United States
Environmental Protection
Agency

Office of Prevention, Pesticides
and Toxic Substances
(7501C)

Pesticide
Fact Sheet

Name of Chemical: Fosthiazate
Reason for Issuance: Conditional Registration
Year Issued: 2004

Appendix I: Glossary of Terms and Acronyms
Appendix II: Bibliography

1. DESCRIPTION OF CHEMICAL

Generic Name:	Fosthiazate (*O*-Ethyl *S*-(1-methylpropyl)(2-oxo-3-thiazolidinyl)phosphonothioate)
Common Name:	Fosthiazate
Trade Name:	Fosthiazate, Nemathorin
EPA PC Code:	129022
Chemical Abstracts Service (CAS) Number:	98886-44-3
Year of Initial Registration:	2004
Registration Expiration Date:	Five years from the date of registration
Pesticide Type:	Nematicide
Chemical Class:	Organophosphate
Registrant:	ISK Biosciences Corporation, Concord, Ohio

2. USE PATTERNS AND FORMULATIONS

Pests/Application Sites:	Controls nematode species on tomatoes
Types of Formulations:	96.0% a.i. technical product 75.0% a.i. emulsifiable concentrate end-use product 50% a.i. emulsifiable concentrate end-use product

Types and Methods:	Drip irrigation under plastic, applied in bands
Application Rates:	1.00 to 1.50 lbs a.i./acre/application Maximum application rate 1.50 lbs a.i./season
Frequency/Timing:	One preplant or pretransplant application per year
Carrier:	Water

3. SCIENCE FINDINGS

Fosthiazate is a member of the organophosphate class of pesticides. Available product chemistry, toxicology, ecological effects and environmental fate data supporting the nematicide use pattern have been reviewed. The data and estimated risks to human health and the environment from its use on field grown tomatoes are summarized below.

PHYSICAL AND CHEMICAL CHARACTERISTICS

Technical fosthiazate is a light gold liquid with a boiling point of 198^{o} C at 0.5 mm Hg, a low vapor pressure of 2.7 x 10^{-6} at 25^{o} C, and a log P_{ow} of 1.752. Fosthiazate has a solubility of 9.85 g/L in water, 15.14 g/L in n-hexane, and is soluble in –methyl-2-pyrrolidinone (NMP), isopropyl alcohol, and xylene.

HAZARD CHARACTERIZATION

Toxicology Characteristics

Technical Fosthiazate has moderate toxicity via the dermal (toxicity category II) and oral (toxicity category II) routes of exposure and slight toxicity via the inhalation (toxicity category III) route of exposure. It is moderately irritating to the eyes (toxicity category II), and moderately irritating to the skin (toxicity category IV). Fosthiazate is classified as a dermal sensitizer. In accordance with the EPA Draft Guidelines for Carcinogen Risk Assessment (July, 1999), and based on lack of evidence for carcinogenicity in mice and rats, the Agency has classified fosthiazate as "not likely to be carcinogenic to humans." There is no concern for mutagenicity resulting from exposure to fosthiazate.

Table 1: Acute Toxicity Profile of Fosthiazate Technical

Guideline Number	Study Type; MRID #	Results	Toxicity Category
870.1100	Acute Oral -Rat; 41347622	LD_{50} = 73 mg/kg- M; = 51-64- F	II
870.1200	Acute Dermal- Rat; 41347625	LD_{50} = 2396 mg/kg- M; =861 mg/kg- F	II
870.1300	Acute Inhalation- Rat (92% ai); 41347626	LC_{50} = 0.83 mg/L- M = 0.56 mg/L- F	III

870.2400	Primary Eye Irritation - Rabbit; 41347627, 41347628	Mildly irritating; corneal opacity reversible within 7 days	II
870.2500	Primary Skin Irritation - Rabbit; 41347629	Non-irritating	IV
870.2600	Dermal Sensitization- Guinea pig; 41347630	Sensitizer	NA

