Graminaceous crops.

Peanuts (proposed use) are generally followed by a winter cover crop and then by a small grain or corn (Attachment IV-L). Again, this precludes the need for a rotational study since the small amount of pesticide residue that may carry over to the next season (Attachments IV-F and IV-G) would not expect to result in detectable residues in either a small grain (Attachment IV-E) or corn (Attachment IV-C).

Cyanamid believes that the above-referenced work provides sufficient assurance that residues of terbufos and its metabolites do not carry through the winter in amounts that could result in detectable residues in any crop involved in rotations with currently registered and proposed crops. In reference to Subdivision 0,65-2(2)(iii)(A), leafy vegetables are not commonly used in rotations with corn, sugar beets, sorghum, soybeans and peanuts.

165 Cyanamid recognizes the need for conducting an environmental monitoring study with COUNTER®, but is of the opinion that 3 studies is excessive. A single study in a Corn Belt state, one where favorable rainfall patterns are most likely to occur, is most appropriate, since this is where COUNTER®'s use is concentrated and a representative site can be located. Further, the great amount of product used versus the very few incidences documented in EPA's Pesticide Information Monitoring System do not warrant such wide testing.

IV. WILDLIFE AND AQUATIC ORGANISMS

The EPA has listed the following areas as data gaps:

Reg. No.	Product data
71-4	Avian reproduction
71-5	Actual field testing
72-3	Acute LC_{50} -estuarine and marine organisms
72-4	Fish early life stage and aquatic invertebrate life cycle

71-4 The Agency's Reregistration Standard stated that "All pen-by-pen data must be provided to enable full statistical evaluation of the results" of Cyanamid's Avian Reproduction Studies (MIRDs 00085177 and 00097892). Individual pen data were utilized within each experimental group and subjected to a thorough statistical analysis sufficient to evaluate the effects of terbufos.

71-5 We recognize the concern of the Agency for the conduct of an actual wildlife monitoring study and suggest integrating this into the field monitoring study discussed under Environmental Fate (165).

72-3 Cyanamid has not registered nor has plans to register COUNTER© for crops or use patterns that potentially threaten estuarine or marine organisms. Further, the acute toxicity of COUNTER© to aquatic organisms is well known. (MIRDs 0037483, 00085176, 00087718 and 00101495; GS0109002, GS0109003, GS0109004) Thus, Cyanamid sees no justification for the conduct of the requested work.

72-4 Cyanamid agrees to conduct the early fish life cycle and aquatic invertebrate life cycle studies.

COUNTER© is recognized as the most effective soil insecticide-nematicide available for corn. Since its registration in 1974 it has been used by thousands of farmers on millions of acres of cropland. When used according to the label it has been shown to adequately protect the environment and the public health. We are confidant that our proposed efforts to fill current data gaps will be sufficient to ameliorate any concerns regarding the continued registration of this product.