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OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

6/12/00

MEMORANDUM

SUBJECT: Phosalone: Revised Human Health Risk Assessment. Chemical I.D.
No. 097701. Case No. 0027. DP Barcode D266577.

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Attached is the revised Human Health Risk Assessment for **Phosalone** developed by the Health Effects Division (HED). This revision serves to update and replace the preliminary Human Health Risk Assessment dated 11/1/99 by responding to public comments and recent data submissions. As phosalone is not an active ingredient in any product registered in the U.S., no occupational, residential, or drinking water exposure will occur. The only source of human exposure is via phosalone residues in imported food. This risk assessment incorporates the salient portions of the following Reregistration Eligibility Decision chapters as well as several memoranda and HED committee reports: the Toxicology Chapter prepared by K. Farwell (9/15/99; D256366), the Residue Chemistry Chapter prepared by K. EL-Attar (11/1/99; D256367), the anticipated residue memorandum by K. EL-Attar (11/1/99; D260579), the dietary risk assessment memorandum by K. EL-Attar (11/1/99; D260580), the Hazard Identification Assessment Review Committee report by K. Farwell dated 8/12/99, the FQPA Safety Factor Committee report by B. Tarplee dated 9/13/99, and the review of product chemistry and apple and cherry field trials conducted in Canada (W. Hazel, 6/5/00, D261763 and D262645).

Aventis CropScience [formerly Rhone-Poulenc Ag Company (RPAC)] is supporting tolerances for phosalone residues in almonds, grapes, pome fruits, and stone fruits to

permit the importation of these commodities. Note that phosalone is reportedly marketed largely in Europe. HED has evaluated the field trial data in terms of the European Union (EU) Good Agricultural Practices (GAPs) including application rate, preharvest intervals, and number of applications as well as registered Canadian uses. Additional field trials conducted in Canada and France (grapes only) are recommended before tolerances can be reassessed.

The acute and chronic dietary risk assessments are considered to be highly refined. Refinements include the use of FDA monitoring data as the principal source of anticipated residues, correction for percent commodity imported from countries having phosalone registrations, and a probabilistic acute assessment. Both acute and chronic dietary risks are well below the Agency's level of concern.

cc: W. Hazel (HED), K. Farwell (HED), K. EL-Attar (HED), List A Reg. Std. File, RF
RRB1:CM2:722J:WHazel:305-7677:wjh:6/7/00
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INTRODUCTION

Phosalone [O,O-diethyl S-[(6-chloro-2-oxobenzoxazolin-3-yl)methyl]phosphorodithioate] is an organophosphate insecticide and acaricide for which U.S. registrations were voluntarily withdrawn in 1989 by the registrant, Rhône-Poulenc Ag Company (RPAC). The Agency proposed revoking tolerances for pesticides with no active registrations, including tolerances for residues of phosalone in/on plant and animal commodities (63 *FR* 3057, 1/21/98). However, in response to this proposal, RPAC requested that the Agency not revoke tolerances for phosalone residues in/on almonds, grapes, pome fruits (apples and pears), and stone fruits (apricots, cherries, peaches, and plums) so that these commodities bearing phosalone residues could continue to be imported legally into the U.S. In the Final Rule published in the Federal Register of 10/26/98 (corrected 1/25/99), the Agency determined to maintain existing tolerances for residues of phosalone in/on the specified commodities while revoking the remaining phosalone tolerances under 40 CFR §180.263 and §186.4800. Aventis CropScience, formerly known as RPAC, continues to support phosalone tolerances in/on these crops.

Phosalone is a List A reregistration chemical that was the subject of a Registration Standard and Final Registration Standard and Tolerance Reassessment (FRSTR) dated 9/81 and 3/17/87, respectively. These documents summarized regulatory conclusions on the available residue chemistry data and specified that additional data were required for reregistration purposes. Several submissions of data have been received since the FRSTR was issued.