Table 2.–Subchronic, Chronic, and Other Toxicity of Fosthiazate

Guideline No.	Study Type; MRID #	Results
870.3100	13-Week Feeding Study-Rat; 41347632	**Systemic Toxicity LOAEL:** 0.08 and 0.09 mg/kg/day for males and females, respectively, based on microscopic lesions in the adrenals (males) and increased ALT (females) levels. **No NOAEL** was established. At higher doses, the severity of vacuolation of cells in zona fasciculata (≥1.07 ppm) and zona glomerulosa (≥53.6 ppm) of the adrenals increased in a dose-dependent manner; at ≥53.6 ppm, the brain cholinesterase inhibition (ChEI) was also noted. In addition, there was increase in adrenal gland weight at 429 ppm **LOAELfor ChEI:** 10.7 ppm (0.77 and 0.89 mg/kg/day for males and females, respectively) based on plasma and RBC ChEI. **NOAEL:** 1.07 ppm (0.08 and 0.09 mg/kg/day for males and females, respectively).
--	4-Week Range-Finding Feeding Study-Rat; 44269905	**Systemic LOAEL:** 400 ppm (equivalent to 40.87 mg/kg/day in males and 43.52 mg/kg/day in females) based on fur loss, muscle tremor, enlarged pale spongiocytes in the adrenals, increased adrenal weights, and increased alkaline phosphatase and alanine aminotransferase levels. **Systemic NOAEL**: 100 ppm (equivalent to 9.69 mg/kg/day in males and 10.67 mg/kg/day in females). **LOAEL for ChEI:** 5 ppm (equivalent to 0.48 mg/kg/day in males and 0.5 mg/kg/day in females) based on decreased plasma butyryl- and acetyl-cholinesterase, and brain acetyl-cholinesterase in females, and erythrocyte acetyl-cholinesterase in males. **NOAEL:** 1 ppm (equivalent to 0.10 mg/kg/day in males and females.
--	28-day Feeding Study- Rat with 2-Butanesulfonic acid **(BSA)**; 43559701	**NOAEL:** 1000 mg/kg/day, the highest dose tested.
--	4-Week Range-Finding Feeding Study - Mice; 43971902	**LOAEL:** 400 ppm (males: 68.99 and females: 82.38 mg/kg/day) based on increased tubular basophilia in the kidney. **NOAEL:** 100 ppm (equivalent to 17.59 mg/kg/day in males and 21.43 mg/kg/day in females).

Guideline No.	Study Type; MRID #	Results
870.3150	13-Weeks Subchronic Toxicity-Dog; 41381108	**Systemic Toxicity LOAEL**: 0.11 mg/kg/day, based on histopathological changes in the adrenal glands. **NOAEL**: 0.054 mg/kg/day. **LOAEL for plasma ChEI:** 0.11 mg/kg/day in females and 0.54 mg/kg/day in males. **NOAEL:** 0.054 mg/kg/day in females and 0.11 mg/kg/day in males.
870.3200	21 - Day Repeated Dermal Toxicity - Rat; 43916806	**Systemic LOAEL**: 250 mg/kg/day for males and females based on mortality, clinical signs (emaciation, torpor [lethargy or dullness], tremor, hunched posture, hypothermia, gasping, hypersensitivity to noise, pallor [paleness], tachypnea [labored breathing], and piloerection), decreased body weight gains, and histopathology of the adrenal cortex observed in both sexes; increased food conversion factor and hematology findings were observed in males only. **Systemic NOAEL**: 25 mg/kg/day. **LOAEL for ChEI**: 25 mg/kg/day in males and 2.5 mg/kg/day in females based on inhibition of plasma, erythrocyte, and brain ChE in both sexes. **NOAEL for ChEI:** 2.5 mg/kg/day in males and 0.5 mg/kg/day in females.
870.3700	Developmental Toxicity-Rat; 43534505	**Maternal Toxicity** **LOAEL** = 10 mg/kg/day, based on reduced body weight gain **NOAEL** = 5 mg/kg/day **Developmental Toxicity** **LOAEL** =Not determined **NOAEL** = 10 mg/kg/day Although data were not provided on clinical signs in the dams during or after dosing no cholinergic signs were seen in neurotoxicity studies at the same dose. Therefore, the study classification is upgraded to acceptable/guideline.
870.3700	Developmental Toxicity- Rabbit; 41381111	**Maternal LOAEL:** 2 mg/kg/day based on weight loss, abortion, and cholinergic clinical signs noted in the range finding study (MRID 41381110). **NOAEL:** 1.5 mg/kg/day. **Developmental toxicity LOAEL:** Not determined. **NOAEL:** 2 mg/kg/day. No developmental toxicity was observed at any dose tested in the definitive prenatal developmental toxicity study. No developmental toxicity was observed at doses up to 2.5 mg/kg in a range-finding study.

