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

AUG 31 1988

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Partial Response (April 7, 1988) by Centre International d'Etudes du Lindane (CIEL) to Data Gap Section 171-4 [Magnitude of Residue in Animals (Sheep)] as Identified in the Residue Chemistry Chapter of the September 30, 1985 Lindane Registration Standard - (DEB No. 4036) MRID Nos. 406605-00 and 406605-03

FROM: Martin F. Kovacs, Jr., Ph.D., Chemist
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TO: Reto Engler, Chief
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and

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and

Edwin Budd, Section Head
Toxicology Branch - Insecticide-Rodenticide Support
Health Effects Division (TS-769C)

THRU: Charles L. Trichilo, Ph.D., Chief
Dietary Exposure Branch
Health Effects Division (TS-769C)

The law firm of McKenna, Conner & Cuneo has submitted a partial response to Residue Chemistry (Section 158.125) data gaps cited in the Lindane Registration Standard (September 30, 1985) on behalf of its client, CIEL, the Centre International d'Etudes du Lindane [Rhone-Poulenc,

Inc.; Celamerck GmbH & Company, KG and its U.S. affiliate, E.M. Industries, Inc.; and Inquinosa (Qimocos de Noroeste SA Industries)]. The submission consists of a letter of transmittal dated June 9, 1988 from Charles A. O'Connor III of McKenna, Conner & Cuneo to Mr. George LaRocca, PM 15, EPA/RD listing Magnitude of the Residue Studies and a Freezer Storage Stability Study including a complete study entitled "Tissue Residue Study in Sheep Using Lindane" conducted by Southwest Bio-Labs, Inc., Las Cruces, NM 88005, Project No. 87050, dated April 7, 1988. In the transmittal letter, the registrant has expressed his concern regarding the results obtained from some of the Magnitude of the Residue Studies as follows:

> Two of the above studies, specifically the residue studies in sheep and in dairy cows, indicate residues that exceed current tolerances. Accordingly, these studies possibly fall within the scope of FIFRA section 6(a)(2), as described in EPA's 1985 Federal Register Notice. 50 Fed. Reg. 38,115 (1985). We would like to discuss these findings with EPA in order to determine whether additional studies are in order, or whether revisions to the existing tolerances must be made.

Summary of Remaining Data Gaps Related to 171-4 - Magnitude of the Residue - Meat (Sheep)

Data gap 171-4 (Magnitude of the Residue - Meat) is not yet fulfilled for sheep.

- The spray and dip treatments impose no limit to the number of applications which can be made to livestock (sheep). A revised label is required which specifies the number of applications permitted and the interval between applications to sheep. The treatment rate should be supported by adequate residue data. This is a data gap.

- The nature of the residue in animals is not adequately understood. If animal metabolism studies reveal the presence of other residues of toxicological concern besides lindane per se, residue data will also be required for these residues.

- Available residue data from the submitted sheep feeding/dipping study do not support the tolerance of 7 ppm for residues of lindane per se, in the fat of sheep. The data also indicated the need for lindane

tolerances in the meat and meat byproducts (kidney, liver) of sheep. Appropriate animal commodity tolerances in sheep will also need to be established when the nature of the residue (ruminants) has been adequately delineated by the registrant.

Recommendations

DEB recommends that the registrant secure and retain his reserve animal commodity samples obtained from the sheep feeding study in the event that possible future reanalysis by appropriate analytical methodology to determine additional residues (metabolites) of toxicological concern is warranted based upon his satisfaction of DEB's and TB's responses to all remaining deficiencies cited in DEB's C. Deyrups March 24, 1988 memorandum re: Lindane Data Gap Section 171-4 (Nature of the Residue in Livestock Ruminants). (Note: If the reserved samples are stored too long, they may not be supported by the present storage stability data.) When all remaining 171-4 data gaps relative to magnitude of the residue in sheep and ruminant metabolism have been satisfied, the registrant should then repropose animal commodity tolerances for sheep to reflect both the nature and magnitude of the total toxic residues resulting from all proposed uses of lindane. DEB also recommends that the registrant respond to all of DEB's Comments/Conclusions outlined below.