This revised human health risk assessment for phosalone represents the first step in the Reregistration Eligibility Decision (RED) process. As all phosalone-containing products registered in the United States have been canceled, human exposure to this pesticide is strictly through the consumption of imported foods. Accordingly, this risk assessment involves consideration of only the hazard component of the risk and food sources of dietary exposure. Probabilistic assessment of acute dietary risk has been conducted using the DEEM™ Software based on anticipated residue data and percent crop imported data. Chronic dietary risk was estimated using DEEM™, anticipated residue data, and phosalone usage data. Both dietary assessments are considered to be highly refined. Residential and occupational exposures as well as dietary exposure through drinking water are not expected because there is no domestic use of phosalone. Therefore, aggregate acute and chronic risks are attributable only to food sources of dietary exposure.

EXECUTIVE SUMMARY

The Health Effects Division (HED) of EPA's Office of Pesticide Programs has evaluated the phosalone toxicology and residue chemistry databases. Although the databases

have some deficiencies, they are sufficient upon which to base a human health risk assessment for phosalone reflecting tolerances with no U.S. registrations, commonly known as "import tolerances."

Phosalone [O,O-diethyl S-[(6-chloro-2-oxobenzoxazolin-3-yl)methyl]phosphorodithioate] is an organophosphate insecticide and acaricide that was previously registered in the U.S. However, Aventis continues to support the use of phosalone outside of the U.S. as a broadcast foliar application to selected fruits and nuts that can be imported into the U.S.

Tolerances are currently established for residues of phosalone *per se* in/on almonds and almond hulls (0.1 and 50.0 ppm, respectively); apples, grapes and pears (10.0 ppm); and apricots, cherries, peaches, and plums (15.0 ppm) under 40 CFR §180.263. No tolerances are established for phosalone residues in processed plant commodities or in livestock commodities. The chemical structure of phosalone is shown in the section entitled Physical/Chemical Properties.

Several submissions of data have been received since the Registration Standard was issued. Also, very recent data submissions have been reviewed involving apple and cherry field trials as well as product chemistry. The information contained in this document outlines the current hazard and dietary exposure assessments with respect to the reregistration of phosalone.

As with other organophosphates, the principal toxic effects induced by phosalone are related to its cholinesterase-inhibiting (ChE) activity. Phosalone is a cholinesterase inhibitor having a Lowest Observed Adverse Effect Level (LOAEL) of 10 mg/kg/day in an acute rat oral neurotoxicity study (a true No Observed Adverse Effect Level or NOAEL was not determined); the effect observed was plasma ChE inhibition. The NOAEL in a 2-year oral rat study used in chronic dietary risk assessment was 0.2 mg/kg/day; LOAELs were 1.8 mg/kg/day in males and 2.5 mg/kg/day in females with the effects being plasma and red blood cell ChE inhibition, decreased testes/epididymal weight, and increased testicular lesion incidence. An additional dose and endpoint were selected from a rabbit developmental toxicity study to be used in acute dietary risk assessment for Females (13+ years) only; the NOAEL was 1 mg/kg/day and the LOAEL was 10 mg/kg/day with the effect being postimplantation loss. Upon applying the appropriate uncertainty factors, the derived Reference Doses (RfDs) used in risk assessment are 0.01 mg/kg/day for acute dietary for Females (13+), 0.03 mg/kg/day for acute dietary for all other population subgroups, and 0.002 mg/kg/day for chronic dietary assessments. Phosalone does not pose a cancer hazard to humans. There was no true qualitative or quantitative increase in offspring sensitivity in the developmental and reproduction studies because any observed effects occurred only at high doses at which significant maternal toxicity occurred. Although phosalone is a ChE inhibitor, no structural neuropathological effects were observed upon histological

examination.