Guideline No.	Study Type; MRID #	Results
870.3800	2-Generation reproduction--Rat; 41381113	**Parental Toxicity** **LOAEL** =100 ppm (equivalent to 9.32 and 7.21 mg/kg/day in females, and males, respectively) based on increased incidences of adrenal zona glomerulosa hypertrophy, centriacinar hepatocytic vacuolation and liver inflammation in F_0 females and periacinar hepatocytic hypertrophy in F_0 males.**NOAEL**: 30 ppm (equivalent to 2.6 and 2.09 mg/kg/day) in females and males, respectively). in F_0 females and in males. **Reproductive Toxicity** **LOAEL** = >100 ppm **NOAEL**=100 ppm. **Offspring Toxicity** **LOAEL** = 30 ppm based on decreased litter size and decreased pup weight and viability index during lactation. **NOAEL**=10 ppm
870.4300	Combined Chronic/carcinogenicity-Rat; 43559703	**Systemic LOAEL:** 50 ppm (2.45 mg/kg/day) for females, based on decreased RBC parameters (packed cell volume, hemoglobin, and RBC count), and increased incidence of atrophy and foamy interstitial cells in the ovaries and 200 ppm (8.34 mg/kg/day) for males, based on increased incidences of retinal atrophy, skeletal degenerative myopathy and non-neoplastic lesions in the adrenal and pituitary glands. **NOAEL:** 10 ppm (0.50 mg/kg/day) and 50 ppm (1.94 mg/kg/day) for female and male rats, respectively. **The test material was not carcinogenic at the doses tested**. **LOAEL for ChEI:** 10 ppm for male rats (0.38 mg/kg/day) and 1 ppm for female rats (0.051 mg/kg/day) based on inhibition of plasma and RBC cholinesterase (ChE) activity. **NOAEL**: 1 ppm for male rats (0.039 mg/kg/day) and a NOAEL was not established for female rats.
870.4200b	Carcinogenicity- Mouse; 43534504	**Systemic LOAEL:** 10.43 mg/kg/day (100 ppm) for females, based on increased adrenal cortico-medullary pigmentation and 30.51 mg/kg/day (300 ppm) for males, based on decreased body weights and non-neoplastic lesions in the adrenals, pituitary and kidney. At 300 ppm, increase in cholinergic signs (ataxia, hunched posture, tremors) was observed. **NOAEL:** 3.20 mg/kg/day (30 ppm) and 10.32 mg/kg/day (100 ppm) for females and males, respectively. **The test material was not carcinogenic at the doses tested**.

Guideline No.	Study Type; MRID #	Results
870.4100	1-Year Chronic Oral Toxicity - Dog; 43534503; 43559702; 43916805	**Systemic LOAEL:** 0.5 mg/kg/day in males based on increased alanine aminotransferase and 5 mg/kg/day in females based on microscopic lesions in the adrenal gland. **NOAEL:** 0.1 mg/kg/day in males and 0.5 mg/kg/day in females. **LOAEL for ChEI:** 0.5 mg/kg/day based on plasma acetyl- and butyryl-cholinesterase activity in males/females. **NOAEL:** 0.1 mg/kg/day based on plasma acetyl- and butyryl-cholinesterase activity. The erythrocyte and brain ChE activity LOAELs were not observed. The erythrocyte and brain cholinesterase NOAELs are 5 mg/kg/day.
870.5265	Gene Mutation Salmonella/ mammalian activation gene mutation assay; 41347633	Negative for mutagenic effects at dose levels up to 5000 ug/plate with or without metabolic activation.
870.5300	*In vitro* Gene Mutation - Mouse Lymphoma Assay; 43534508	No evidence of increased mutation frequency at the thymidine locus in cells treated up to cytotoxic concentration with or without S-9. Cytotoxicity was evident at ≥640 μg/ml (-S9) and ≥160 μg/ml (+S9).
870.5375	*in vitro* Cytogenetics (CHO) Assay; 41347634	No effects at concentrations up to 200 ug/ml (without S9) or 750 ug/mL (with S9). Cytotoxicity was evident at ≥50 μg/mL (-S9) and ≥93.75 μg/mL (+S9).
870.5395	*in vivo* mammalian cytogenetics assay; 43559704	No evidence of clastogenic or aneugenic effect at doses tested. Negative for induction of micronuclei at a dose approaching oral MTD, 50 mg/kg.
870.5500	*In Vitro* DNA Repair Test; 41347635	Negative in the DNA repair test. Fosthiazate did not induce any clear differences in the diameter of growth inhibitory zones between H17 (rec^+) and M 45 (rec^-), either in the presence or absence of metabolic activation.
870.5100	Gene Mutation Salmonella/ mammalian activation gene mutation assay with **BSA;** 43534506	Negative in Salmonella strains with or without S-9 activation. No cytotoxicity response up to the limit dose.

