

US EPA ARCHIVE DOCUMENT



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

APR 2 1991

MEMORANDUM

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

Subject: Dithiopyr Herbicide Avian Reproduction and Residue
Study Analysis Protocol Review

From: James W. Akerman, Chief
Ecological Effects Branch
Environmental Fate and Effects Division (H7507C)

To: Joan Miller, Product Manager 23
Herbicide / Fungicide Branch
Registration Division (H7505C)

Monsanto Agricultural Company's letter of January 25, 1991, raised questions concerning the requirement for residue analysis in an avian reproduction study in addition to requesting comments on the specific protocols of Wildlife International Ltd. for residue analysis and avian reproduction. The specific questions are addressed first followed by comments on the residue analysis and avian reproduction study, respectively.

- 1) 71-4(d) Diet Preparation - What are the specific triggers for requiring tissue residue analysis on avian reproduction studies?

The decision to require additional residue testing in birds is made on a case by case basis and relies on a combination of three elements reported in the guidelines:

1. Partition coefficient (octanol water coefficient)
2. Bioconcentration Factor (BCF) (e.g. 1000)
3. Structural similarity to known bioaccumulative chemicals

In the case of dithiopyr the BCF of 1100 confirms the potential for bioconcentration suggested by the octanol water partition coefficient 5.6×10^4 . EEB therefore has decided that the avian potential for bioconcentration should be investigated.

- 2) Bioconcentration factors ranging from 760 to 1100 have been determined for dithiopyr in bioaccumulation studies with bluegill sunfish and common carp. Although dithiopyr

does bioconcentrate, it has been shown to readily deplete on removal of the fish from exposure. An octanol water partition coefficient of 5.625×10^4 has been determined for dithiopyr. Is tissue residue analysis required for the dithiopyr avian reproduction studies?

Yes, fish may trigger but cannot always be relied upon to accurately reflect the situation in avian species.

3) If tissue residue analysis is required, is it needed for both species (i.e. mallard and bobwhite)?

Yes, these two birds are the indicator species for all birds in the potential areas of use. This may be over 600 species if the chemical is used in the majority of United States. Therefore, to insure differences in avian reproductive physiology has been taken into consideration both species should be tested.

4) What tissue residue analysis? Based on the results of the rat metabolism and pharmacokinetics studies the highest residues of dithiopyr derived- ^{14}C were measured in the following three: fat, blood, and liver. We propose to analyze composite samples of subcutaneous fat, liver, and blood obtained from adult birds at each dose level for residues of dithiopyr; concentrations of parent molecule will be measured. Each composite will be comprised of a tissue sample obtained from each adult bird of a given sex at each treatment level. This approach to residue analysis is similar to that used on poultry and livestock residue studies.

The tissues you suggest would be sufficient if the EEB was interested in determining the maximum possible concentration. However, EEB is interested in the reproductive effects. Therefore, the amount found in the whole egg rather than the blood is needed. Composite samples are not acceptable. The residue in each tissue will provide site specific information which may be related to reproductive effects.

5) If residue analysis is necessary, we propose to add a small group of birds at the high exposure level to investigate dithiopyr depuration. At the end of the egg production phase, 4 pairs of adult birds will be removed from the treated diet and placed on control diet. After 14 days on the control diet, these birds will be killed and composite residue analysis for dithiopyr will be performed on fat, liver, and blood tissues.

As previously indicated EEB is interested in the residue data not only to determine depuration rates but

also the concentration in the different tissues. Therefore, tissue concentrations at the end of the egg laying period, as well as at the end of the 14 day depuration period for birds on the control diet. The egg contents should be collected after 15 or more weeks from sixteen additional females (16 pairs) on the highest test concentration. Eight females should be randomly selected for the 14 day depuration period or control diet portion of the test. After the end of the 14 day period, samples of the liver and fat should be taken. After the end of the egg laying period the those birds left on treated diet should be sampled. It is important to identify all samples by time, hen, and test group.

Residue Study Analysis Protocol

Ecological Effects Branch Comments:

"9. Sample Analysis:"

"1." EEB recommends:

1. Tissue specific samples, not composite samples, be taken.
2. Sampling of the egg contents, rather than the blood, should be done.
3. Treatment level sampling (highest treatment level) should be as indicated.

"2." Analysis of samples at the end of the treated period, as well as, after the 14 day control diet period, are essential.

Avian Reproduction Protocol

Ecological Effects Branch Comments:

1. Description of the test substance did not indicate if the technical grade material will be used.
2. Description of the diet did not report the maximum acceptable percent of solvent in the diet.
3. Description of the test birds does not mention the breeding history, pen reared, phenotypically indistinguishable from wild birds, and that they are healthy.
4. Under housing and environmental conditions ventilation was not reported.

5. The temperature and relative humidity were 15-30°C and ambient, respectively. The guidelines recommend a temperature of 21°C and a relative humidity of 55%.

6. The report states, "During the first seven weeks, the photoperiod for the adults will be 8 hours of light per day." (bobwhite quail). The guidelines indicate eight weeks and 7 hours of light for bobwhite. For mallards 8 hours of light are reported, whereas, the guidelines indicate that 7 hours.