The Food Quality Protection Act (FQPA) of 8/3/96 requires that a 10-fold safety factor be applied to risk assessments to protect against the potential increased sensitivity of infants and children unless there is evidence supporting reduction of this factor. In the case of phosalone, hazard and exposure considerations led to the conclusion that this factor should be removed (reduced to 1X) for the following reasons:

- i. The current toxicology database is adequate for FQPA assessment;
- ii. The HIARC concluded that the toxicity data provide no indication of qualitative or quantitative increased susceptibility of young rats or rabbits to phosalone;
- iii. Adequate actual data, surrogate data, and/or modeling outputs are available to satisfactorily assess dietary exposure (since the reregistration only supports import tolerances, no drinking water or residential assessment is required for phosalone).

To derive the Population Adjusted Doses (PADs) the acute and chronic RfDs must be divided by the FQPA factor. In the case of phosalone, as the FQPA factor is 1X, the aRfD and the cRfD are identical to the respective aPADs and cPAD, i.e., **the aPADs are 0.03 mg/kg/day for cholinesterase inhibition (all population subgroups) and 0.01 mg/kg/day for developmental effects (Females 13+) and the cPAD is 0.002 mg/kg/day**. These are the hazard components to be used in the dietary risk assessments, i.e., the target or allowable level of dietary exposure to phosalone in units of mg/kg/day.

Dietary risk assessments reflected highly refined exposure estimates. The exposure components consisted of anticipated residues derived largely from FDA surveillance monitoring data although field trial data were used in the case of almonds and cherries. Although USDA/Pesticide Data Program (PDP) monitoring data were available for some commodities, the FDA data were preferable to the PDP data due to a larger number of samples imported from countries having phosalone registrations. Anticipated residues were adjusted by percent crop imported from countries having phosalone registrations; of this percent, all was assumed to have been treated thus introducing a conservatism. A Tier 3 probabilistic/Monte Carlo type of acute dietary risk assessment was conducted. These refined dietary exposure values were then compared to the aPAD and cPAD to estimate dietary risk. **Acute risks to all population subgroups were $\leq 0.74\%$ of the aPAD and chronic risks to all population subgroups were $\leq 0.1\%$ of the cPAD.**

Aggregate exposure is comprised solely of food sources as there are no drinking water or residential exposures to phosalone. Thus, acute and chronic dietary (food only) assessments of risk are identical to the corresponding aggregate risks. **These risks**

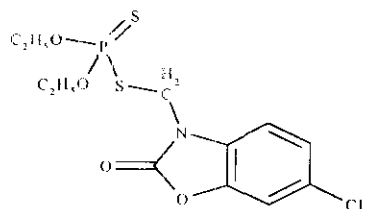
are well below the Agency's level of concern.

As there is no use of phosalone-containing products in the United States, an occupational risk assessment is not necessary or appropriate.

The phosalone database, while not being complete, is adequate for the conduct of this revised human health risk assessment. The following confirmatory toxicology data remain outstanding: (i) the rat metabolism study should be upgraded by the identification of sufficient urine radioactivity or, if identification is not possible, an explanation should be provided; (ii) the *in vitro* unscheduled DNA synthesis (UDS) assay should be repeated to confirm or refute the findings of an earlier study indicating weak UDS-inducing activity; and (iii) a developmental neurotoxicity study in the rat. The following residue chemistry data are required to reassess phosalone tolerances: additional field trials conducted on apples, peaches, plums, and grapes. In response to Aventis comments, the Agency has decided to waive pear field trials and reduce the number of trials required on peach and plum. However, several side-by-side field trials have been determined to be necessary to compare residues resulting from application of two major formulation classes. Depending on the outcome of these side-by-side studies, additional cherry field trials may be required. Note that a Pome Fruits Crop Group tolerance cannot be established without pear field trials in which side-by-side comparisons of the two major formulation classes are made.

PHYSICAL/CHEMICAL PROPERTIES

Phosalone [O,O-diethyl S-[(6-chloro-2-oxobenzoxazolin-3-yl)methyl]phosphorodithioate] is an organophosphate insecticide for which all U.S. registrations have been voluntarily canceled. The chemical structures of phosalone as well as several properties and identifying characteristics are presented below.