Guideline No.	Study Type; MRID #	Results
870.5300	*In vitro* Mammalian Gene Mutation - Mouse Lymphoma Assay with **BSA;** 43534507	No evidence of increased mutation frequency in cells treated up to the limit dose with or without S-9.
870.5395	*In vivo* Mammalian Cytogenetics Micronucleus Assay with **BSA;** 43534509	No evidence of clastogenic or aneugenic effect at doses tested. Negative for induction of micronuclei.
870.6100	Acute Delayed Neurotoxicity Study-Hen; 41347631	Six hens treated with IKI-1145 (fosthiazate technical) died within 6 days; 2 had relapses and progressed to moribundity on days 13 and 26; 9 hens survived. No abnormal neuropathological changes were observed except for a minimal case of focal gliosis in the lumbar sacral area of one of the two relapsing hens. IKI-1145 did not cause ADNT.
870.6200a	Acute neurotoxicity screening battery; 44269907	**Neurotoxicity LOAEL:** 10 mg/kg/day based on decreased forelimb grip strength in females. No abnormal neuropathological changes were observed. **NOAEL:** 0.4 mg/kg/day. **LOAEL for ChEI:** 10 mg/kg/day based on inhibition of plasma. Erythrocyte, and brain 3 hrs postdosing (plasma ChEI was reversible). **NOAEL:** 0.4 mg/kg/day.
_ _	Special Cholinesterase Inhibition study-rat; 43534502	**LOAEL:** 4.0 mg/kg/day based on plasma ChEI. **NOAEL:** 0.4 mg/kg/day. Decrease plasma ChE activity was noted in the male and female rats 3 hours after a single dose at 4.0 mg/kg body weight. Brain and RBC ChE activities were unaffected
870.6200b	Subchronic neurotoxicity screening battery; 44269908	**Systemic LOAEL:** 2.5 mg/kg/day based on decreased hind limb grip strength (21%; $p<0.01$) in females. No abnormal neuropathological changes were observed. **NOAEL:** 0.5 mg/kg/day. **LOAEL for ChEI:** 0.5 mg/kg/day based on significant inhibition of plasma, erythrocyte and brain ChE in females at weeks 5 and/or 9 and 14. **NOAEL:** 0.05 mg/kg/day.

Guideline No.	Study Type; MRID #	Results
870-7485	Metabolism- Rat; 43534511, 43534513, 43534515, 43534519	IKI-1145 (fosthiazate technical) was rapidly absorbed and widely distributed with only >5% detected in the tissues. No sex-related differences noted in the absorption and distribution; absorption was not dose dependent. Peak concentration in the blood was at 0.33 hr in both sexes. Only one metabolite, BESxP, represented > 10% of the administered dose. Test material was rapidly eliminated primarily in the urine (57%-72%) within 24 hrs. Unacceptable/Guideline due to lack of identification of metabolites in fecal radioactivity (accounted for 9-15% of the administered dose). Mean recovery was 95%-99%. IKI-1145 was metabolized by multiple processes including hydrolysis, oxidation, methylation and glutathione conjugation.
870.7485	Metabolism- Rat; 43534510, 43534512, 43534514, 43534518	IKI-1145 was rapidly and extensively absorbed independent of dose; rapidly metabolized and excreted in the urine (>65%), expired air (>10%) and in feces (<9%). Elimination was biphasic with first phase elimination half-life (t1/2) of 5-6 hrs and second phase of 85-112 hrs. Metabolism and excretion was rapid within 24 hrs. IKI-1145 was metabolized by multiple processes including hydrolysis, oxidation, methylation and glutathione conjugation. Female rats tended to excrete a metabolite containing a methylsulfinylethyl group while male rats excreted more containing a sulfoethyl group.
870.7485	Metabolism- Rat with **BSA**; 43534516, 43534517	Recovery was 100-108%. BSA was rapidly eliminated unchanged following dosing via the iv (approx. 100% in the urine) or oral (63%-89% in the urine and 10%-28% in feces) routes. Tissue burden was low.