The data gaps associated with magnitude of the residue - sheep meat - after reviewing the present submission are discussed in detail under DEB's Comments/Conclusions below.

DEB's Comments/Conclusions re: Magnitude of the Residue - Sheep

1. In conjunction with the submitted sheep feeding/ dipping study, DEB reiterates the following data gap cited in the Lindane Registration Standard (September 30, 1985):

> The spray and dip treatments impose no limit to the number of applications which can be made to livestock. A revised label is required which specifies the number of applications permitted and the interval between applications. The treatment rate should be supported by adequate residue data. This is a data gap.

The submitted sheep feeding/dipping study employed two dipping treatments at a 1-week interval with a preslaughter interval of less than 1 day. If this treatment schedule supports the registrant's proposed use then the revised labels requested by DEB on the Lindane Registration Standard should also reflect this treatment schedule.

2. A freezer storage stability study for lindane residues in poultry and cattle (covering 2 through 9 or 12 months) has been submitted in a separate submission (see DEB's review of August 23, 1988). In the subject feeding and dipping study, samples were stored up to 31 weeks at -20 `C from time of animal slaughter to time of analysis. Therefore, DEB concludes that the preceding storage stability study supports the residue data obtained for the parent compound lindane.

3. DEB concurs with the registrant that a linear concentration dependence on lindane feeding level was evident for fat tissue. Although not noted by the registrant, this same linear relationship was observed by DEB for lindane residues in muscle tissue but not for kidney and liver tissues.

4. DEB has calculated that average lindane residue levels in fat, muscle, kidney, and liver samples increased approximately 5X, 6X, 5X, and 10X, respectively, in animals exposed both (1X) orally and dermally as compared to animals exposed (1X) orally only.

5. DEB concludes that the current 7 ppm tolerance for residues of lindane per se in fat of sheep is inadequate to support lindane residues (ca. 20 ppm) resulting from a 17.5 ppm (1X) feeding level or oral exposure only. Based on the results of these same 1X feeding levels, tolerances for lindane per se would also need to be proposed by the registrant for meat (muscle, ca. 1 ppm) and meat byproducts (kidney, ca. 1 ppm and liver, ca. 0.02 ppm). Provided the current lindane label is retained and revised to permit two sheep dipping treatments at a 1-week interval followed by no preslaughter interval, then the tolerances proposed by the registrant for lindane per se reflecting oral exposure only in fat, meat, and meat byproducts (kidney and liver) will need to be increased approximately 5X, 6X, 5X, and 10X, respectively.

6. DEB, however, cannot at the present time arrive at any final conclusion regarding the adequacy of the submitted sheep feeding/dipping study to establish appropriate animal commodity tolerances until all remaining deficiencies [See DEB's C. Deyrup March 24, 1988 memorandum re: Lindane Data Gap section 171-4 (Nature of the Residue in Livestock Ruminants)] have been adequately addressed by the registrant including the identity of unidentified ^{14}C residues in goat liver and kidney which are of concern to TB (see TB's J. Doherty May 19, 1988 memorandum re: Lindane: TB's response to DEB inquiry concerning more adequate identification of lindane residues in goat liver and kidney). If these ^{14}C residues (metabolites), once identified, are then determined by TB to be of toxicological concern then they would also need to be included in future tolerance expressions for animal commodities. Accordingly, the registrant should now secure and retain his reserve animal commodity samples obtained from the sheep feeding/dipping study for possible future reanalysis by appropriate analytical methodology to determine these additional residues (metabolites) of toxicological concern.

   An updated section of table A containing the pertinent data requirements addressed in this submission is attached to this review.

Detailed Considerations

Pertinent data gaps cited in the Registration Standard will be restated below followed by CIEL's response.