7. Under Incubation and Hatching, cracked or abnormal eggs will be recorded and discarded. It is unclear as to whether eggs damaged by handling would be recorded. Under this same heading it indicates that between Days 20-22 eggs will be candled for embryo survival. The guidelines indicate that Day 18 for bobwhite's. Also the temperature in the hatchery average approximately 37.0-37.5°C. The guidelines recommend 39°C.

8. The guidelines state that, "The [test] concentrations should include an actual or expected field residue exposure level and a multiple level such as five." The propose of this is to establish an effect level and a no-effect level, in addition to the effects expected at field residue level. This allows EEB to evaluated any new uses which may have higher applications rates than the current submission without another avian reproduction at higher concentrations.

Please contact Dennis McLane (557-1993) if any further information is required.

Monsanto

MONSANTO AGRICULTURAL COMPANY

800 N. Lindbergh Boulevard
St. Louis, Missouri 63167
Phone: (314) 694-1000

January 25, 1991

Office of Pesticide Programs - H7505C
Document Processing Desk (APPL)
U.S. Environmental Protection Agency
Room 266A, Crystal Mall 2
1921 Jefferson Davis Highway
Arlington, VA 22202

Attention: Ms. Joanne I. Miller
Product Manager (23), Registration Division

Subject: Request for expedited review of protocols for avian reproduction studies with dithiopyr herbicide (MON 7200/MON 15100).
EPA ID # 524-UGN: Dithiopyr herbicide

Dear Ms. Miller:

Subsequent to review of studies contained in the initial registration submission for dithiopyr herbicide (Monsanto code numbers: MON 7200 and MON 15100) the Ecological Effects Branch (EEB) requested reproduction studies with the mallard duck and bobwhite quail. Prior to initiating these studies we would like to obtain answers to a number of questions concerning conduct of these studies. In a telephone conversation of January 15, 1991, Mr. Douglas J. Urban, Deputy Branch Chief of EEB, indicated that the appropriate mechanism for addressing these questions was to submit draft protocols for expedited review. He further indicated that the protocols should be routed to his attention.

We are requesting expedited review of the attached protocols for reproduction studies with the mallard duck and bobwhite quail. We would also appreciate obtaining answers to the following specific questions pertaining to conduct of the studies:

- 1) §71-4 (d) Diet Preparation - What are the specific triggers for requiring tissue residue analysis on avian reproduction studies?
- 2) Bioconcentration factors ranging from 760 to 1100 have been determined for dithiopyr in bioaccumulation studies with the bluegill sunfish and common carp. Although dithiopyr does bioconcentrate, it has been shown to readily deplete on removal of the fish from exposure. An octanol water partition coefficient of 5.625×10^4 has been determined for dithiopyr. Is tissue residue analysis required for the dithiopyr avian reproduction studies?
- 3) If tissue residue analysis is required, is it needed for both species (*i.e.* mallard and bobwhite)?
- 4) What tissues should be analyzed? Based on the results of rat metabolism and

Ms. J. I. Miller
January 25, 1991
page -2-

pharmacokinetics studies the highest residues of dithiopyr derived-¹⁴C were measured in the following three tissues: fat, blood and liver. We propose to analyze composite samples of subcutaneous fat, liver and blood obtained from adult birds at each dose level for residues of dithiopyr; concentrations of parent molecule will be measured. Each composite will be comprised of a tissue sample obtained from each adult bird of a given sex at each treatment level. This approach to residue analysis is similar to that used on poultry and livestock residue studies.

- 5) If residue analysis is necessary, we propose to add a small group of birds at the high exposure level to investigate dithiopyr depuration. At the end of the egg production phase, 4 pairs of adult birds will be removed from the treated diet and placed on control diet. After 14 days on control diet, these birds will be killed and composite residue analysis for dithiopyr will be performed on fat, liver and blood tissues.

The avian reproduction studies are scheduled to start in early March and will be conducted at Wildlife International in Easton, Maryland. If residue analysis is necessary, tissue samples will be sent to St. Louis and analyzed by Monsanto's Residue Chemistry Department. We would appreciate the Agency's earliest possible response to the above questions. If further information is needed, please contact Dr. Kevin Cannon in Monsanto's Washington Office (202-783-2460) or myself (314-694-3277). Thank you.

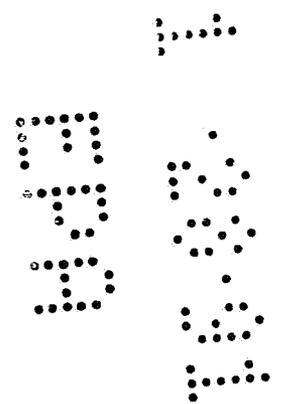
Sincerely,



Roy G. Danhaus
Registration Manager

Att: Mallard and Bobwhite reproduction study protocols
Residue analysis protocols

cc: Mr. Douglas J. Urban, Ecological Effects Branch (H7507C)
K. F. Cannon (Monsanto Washington D.C. Office)



6 7