Developmental/Reproductive toxicity

In a 2-generation reproduction study, there is qualitative and quantitative evidence of increased susceptibility in offspring following pre- and post-natal exposure to fosthiazate since the effects on pups are considered to be severe and occurred at a lower dose than those on parental animals. Since there is evidence of increased susceptibility of the young following pre- and post-natal exposure to fosthiazate in the rat reproduction study, the Agency performed a Degree of Concern Analysis to: 1) determine the level of concern for the effects observed when considered in the context of all available toxicity data; and 2) identify any residual uncertainties after establishing toxicity endpoints and traditional uncertainty factors to be used in the risk assessment of this chemical. In determining the degree of concern for these findings in the reproduction study, the Agency considered the overall quality of the study; the dose levels at which the pup effects were observed; the dose response of the pup effects; and the comparative severity of the effects seen. It was determined that there is a low degree of concern and no residual uncertainties for the susceptibility since: 1) the study was well conducted; 2) the dose-response in the offspring is well characterized; 3) clear NOAEL and LOAEL were established for the effects on the offspring; 4) although the decrease in pup survival seen at the LOAEL is

severe, this could be attributed to exposure to higher levels of the chemical since the mortalities occurred during early lactation; and 5) although cholinesterase activity was not measured in this study, cholinergic signs and cholinesterase inhibition were seen at comparable doses in other studies and thus could have been a cause for the pup mortality

Carcinogenicity

Fosthiazate has been classified into the category "Not likely to be carcinogenic to humans." This classification is based on the lack of evidence for carcinogenicity in mice and rats.

Mutagenicity

Submitted studies were found to be acceptable. There is no concern for mutagenicity resulting from exposure to fosthiazate.

DOSE RESPONSE ASSESSMENT

Toxicological Endpoints Determination

The primary target for fosthiazate appears to be the nervous system, with a secondary target, the adrenal system. Inhibition of plasma, red blood cell (RBC), and brain cholinesterase (ChE) activities was noted in the acute, subchronic and chronic toxicity studies. Evidence of neurological impairment included impaired grip strength in female rats in the acute and subchronic neurotoxicity studies; ataxia, hunched posture, gasping, and tremors in male mice in the carcinogenicity study and in male and female rats in the 21-day dermal toxicity study; and inhibition of brain ChE in the 13-week and 4-week rat feeding studies, subchronic neurotoxicity rat feeding study, and the 21-day dermal toxicity study.

The regulatory dose level for acute dietary risk assessment is the NOAEL of 0.4 mg/kg/day selected from the acute neurotoxicity study in adult rats (MRID # 44269907). The regulatory dose level for chronic dietary risk assessment is the NOAEL of 0.05 mg/kg/day from the 2-year chronic/carcinogenicity toxicity study in rats (MRID # 43559703, 43534502) . The short- and intermediate-term dermal endpoint is based on a 21-day dermal toxicity study in the rat (MRID # 43916806). The NOAEL of 0.5 mg/kg/day in females is based on inhibition of plasma, RBC, and brain ChE, and absorption factor of 100% should be applied. The short term inhalation endpoint (NOAEL of 0.10 mg/kg/day) is based on plasma, RBC, and brain ChEI from the oral 4- week range finding study in rats (MRID # 44269905). The intermediate term inhalation endpoint (NOAEL of 0.05 mg/kg/day) is based on plasma, RBC, and brain ChEI from the 90-day subchronic neurotoxicity study (MRID # 44269908).

It can be assumed that doses used in a DNT study may be similar to those used in the reproductive toxicity study. ChEI has been shown to be the most sensitive endpoint for fosthiazate in adults; it can also be assumed that ChEI may potentially be the most sensitive endpoint for pups.