158.125 - Residue Chemistry

171-4 - Magnitude of the Residue - Meat (includes meat, fat, and meat byproducts)

The following additional data are required:

- Available residue data do not support the tolerance of 7 ppm for residues of lindane in the fat from cattle, goats, horses, and sheep and 4 ppm in the fat from hogs because much of the data were generated by questionable or unspecified methods and most of the studies did not specify the conditions under which the samples were stored or give the duration of the storage period before analysis. Residue data using adequate methodology must be submitted for residues of lindane in animal fat resulting from the various

methods of application and at appropriate dosages. Unless the requested animal metabolism studies establish the absence of radioactive residues in other tissues, residue data on meat and meat byproducts are needed in order to establish tolerances on these commodities for residues of parent lindane. If animal metabolism studies reveal the presence of other residues of toxicological concern besides parent lindane, residue data will also be required for these residues.

- o The results of previous studies indicating the presence of lindane residues in cattle fat following spray application of 0.075 percent lindane but not after application of 0.03 percent lindane need to be verified. The spray and dip treatments impose no limit to the number of applications which can be made to livestock. A revised label is required which specifies the number of applications permitted and the interval between applications. The treatment rate should be supported by adequate residue data. Preslaughter intervals of 30 days are imposed following spray treatment and 60 days following dip treatment. Preslaughter intervals greater than 3 days are not practical since animals may be sent to slaughter over an extended period of time, and, if sold, the pesticidal history of the animals may not be known to the new owner. Residue data reflecting preslaughter intervals of 3 days or less are required for spray and dip applications.

- o Available data indicate that unshorn lambs have much higher residues in the fat after dipping than shorn sheep. More residue data on unshorn lambs and sheep reflecting the maximum treatment rate are required to support the tolerance.

CIEL's Response

The registrant has submitted a sheep feeding/dipping study in which lindane residues only were determined in tissues following both oral and dermal dosing of the animals with lindane.

Partial Summary of Study

". . . Eighteen predominantly Hampshire cross-bred sheep (nine male; nine female) approximately 18 weeks of age (38-49 kg) were treated for 28 days with Lindane administered by oral capsule given daily. Animals were randomly divided into three treatment groups of six animals each, but with equal numbers of each sex. Animals were treated at nominal

levels of 17.5 ppm (1X), 52.5 ppm (3X), and 175 ppm (10X). These levels were designed to provide the maximum calculated pesticide exposure by animals via the diet. Two male and two female animals at each exposure level were dip treated on treatment days 21 and 28 with a 0.06% Lindane solution supplied from water dilution of a 20% emulsifiable concentrate of Prentox Lindane. Two additional animals (one male; one female) served as controls and were housed in the same room and conditions as the treated animals. Animals were sacrificed at approximately 10-12 hours post last dose. Fat, kidney, liver and muscle tissue samples were collected and analyzed for Lindane residues by validated AOAC Multiresidue GLC methodology with electron capture detection . . . ."

Sample Collection and Preparation

". . . Tissue samples taken from each animal consisted of: (1) liver (whole, less gallbladder), (2) muscle, various muscle groups, (3) kidneys, both, and (4) a composite fat sample taken from subcutaneous, perirenal, and omental fat. Tissue samples were collected, wrapped in aluminum foil, and placed into labeled plastic storage bags (Zip-Loc\); then placed inside an additional plastic bag. All samples were frozen and maintained at -20°C until further processing for residue analysis.

"All tissues except kidney were ground through a coarse aperture plate in a food grinder/chopper. Samples were thoroughly mixed and then reground through a finer aperture plate. Samples were again mixed and subsampled for analysis. Kidney samples were processed for analysis by blending at low speed with an approximately equal weight of distilled water (weights recorded to 0.01 gram) in a one quart blender jar."

Sample Analysis/Validation

According to the registrant, each tissue sample was analyzed in triplicate by Southwest Bio-Labs Operating Procedure No. 81.00 to 87.