Physical Properties:

Physical state.	Solid
Melting point.	40 C
Solubility.	Water: 0.017 g/L

	Hexane: 11.65 g/L
	Methanol: 237 g/L
Vapor pressure.	0.96×10^{-6} mmHg at 40 C ($<0.5 \times 10^{-6}$ mmHg at 24 C)
Octanol/H ₂ O coeff.	5.89×10^3
Stability.	Fairly stable to heat and at pH 5 & 7; moderately at pH 9

Other Identifying Characteristics and Codes:

Empirical Formula.	C ₁₂ H ₁₅ ClNO ₄ PS ₂
Molecular Weight.	367.80
CAS Registry No.	2310-17-0
Chemical I.D. No.	097701

HAZARD ASSESSMENT

The Toxicology Chapter of the RED was prepared by K. Farwell (9/15/99; D256366). The phosalone toxicology data base is adequate; there are sufficient data from which to select acute and chronic dietary endpoints for assessment of dietary risks associated with **imported foods** that may bear phosalone residues.

Phosalone is an organophosphate (OP) insecticide and acaricide; its mode of toxic action is the inhibition of cholinesterase (ChE). Phosalone is in acute Toxicity Category II by the oral route. The main toxic effects seen in the subchronic and chronic studies were inhibition of plasma, red blood cell, and brain cholinesterase, and associated clinical signs due to ChE inhibition. In some studies, No Adverse Effect Levels (NOAELs) for cholinesterase inhibition were not determined because cholinesterase activity was inhibited even at the lowest dose; however, this did not interfere with toxicity endpoint selection.

There was no increased susceptibility to offspring from *in utero* or postnatal exposure to phosalone. Toxic effects in the developmental rat and rabbit studies included increased postimplantation loss. Toxic effects observed in the rat reproduction study included body weight decrements and pup mortality. Phosalone was recently the subject of a data call-in for a developmental neurotoxicity study.

The mouse carcinogenicity study and the rat combined chronic toxicity/carcinogenicity study showed no treatment-related increase in tumor incidence. The Hazard Identification Assessment Review Committee (HIARC) classified phosalone is a "not likely" human carcinogen.

A microbial mutagenicity assay with *Salmonella typhimurium* did not result in mutagenic effects and there was no evidence of a clastogenic effect in an *in vitro* cytogenetic

assay. In an *in vitro* unscheduled DNA synthesis (UDS) assay, phosalone was found to be weakly active for UDS induction.

In a rat metabolism study, phosalone was rapidly absorbed orally and extensively metabolized. The major route of elimination was urinary. Tissue residues were low with minimal potential for bioaccumulation.

Table 1 contains the acute toxicity endpoints which are especially important for labeling purposes. As phosalone is only applied outside the U.S., these data are presented largely for informational purposes. Because dermal, inhalation, and ocular exposure to phosalone will not occur in the U.S., acute toxicity studies reflecting administration via these routes of exposure are not required.

Table 1. Acute Toxicity Profile of Phosalone.

GDLN	Study Type	MRID	Results	Tox Category
81-1	Acute Oral	00006716, 00006643	Male: 120-155 mg/kg Female: 90-135 mg/kg	II
81-7	Delayed Neurotoxicity, Hen	00137037 00137038	Negative for OPIDN ¹	—

¹OPIDN = organophosphate induced delayed neurotoxicity.

DOSE RESPONSE AND HAZARD ENDPOINT SELECTION

A summary of the phosalone toxicology studies and hazard dose and endpoint selections made by HED is provided in the HIARC report by K. Farwell dated 8/12/99. Table 2 contains a summary of the doses and toxicity endpoints selected for use in the human health risk assessments.

