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WASHINGTON, D.C. 20460

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OFFICE OF  
PREVENTION, PESTICIDES AND  
TOXIC SUBSTANCES

Memorandum of Conference:

**SUBJECT:** Pendimethalin. Discussion of Need for Processing Studies for Oilseeds. Discussion of Adequacy of Ruminant Metabolism Study. Discussion of Other Chemistry Data Requirements. (No MRID#. CBTS#15373. DP Barcode D212340.).

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**THRU:** Ed Zager, Acting Branch Chief  
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**TO:** Walter Waldrop/Jane Mitchell (PM-71)  
Reregistration Branch  
Special Review & Reregistration Division (7508W)

Attendees:

American Cyanamid:

Zareem Ahmed  
Bill Steller  
Phil Miller  
John Wrebel  
Jack Arthur

EPA:

F. Bart Suhre, HED/CBRS  
Paula Deschamp, HED/CBRS  
Walter Waldrop, SRRD  
Jane Mitchell, SRRD  
Bonnie Cropp-Kohlligian, HED/CBRS  
Jerry Stokes, HED/CBTS

In a letter dated February 22, 1995, the registrant, American Cyanamid Company, requested a meeting with CBRS and CBTS to discuss the data requirements for processing studies and the adequacy of



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the previously submitted and CBTS-reviewed ruminant metabolism study (MRID# 417139-01, PP#3F2788).

Representatives of CBRS and CBTS met March 22, 1995, to discuss specific residue data requirements for the herbicide pendimethalin. CBRS and CBTS have previously reviewed this chemical for established and pending tolerances and for reregistration actions.

CBRS and CBTS (F. Suhre, M. Metzger, P. Deschamp, B. Cropp-Kohlligian, E. Zager, R. Perfetti, J. Stokes) concluded the following at this in-house meeting based on the data available from Agency files.

- CBRS/CBTS have adequate processing data for oilseed crops. Pendimethalin will not concentrate in oilseeds. No additional processing data are needed for oilseed crops.
- CBRS/CBTS will require a rice processing study. Data could be translated from the rice study to support the proposed wheat/barley use (PP#3F2788).
- CBRS/CBTS agreed that the ruminant metabolism study (MRID#417139-01) is adequate to support the established uses and tolerances, and to support the proposed use on wheat/barley. No additional data are needed.
- CBRS/CBTS has determined that based on existing tolerances in CFR 40 §180.361 and on the pending wheat/barley tolerances on animal feed items, there is no reasonable expectation of finite residues of concern in animal tissues, milk, and eggs. This should be handled as a 40 CFR § 180.6 (a)(3) situation. No additional animal metabolism, analytical methodology, storage stability, or magnitude of the residue are required for livestock. No tolerances for residues of pendimethalin in animal tissues, milk, and eggs are required.
- CBRS/CBTS have determined that 28-day feeding studies (ruminant or poultry) will not be needed to support the established uses and tolerances, and to support the proposed use on wheat/barley.

CBRS and CBTS and SRRD met with representatives of American Cyanamid Company to discuss processing studies and the ruminant metabolism study on March 23, 1995.

#### Background/Processing Studies:

CBRS has determined that the nature of the residue in plants is adequately understood based on accepted plant metabolism studies

for sweet corn and potato. (See memos of 11/15/94, B. Cropp-Kohlligian, and 06/16/93, P. Deschamp). The residues of concern are the parent pendimethalin and its metabolite 4-[(1-ethylpropyl)amino]-2-methyl-3,5-dinitrobenzyl alcohol as defined in the current tolerance expression (40 CFR §180.361).

CBRS and CBTS had previously accepted the registrant's argument that residues of pendimethalin in corn oil could not exceed the currently established tolerance on corn based on the maximum concentration factor of 25X for corn oil and no detectable residues in the mature corn grain measured at 0.002 ppm. However, CBRS and CBTS jointly required the registrant to provide processing studies for "all other oilseed crops on which pendimethalin is registered". (See memo of 01/29/91, R. Loranger and R. Perfetti). Pendimethalin is registered for use on cottonseed, peanut, soybean, and sunflower. Based on the high solubility of pendimethalin in hexane, concentration of residues would be possible in the processed oil of treated oilseed crops. Maximum theoretical concentration factors for the oils are 6X for cottonseed, 5X for peanut, 12X for soybean, and 5X for sunflower seed.

#### Registrant's Presentation and Discussion:

The registrant presented a short summary of the history of processing data needs and the registrant's efforts to address these needs.

#### CBRS and CBTS Comments/Conclusions:

As in the past, CBRS and CBTS accepts the registrant's argument that residues of pendimethalin in corn oil are not expected to exceed the currently established tolerance on corn. Furthermore, data reviewed in the Pendimethalin Reg. Std. clearly indicated that residues <0.1 ppm (established RAC tolerances are 0.1 ppm) are found in cottonseed oil, peanut oil, soybean oil, and sunflower seed oil. This is supported by additional data from the previously submitted plant metabolism studies for soybean, cotton, and corn, where radioactive residues measured in the early growth of leafy plant parts are diluted as the plant matures. Residues are not translocated to the oilseed.

Additional processing studies for the oilseed crops are not required. Likewise, FAT's for processed commodities of the oilseed crops are not required. This would also include the pending use on safflower. The registrant has offered to conduct a rice processing study at an exaggerated rate (not specified) since the rice growing culture is different from that of oilseed crops. CBRS and CBTS agreed that this rice processing study must be submitted. CBRS and CBTS also agreed that this rice processing study could be translated to support the pending wheat/barley use (PP#3F2788).

Background/Ruminant Metabolism Study:

A goat metabolism study (MRID#417139-01) was reviewed by CBTS (See memo of 03/05/91, F. Griffith). CBTS had asked for additional characterization/identification of unknown pendimethalin metabolites in the liver.