The registrant indicated further that the method of analysis is essentially the Multiresidue Method of the AOAC with slight modifications in the concentration/final volume steps to simplify analysis of the higher than normal residue levels found in this study. The results of analysis for lindane residues in the four analyzed tissues were summarized by the registrant. The reported residue results were not corrected for control tissue background or method recovery.

Two tissue types were used for method validation; muscle, representing a nonfatty food tissue and fat, a fatty food type.

One problem of note surfaced during the validation of fat tissue. Both control animals contained lindane residues in fat tissues. Consequently, sheep fat was purchased at a local grocery for all fortification and control samples for analyzing fat tissue samples. The contamination probably occurred from being housed in the same room with the treated animals. The dipped animals were placed back into the study room shortly after being dipped. As a result, the control animals were exposed to sufficient levels of lindane in the air to provide residues in fat. Other control tissues did not contain significant lindane residues.

DEB's Comments/Conclusions re: Conduct of Study

The overall conduct of the registrants submitted sheep feeding/dipping study generally conforms to the suggestions made by DEB in a meeting with the registrant following the issuance of the September 30, 1985 Lindane Registration Standard (see February 10, 1986 memorandum of R. Perfetti). In that memorandum DEB suggested the following relative to the animal feeding studies:

6. In the case of feeding studies, three animals at three dose levels should be used.

7. The animals in the feeding studies above should receive both oral and dermal medications with lindane. The dermal treatments should reflect maximum concentrations and the maximum number of dips expected in actual use.

8. The feeding/dermal studies should be carried out on lactating cows, unshorn sheep, and hogs.

9. Dipping of the animals will suffice for requirements for experiments with other forms of treatment.

10. As far as the oral doses are concerned, the levels for the lowest dose could be calculated from theoretical dry-down factors for grape and apple pomace.

11. In the dip/oral dosing experiments it will be acceptable to perform the last dip of the animals then continue to feed them labeled lindane for 3 days and finally sacrifice them within 24 hours of the last oral dose (within 3 days of the last dip).

The aforementioned suggestions were emphasized in part by DEB in its C. Deyrup March 24, 1986 protocol review re: a lindane dermal application metabolism study as follows:

> DEB agrees that the dip application would represent the worst case for dermal application and recommends that the dip application would be adequate for the purpose of assessing the levels of residues arising in animal commodities from dermal treatment.
>
> However, unshorn lambs should be subjected to dipping, in addition to the cattle and hogs. The available residue data, though scanty, indicate that the highest residues were found in unshorn lambs, which exhibited lindane levels of 21-51 ppm in the fat 3 weeks after treatment. In a meeting with DEB, representatives of Rhone-Poulenc have agreed to dip unshorn lambs (memo of R. Perfetti, 2/10/86).
>
> The registrant was not specifically asked to conduct a feeding study using lambs in the Lindane Registration Standard because residue data from cattle would be translatable to lambs.

In regard to Item 10 of the February 10, 1986 R. Perfetti memorandum, the registrant's calculated level for the lowest dietary dose was based on theoretical dry-down factors for apples, grapes, and tomatoes since those commodities appear to contribute the most to the dietary burden of lindane. These values were calculated for the sheep diet as follows:

RAC	Tolerance (ppm)	Dry-Down Factor (Pomace)	ppm in Pomace	% in Diet (Sheep)	Lindane in Diet (ppm) (Sheep)
Apple	1.0	8	8	50	4.0
Grape	1.0	4.3	4.3	30	1.29
Tomato	3.0	20	1.0	20	12.0
					17.29

1X feeding level = 17.5 (ppm).

Since it is unlikely that sheep would receive a ration consisting of all pomace, DEB concludes that the calculated

dietary exposure would represent a theoretical worst-case situation.