TABLE 2. Toxicological endpoints for use in human risk assessment

EXPOSURE	DOSE (mg/kg/day)	ENDPOINT	STUDY
Acute Dietary (General population including infants and children)	LOAEL = 10	Plasma ChE inhibition	Acute neurotoxicity in rats
	UF =300 Acute RfD = Acute PAD = 0.03 mg/kg /day		
Acute Dietary (Females 13+)	Developmental NOAEL = 1	Post-implantation loss	Developmental toxicity in rabbits
	UF =100 Acute RfD = Acute PAD = 0.01 mg/kg /day		
Chronic Dietary	NOAEL = 0.2	Plasma and RBC ChE inhibition (both sexes), decreased testicular weight and lesions	2-Year Rat Study
	UF =100 Chronic RfD = Chronic PAD = 0.002 mg/kg/day		
Dermal or Inhalation Endpoints	---	None selected. Phosalone reregistration is for import tolerances only.	—

FQPA Safety Factor

The Food Quality Protection Act (FQPA) of 8/3/96 requires that a 10-fold safety factor be applied to risk assessments to protect against the potential increased sensitivity of infants and children unless there is evidence supporting reduction of this factor. The FQPA Safety Factor Committee met 8/16/99 to evaluate the hazard and exposure data for phosalone as bases for making a recommendation on the magnitude of the FQPA Safety Factor (as required by FQPA). The FQPA Safety Factor Committee's 9/13/99 report recommends removal (reduction to 1X) of the 10X FQPA Safety Factor as initially recommended by HIARC in its 8/12/99 report. The rationale for reduction of the FQPA Safety Factor to 1X is:

- The toxicology database is adequate for FQPA assessment;
- The HIARC concluded that the toxicity data provide no indication of qualitative or quantitative increased susceptibility of young rats or rabbits to phosalone;
- Adequate actual data, surrogate data, and/or modeling outputs are available to

satisfactorily assess dietary exposure (since the reregistration only supports import tolerances, no drinking water or residential assessment is required for phosalone).

To derive the acute and chronic Population Adjusted Doses (PADs), the acute RfDs (0.01 and 0.03 mg/kg/day for Females 13+ and All other subpopulations, respectively) and the chronic RfD (0.002 mg/kg/day) must be divided by the relevant FQPA Safety Factor. As the FQPA Safety Factor was reduced to 1X, the RfDs and PADs are identical, i.e., **the aPAD for females (13+ years) is 0.01 mg/kg/day for developmental effects; the aPAD for all subpopulations is 0.03 mg/kg/day for cholinesterase inhibition; and the cPAD is 0.002 mg/kg/day for all population subgroups.** These are the hazard components to be used in the dietary risk assessments, i.e., the maximum allowable level of dietary exposure to phosalone in units of mg/kg/day.

DIETARY EXPOSURE AND RISK ASSESSMENT

Food Sources of Dietary Exposure

The residue chemistry database, tolerance reassessment summary, and details of outstanding data are presented in the Residue Chemistry Chapter of the RED (K. EL-Attar, D256367, 11/1/99). The nature of phosalone residues in plants and livestock is adequately understood for purposes of the supported import tolerances based on available metabolism studies. HED's Metabolism Assessment Review Committee (MARC) determined that the phosalone residue to be regulated in plant commodities is the parent compound only (K. EL-Attar, D255208, 10/4/99). Tolerances are currently established for residues of phosalone *per se* in/on almonds and almond hulls (0.1 and 50.0 ppm, respectively); apples, grapes and pears (10.0 ppm); and apricots, cherries, peaches, and plums (15.0 ppm) under 40 CFR §180.263. No tolerances have been established for phosalone residues in processed plant commodities. Adequate data collection and enforcement methods are available to detect phosalone residues in plant commodities. The chemical name and structure of phosalone are provided in the section on Physical/Chemical Properties.

Based on available livestock metabolism and feeding studies, it has been determined that there is no reasonable expectation of finite residues being transferred to livestock commodities from feed items bearing phosalone residues, i.e., a 180.6(a)(3) classification is appropriate (K. EL-Attar, D260637, 11/1/99). This classification is further supported by the estimation that only 0.2% of beef consumed in the U.S. could even theoretically bear phosalone residues and that potential livestock exposure is limited to consumption of the very minor, localized, and seasonal feed item wet apple pomace by beef cattle to be exported from Canada to the U.S. Almond hulls, the other potential feed item, are not imported into the U.S. As a result, tolerances for phosalone residues in livestock commodities are not necessary. Likewise, the dietary exposure assessments reflected no consumption of livestock commodities.