Registrant's Presentation and Discussion:

The registrant has expressed disagreement with CBTS's conclusion as to the adequacy of the ruminant study. The low levels of the residue (<0.005 ppm) lend themselves to possible chemical characterization based on the HPLC behavior of synthetic standards, but these levels do not allow identification by confirmatory structure analysis using spectrophotometric methods.

CBTS Comments/Conclusions:

CBTS has again reviewed this ruminant study. CBTS agrees that the very low levels of residues in the liver hinder the use of confirmatory spectrophotometric methods. Two goats treated at a 6.5 ppm dose level yielded total radioactive residues in milk at <0.01 ppm, in muscle, fat, and kidney at <0.05 ppm, and in liver at 0.077 and 0.096 ppm. The Pendimethalin Reg. Std. had suggested that a new ruminant metabolism study be performed using a 10.0 ppm dose rate in order to provide adequate residues for chemical structure identification. However, based on the very low levels observed at the 6.5 ppm dose, extrapolating to a 10.0 ppm dosage would only increase the highest single residue, as shown by HPLC separation and radiochemical detection, from 0.005 ppm to 0.008 ppm. According to the Chemistry Branches' guidelines, only characterization by comparison to synthetic chemical standards is expected at these levels. HPLC charts submitted in this study (MRID#417139-01, pp. 141, 142, and 143) of the methanol/water, hexane-methylene chloride (partition composite), and acidic methanol/water extracts of the ruminant liver indicated the presence of the parent pendimethalin and its 3,5 d-NO<sub>2</sub> metabolite. These residues appear to be present based on HPLC retention times of the parent pendimethalin and this metabolite.

The 6.5 ppm dose level, according to the registrant, represents a 90X feeding level. CBTS, however, has included the proposed 0.1 ppm tolerance on wheat and barley to achieve a worst case diet. This diet contains wheat/barley milled byproducts and forage. CBTS has also assumed a maximum concentration factor for pendimethalin residues in milled byproducts at 9X. Thus beef and dairy cattle could be exposed to a dietary burden of 0.7 ppm.

$$\frac{50\% \text{ milled bypdts}}{88\% \text{ DM}} \times 0.9 = 0.5 \text{ ppm}$$

$$\frac{50\% \text{ forage}}{25\% \text{ DM}} \times 0.9 = 0.2 \text{ ppm}$$

Total; 0.7 ppm

Thus using this approach, the 6.5 ppm dosage level now represents a 9X feeding level ( $6.5 \div 0.7 \approx 9$ ).

[Please Note: These values are intended to be highly exaggerated in order to provide a worst case estimate in the absence of processing data for wheat/barley. These estimates should never be used in subsequent memoranda as they are based on gross assumptions concerning the likelihood of concentration in processed wheat/barley products. Based on currently established tolerances, CBRS/CBTS would estimate a more reasonable worst case dietary burden for livestock at 0.1 ppm.]

Therefore, at a 1X feeding level any secondary pendimethalin residues in meat, meat byproducts, fat, or milk would be below 0.5 ppb for parent and any metabolite. This is well below the LOQ (0.1 ppm combined) of the acceptable analytical methodology for pendimethalin and/or its 3,5 di-NO<sub>2</sub> metabolite.

CBTS finds the ruminant metabolism study adequate to support not only the established tolerances (40 CFR §180.361), but also the pending use on wheat and barley (PP#3F2788). CBTS finds this to be a 40 CFR § 180.6(a)(3) situation. Therefore, based on the above data, a 28-day feeding study will not be needed to support the existing tolerances nor the pending tolerances on wheat/barley. However, any additional uses on other animal feeds could trigger the need for a 28-day study and additional data for the ruminant metabolism.

#### General Questions from Registrant:

The registrant stated that he is considering a registration of pendimethalin for use on alfalfa. Field trials indicate residues of 1.5 ppm on harvested mature alfalfa. The registrant also stated that 1 trial in the Great Lakes area (Region V) showed residues between 4.5 - 6.5 ppm. However, the registrant expressed concern about the reliability of these data. The trial in question was damaged by 3 hail storms and drought conditions during the growing season. The registrant asked if a regional registration would be possible?

CBTS Comments/Conclusions:

CBTS stated that a regional use would not be considered for alfalfa. CBTS suggested that if the registrant expected to find lower residues in alfalfa under normal growing conditions, then it would be necessary to also provide the Agency with a least two additional trials from Region V. The registrant was also told to submit the abnormal trial with their comments on the reliability of the data. CBTS also stated that a 28-day ruminant feeding study would be necessary to support the alfalfa use. If the real weathered field residues are 1.5 ppm, CBTS did state that the alfalfa use would require characterization of the highest residue in goat liver (HPLC peak measured at 0.005 ppm). This could be achieved by HPLC retention time comparison of synthetic chemical standards of possible pendimethalin metabolites. CBTS believes that adequate characterization of this unknown by this method should be sufficient, and that the ruminant metabolism study conducted at 6.5 ppm should then be adequate to also support an alfalfa use. This metabolism without this characterization will not adequately support an alfalfa use. The registrant should submit this information prior to analysis of any ruminant tissue samples from the feeding study. CBTS will determine what pendimethalin residues should be analyzed.

cc: J. Stokes (CBTS); Bonnie Cropp-Kohlligian (CBRS); PP#3F2788;  
Pendimethalin Reg. Std. F.; R.F.; Circu.  
RDI: RPerfetti:04/06/95:RLoranger:04/05/95:EZager04/05/95  
7509C:CBTS:JStokes:js:Rm 803:CM#2:305-7561:04/06/95