In regard to Item 11 of the R. Perfetti February 10, 1986 memorandum, animals were not fed for 3 days beyond the last dipping treatment and then sacrificed within 24 hours of the last dose. In the submitted experiment, all animals were sacrificed within 10 to 12 hours of the last dose and/or dipping treatment. DEB has no objection to the protocol utilized in the submitted study, although it deviates somewhat from the original protocol suggested by DEB.

In conjunction with the submitted sheep feeding/dipping study, DEB reiterates the following data gap cited in the Lindane Registration Standard (September 30, 1985):

2. The spray and dip treatments impose no limit to the number of applications which can be made to livestock. A revised label is required which specifies the number of applications permitted and the interval between applications. The treatment rate should be supported by adequate residue data. This is a data gap.

The submitted sheep feeding/dipping study employed two dipping treatments at a 1-week interval with a preslaughter interval of less than 1 day. If this treatment schedule supports the registrant's proposed use then the revised labels requested by DEB in the Lindane Registration Standard should also reflect this treatment schedule.

Results of Tissue Residue Study in Sheep Using Lindane

Lindane residue values discussed below were not corrected for control tissue background or average recovery values of concurrently fortified controls which were respectively reported for muscle, kidney, liver, and fat as; (0.011 ppm/90.7%), (0.006 ppm/92.0%); (0.000 ppm/97.2%), and (0.017 ppm/113.0%).

Representative gas chromatograms were submitted for only one treated animal fat and one treated animal kidney sample.

Lindane residues were reported in sheep tissues as a result of all treatments and treatment levels as follows:

1. Feeding (Oral Exposure)

   Muscle - Total maximum (average) residues at the 17.5 (1X), 52.5 (3X), and 175.0 ppm (10X) feeding levels were 1.04 (0.73); 2.10 (1.58), and 9.65 (7.69) ppm, respectively.

Kidney - Total maximum (average) residues at the 1X, 3X, and 10X feeding levels were 0.98 (0.74), 2.32 (1.75), and 5.80 (4.81) ppm, respectively.

Liver - Total maximum (average) residues at the 1X, 3X, and 10X feeding levels were 0.02 (0.02), 0.04 (0.02), and 0.15 (0.13) ppm, respectively.

Fat - Total maximum (average) residues at the 1X, 3X, and 10X feeding levels were 21.68 (19.37); 45.73 (42.60), and 228.65 (197.87) ppm, respectively.

2. Feeding and Dipping (Oral and Dermal Exposure)

Muscle - Total maximum (average) residues following two dipping treatments at a 1-week interval with simultaneous feeding at the 17.5 (1X), 52.5 (3X), and 175.0 ppm (10X) levels were 6.00 (4.40), 5.22 (4.41), and 18.63 (15.31) ppm, respectively.

Kidney - Total maximum (average) residues following dipping treatments and feeding at the 1X, 3X, and 10X levels were 4.74 (3.83), 4.66 (3.87), and 15.22 (11.51) ppm, respectively.

Liver - Total maximum (average) residues following dipping treatments and feeding at the 1X, 3X, and 10X levels were 0.56 (0.22), 0.16 (0.06), and 0.33 (0.14) ppm, respectively.

Fat - Total maximum (average) residues following dipping treatments and feeding at the 1X, 3X, and 10X levels were 123.69 (105.04); 134.13 (124.27), and 408.19 (316.70) ppm respectively.

The above residue data can be tabulated as follows:

		Total (Average) Lindane Residues (ppm) Resulting From	
Matrix	Feeding Level	Feeding	Feeding + Dipping
Fat	1X	19.37	105.04
	3X	42.60	124.27
	10X	197.87	316.70
Muscle	1X	0.73	4.40
	3X	1.58	4.41
	10X	7.69	15.31

Matrix	Feeding Level	Total (Average) Lindane Residues (ppm) Resulting From Feeding	Feeding + Dipping
Kidney	1X	0.74	3.83
	3X	1.75	3.87
	10X	4.81	11.51
Liver	1X	0.02	0.22
	3X	0.02	0.06
	10X	0.13	0.14

The registrant summarizes the reported lindane residue data in sheep tissue as follows:

> Zero-day withdrawal residue levels ranged from very low (< 0.025 ppm) in liver to more than 300 ppm in fat. Residue levels were consistently higher in all tissues from animals dip treated in addition to the exposure provided orally. The increased residues ranged from approximately 10X (in the 1X treatment group) down to about 2X in the 10X dip treated group. The 3X treatment group had residues of approximately 3-5X the level found in nondipped animals. There was an approximate 1:1 ppm ratio of lindane in the diet to fat residues in the nondipped animals.