There are no registered domestic uses of phosalone on food/feed crops. There are three basic formulations of Phosalone manufactured by Aventis that are registered for use on food/feed crops in countries that export treated commodities into the U.S. These include emulsifiable concentrate (350 g/L EC), flowable concentrate (500 g/L FIC), and wettable powder (30% WP) formulations marketed, primarily in Europe, under the trade names Zolone® and Rubitox®. Local formulations, which represent more dilute versions of the EC or WP products formulated with the same inerts, are also available in a few countries. These products may be applied as broadcast foliar applications using either ground or aerial equipment.

Dietary risk assessments reflected highly refined exposure estimates. The phosalone dietary exposure analyses were based largely on FDA monitoring data. Field trial data were used in the cases of almonds and cherries. Although USDA/Pesticide Data Program (PDP) monitoring data were available for some commodities, the FDA data were preferable to the PDP data due to a larger number of samples imported from countries having phosalone registrations. Residues were typically below the limit of detection (LOD), between the LOD and the limit of quantitation (LOQ), or at or just above the LOQ. Available field trial and monitoring data reflected analyses of phosalone *per se*, the only residue of regulatory and toxicological concern.

HED conducts dietary risk assessments using the Dietary Exposure Evaluation Model (DEEM™), which incorporates consumption data generated in USDA's Continuing Surveys of Food Intakes by Individuals (CSFII), 1989-1992. For chronic dietary risk assessments, the three-day average of consumption for each subpopulation is combined with residues in commodities to determine average exposure in mg/kg/day. For refined acute dietary risk assessments, the entire distribution of consumption events for individuals is multiplied by a distribution of residues to obtain a distribution of exposures in mg/kg/day; this is a probabilistic analysis, referred to as "Monte Carlo," with risk at the 99.9th percentile of exposure reported.

In the acute dietary exposure assessment, risk at the 99.9th percentile of exposure is reported since the probabilistic analysis was highly refined using residue distribution files adjusted by the percent of U.S. consumption of each food that has been imported from countries having phosalone registrations; of this percent, all was assumed to have been treated thus introducing a conservatism. A Tier 3 probabilistic/Monte Carlo type of acute dietary risk assessment was conducted by comparing these refined exposure values to the aPADs. Average exposure values corrected by percent crop treated were compared to the cPAD to estimate chronic dietary risk. **Acute risks to all population subgroups were ≤0.74% of the aPAD and chronic risks to all population subgroups were ≤0.1% of the cPAD, well below the Agency's levels of concern (Table 3).**

The chronic and acute analyses take into consideration the reduction of phosalone residues in certain processed foods based on a chemical-specific apple processing study.

Table 3. Summary of Phosalone Acute & Chronic Non-cancer Dietary Exposure and Risk Estimates ¹

Population Subgroup	Acute Assessment (99.9th %-ile of Exposure)				Chronic Assessment	
	General U.S. Population Including All Infants and Children Subgroups		Females 13+			
	Exposure (mg/kg/day)	% aPAD	Exposure (mg/kg/day)	% aPAD	Exposure (mg/kg/day)	% cPAD
General U.S. Population	0.000049	0.16	N/A	N/A	0.000001	0.0
All Infants (<1 yr)	0.000084	0.28	N/A	N/A	0.000001	0.1
Children (1-6 yrs)	0.000221	0.74	N/A	N/A	0.000002	0.1
Children (7-12 yrs)	0.000132	0.44	N/A	N/A	0.000001	0.0
Females (13-50 yrs)	0.000016	0.05	0.000017	0.17	0.000000	0.0
Males (13-19 yrs)	0.000014	0.05	N/A	N/A	0.000000	0.0
Males (20+ yrs)	0.000017	0.06	N/A	N/A	0.000000	0.0

¹ The Acute Population Adjusted Doses (aPADs) are 0.03 mg/kg/day for the "General U.S. Population Including All Infants and Children Subgroups" and 0.01 mg/kg/day for "Females 13+." The Chronic PAD (cPAD) is 0.002 mg/kg/day for all population subgroups.