In connection with the sheep feeding and dipping study, DEB notes that all fat, kidney, liver, and muscle samples were stored at -20 `C for (29.6 to 31.1), (25.3 to 27.7), (25.6 to 30.3), and (22.1 to 22.7 weeks), respectively from time of sheep slaughter to time of analysis. The registrant provides validation data indicating recoveries of (78.7 to 94.7) X = 86 percent and (52 to 68) X = 63 percent lindane from stored (-20 `C) samples of fat and liver fortified respectively with lindane at 2.5 and 0.025 ppm.

DEB's Comments/Conclusions re: Results of Study

DEB concurs with the registrant that a linear concentration dependence on lindane feeding level was evident for fat tissue. Although not noted by the registrant, this same linear relationship was observed by DEB for lindane residues in muscle tissue but not for kidney and liver tissues.

DEB also calculates that average lindane residue levels in fat, muscle, kidney, and liver samples increased approximately 5X, 6X, 5X, and 10X, respectively in animals exposed both (1X) orally and dermally as compared to animals exposed (1X) orally only.

DEB concludes that the registrant has provided storage stability data (see DEB's review of August 23, 1988) that support the residue data obtained for the parent compound lindane.

DEB concludes that the current 7 ppm tolerance for residues of lindane per se in fat of sheep is inadequate to support lindane residues (ca. 20 ppm) resulting from a 17.5 ppm (1X) feeding level or oral exposure only. Based on the results of these same 1X feeding levels, tolerances for lindane per se would also need to be proposed by the registrant for meat (muscle, ca. 1 ppm) and meat byproducts (kidney, ca. 1 ppm and liver, ca. 0.02 ppm). Provided the current lindane label is retained and revised to permit two sheep dipping treatments at a 1-week interval followed by no preslaughter interval, then the tolerances proposed by the registrant for lindane per se reflecting oral exposure only in fat, meat, and meat byproducts (kidney and liver) will need to be increased approximately 5X, 6X, 5X, and 10X, respectively.

DEB, however, cannot at the present time, arrive at any final conclusion regarding the adequacy of the submitted sheep feeding/dipping study to establish appropriate animal commodity tolerances until all remaining deficiencies [see DEB's C. Deyrup March 24, 1988 memorandum re: Lindane Data Gap Section 171-4 (Nature of the Residue in Livestock Ruminants)] have been adequately addressed by the registrant including the identity of unidentified ^{14}C residues in goat liver and kidney which are of concern to TB (see TB's J. Doherty May 19, 1988 memorandum re: Lindane: TB's response to DEB inquiry concerning more adequate identification of lindane residues in goat liver and kidney). If these ^{14}C residues (metabolites) once identified are then determined by TB to be of toxicological concern, then they would also need to be included in future tolerance expressions for animal commodities. Accordingly, the registrant should now secure and retain his reserve animal commodity samples obtained from the sheep feeding/dipping study for possible future reanalysis by appropriate analytical methodology to determine these additional residues (metabolites) of toxicological concern (Note: If the reserved samples are stored too long, they may not be supported by the present storage stability data).

Attachment
cc: Reviewer (M. Kovacs), TOX, Registration Standard (Lindane), RF, SF (Lindane), Circulation (7), E.Eldredge (ISB/PMSD), A. Rispin-EFCD

TS-769C:DEB:M.Kovacs:CM#2:Rm.810:557-7324:Typist Kenco, 8/25/88:Edited by:MT, 8/30/88
RDI:J.H.Onley, 8/23/88:R.D.Schmitt, 8/24/88.