Drinking Water Sources of Dietary Exposure

Products containing phosalone are not registered for use within the United States. Therefore, no contamination of drinking water sources is expected. As a result, drinking water is not a contributor to the aggregate risk and a water assessment has not been conducted.

AGGREGATE EXPOSURE AND RISK ASSESSMENT

Acute Aggregate Exposure and Risk

Acute aggregate risk consists solely of food sources of dietary exposure because dietary exposure to phosalone through drinking water is not expected. Acute dietary (food only) risks do not exceed the Agency's level of concern as the most exposed population subgroup, children (1-6 years), has a risk that is 0.74% of the aPAD (Table 3) based on highly refined exposure estimates.

Aggregate Short-term and Intermediate-term Exposures and Risks

Aggregate short-term and intermediate-term exposures were not estimated because there are no residential exposures to phosalone expected based on the use pattern.

Chronic Aggregate Exposure and Risk

In the case of chronic aggregate risk, food sources of dietary exposure are the only contributor because drinking water exposure is not expected. Chronic (food only) risks are below the Agency's level of concern. Risks to all population subgroups are $\leq 0.1\%$ of the cPAD (Table 3); these risk values are based on highly refined dietary exposure estimates.

OCCUPATIONAL AND RESIDENTIAL EXPOSURE AND RISK ASSESSMENT

Products containing phosalone are not registered for use within the United States. Therefore, no occupational or residential exposure is expected. As a result, these risk assessments have not been conducted.

ENDOCRINE DISRUPTER EFFECTS

The Food Quality Protection Act (FQPA; 1996) requires that EPA develop a screening program to determine whether certain substances (including all pesticides and inerts) "may have an effect in humans that is similar to an effect produced by a naturally occurring

estrogen, or such other endocrine effect...." EPA has been working with interested stakeholders, including other government agencies, public interest groups, industry and research scientists to develop a screening and testing program as well as a priority setting scheme to implement this program. The Agency's proposed Endocrine Disrupter Screening Program was published in the Federal Register of December 28, 1998 (63 FR71541). The Program uses a tiered approach and anticipates issuing a Priority List of chemicals and mixtures for Tier 1 screening in the year 2000. As the Agency proceeds with implementation of this program, further testing of phosalone and its end-use products for endocrine effects may be required.

CUMULATIVE EXPOSURE AND RISK

EPA has determined that phosalone has a common mechanism of toxicity with other members of the organophosphate class of pesticides. However, the Agency is in the process of developing methodology to conduct a cumulative risk assessment. At this time, therefore, EPA will not conduct a cumulative risk assessment.

DATA NEEDS

The following data requirements have been identified for phosalone:

Toxicology (Confirmatory Data Requirements)

- The rat metabolism study should be upgraded by the identification of sufficient urine radioactivity or, if identification is not possible, an explanation should be provided.
- The *in vitro* unscheduled DNA synthesis (UDS) assay should be repeated to confirm or refute the findings of an earlier study indicating weak UDS-inducing activity.
- A developmental neurotoxicity study in the rat.

Residue Chemistry Data Necessary for Tolerance Reassessment

- Additional field trials conducted on apples, peaches, plums, and grapes. In response to Aventis comments, the Agency has decided to waive pear field trials and reduce the number of trials required on peach and plum. However, several side-by-side field trials have been determined to be necessary to compare residues resulting from application of two major formulation classes. Depending on the outcome of these side-by-side studies, additional cherry field trials may be required. Note that a Pome Fruits Crop Group tolerance cannot be established without pear field trials in which side-by-side comparisons of the two major formulation classes are made.



13544

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