ATTACHMENT

GENERIC DATA REQUIREMENTS FOR LINDANE

TABLE A

[EDEB # 4036; MRID #'s 406605-00 & -03]

Data Requirement	Composition 1/	Does EPA Have Data To Satisfy This Requirement?	Bibliographic Citation	Must Additional Data Be Submitted Under FIFRA § 3(c)(2)(B) ?	Time Frame For Data Submission 2/
158.125 Residue Chemistry (Continued)					
171-4 - Magnitude of the Residue - Residue Studies 8/,9/,10/ (Continued)					
- Meat (includes meat, fat, and meat by-products)	TGAI and Plant Metabolites	Partially	00045126 00088165 00089592 00101478 00118724 00118725 MRID # 406605-03	Yes108/	18 Months
- Milk	TGAI and Plant Metabolites	Partially	00104441 00025685 00075989 00088048 00118722 00118723 00118725 00118739 00098785 GS0315009 GS0315010	Yes109/	18 Months
- Poultry and Eggs	TGAI and Plant Metabolites	No	-	Yes110/	18 Months

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§ 158.125 Residue Chemistry (continued)

106/ [Continued from previous page] A food additive tolerance will not be necessary for refined suntlower oil from second generation sunflower seed, if it is established that sunflower oil is always deodorized and/or hydrogenated during the refining process. It has been shown that residues of lindane do not survive the hydrogenation of deodorization step in the refinement of oil. If the required plant metabolism studies indicate the presence of other residues besides parent, and if significant levels of these metabolites are found in second generation sunflower seed, then a processing study will be required to determine if these residue concentrate in processed commodities.

107/ The use of lindane on tobacco does not require a tolerance or an exemption from tolerance, but data are needed to assess the exposure to residues resulting from the use of lindane. There are no lindane residue data on tobacco which reflect the present uses. Residue data from field trials in Kentucky/Virginia/Tennessee, and Georgia/North Carolina/South Carolina are required. Residue data reflecting application of the EC formulations should be included, as residues would be expected to be higher from that type of formulation. Since tobacco plants can be subjected to both foliar and transplant water treatment, residue data reflecting both foliar and transplant treatment at the maximum application rates are needed. If use is limited to foliar or transplant treatment (rather than both), revised labeling with this restriction must be submitted. A residue profile on tobacco smoke is also required. It residues of 0.1 ppm or more are found on green freshly harvested tobacco, pyrolysis products from the active ingredient must be characterized. The total number of foliar applications and the interval between application should be specified in a revised label.

108/ ALL METHODS OF APPLICATION TO LIVESTOCK

Available residue data do not support the tolerance of 7 ppm for residues of lindane in the fat from cattle, goats, horses, and sheep and 4 ppm in the fat from hogs because much of the data were generated by questionable or unspecified methods and most of the studies did not specify the conditions under which the samples were stored or give the duration of the storage period before analysis. Residue data using adequate methodology must be submitted for residues of lindane in animal fat resulting from the various methods of application and at appropriate dosages. Unless the requested animal metabolism studies establish the absence of radioactive residues in other tissues, residue data on meat and meat by-products are needed in order to establish tolerances on these commodities for residues of parent lindane. If animal metabolism studies reveal the presence of other residues of toxicological concern besides parent lindane, residue data will also be required for these residues.

SPRAYS AND DIPS

The results of previous studies indicating the presence of lindane residues in cattle fat following spray application of 0.075% lindane but not after application of 0.03% lindane need to be verified. The spray and dip treatments impose no limit to the number of applications which can be made to livestock. A revised label is required which specifies the number of applications permitted and the interval between applications. The treatment rate should be supported by adequate residue data. Pre-slaughter intervals of 30 days are imposed following spray treatment and 60 days following dip treatment. [Continued on next page]

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