Safety Factor Determinations

The acute ChE NOAEL for pups may be lower than the established offspring NOAEL of 0.69 mg/kg/day and could be as low as 0.02 mg/kg/day (ie., 10x lower than the lowest dose in the reproductive toxicity study). In the absence of ChE data to compare the relative sensitivity of pups and adults to acute fosthiazate exposure, it is prudent to assume that the potential acute ChE NOAEL from a DNT study may be lower than the NOAEL of 0.4 mg/kg/day currently used for establishing the acute RfD. Therefore, a 10x UF_{DB} is required for acute dietary risk assessment.

The multi-dosing ChE NOAEL for pups may be lower than the established chronic ChE NOAEL of 0.05 mg/kg/day from the 2-year chronic/carcinogenicity study and could be as low as 0.02 mg/kg/day (ie., 10x lower than the lowest dose in the reproductive toxicity study). In the absence of ChE data to compare the relative sensitivity of pups and adults to exposure to fosthiazate, it is prudent to assume that the potential multi-dosing ChE NOAEL from a DNT study may be lower than the established chronic ChE NOAEL. As opposed to a 10X, a 3X factor is considered adequate for chronic dietary risk assessment, because, the 0.05 mg/kg/day NOAEL currently used for risk assessment is approximately 3x higher than the potential lower NOAEL (0.02 mg/kg/day) that could be attained in the DNT study. Therefore, a 3x UF_{DB} is required for chronic dietary risk assessment.

The dietary food exposure assessment is conservative, using field trial level residues and assuming 100% CT. Dietary drinking water exposure is based on conservative modeling estimates and there are no residential uses. These assessments will not underestimate the exposure and risks posed by fosthiazate.

Table 3: Summary of FQPA Safety Factors for Fosthiazate

	LOAEL to NOAEL (UF_L)	**Subchronic to Chronic (UF_S)**	**Incomplete Database (UF_{DB})**	**Special FQPA Safety Factor (Hazard and Exposure)**
Magnitude of Factor	1X	1X	**10X acute & 3X chronic**	**1X**
Rationale for the Factor	No LOAEL to NOAEL extrapolations performed	No subchronic to Chronic extrapolations performed	**For the lack of a Developmental Neurotoxicity Study and Comparative Cholinesterase Measures (adult/young).**	**No residual concerns regarding pre- or post-natal toxicity or completeness of the toxicity or exposure databases**
Endpoints to which the Factor is Applied	Not Applicable	Not Applicable	**All Dietary and Residential (when applicable) Non-Dietary exposure assessments. 10X for acute dietary & 3X for chronic dietary.**	**Not Applicable**

4. HUMAN HEALTH EXPOSURE AND RISK ASSESSMENT

Acute and Chronic Dietary Exposure Assessment

Acute and chronic dietary exposure assessment was conducted for fosthiazate on tomatoes using the Dietary Exposure Evaluation Model (DEEM-FCID™, version 1.3). Fosthiazate tomato field trial data were used, assuming 100%CT and incorporating the default DEEM processing factors as well as processing data for tomato juice and puree, to estimate the acute and chronic dietary risk associated with the use of fosthiazate on tomatoes. Since no residues of concern were detected in the edible portion of the tomato plants in field trial studies, the residue value used consisted of half the LOQ for the parent, and half the LOQ for the metabolite ASC-67131; therefore, the residue value used in the dietary assessment was the LOQ (0.01 ppm). DEEM default values were used for all processed tomato commodities with the exception of tomato juice and puree. Dietary risk estimates are provided for the U.S. population (total) and various population subgroups.

A drinking water assessment for fosthiazate was conducted based on Tier 2 surface water modeling (PRZM-EXAMS) and Tier 1 groundwater modeling (SCI-GROW) results. The Agency has determined that only the parent fosthiazate is to be included in the drinking water risk assessment. The metabolite of toxicological concern, ASC-67131, is not found in soil or water.

Acute Dietary Risk Assessment

The acute dietary risk assessment was based on field trial residues in tomato (½ LOQ parent + ½ LOQ ASC-67131) and 100% CT. Risks of concern were considered at the 95th percentile because field trial data with 1.3x application rate, minimum preharvest interval (PHI), and 100% CT were used, which are considered conservative inputs. No detectable residues of either the parent or its metabolite of concern were found in the edible portion during these trials at a LOD of 0.01 ppm. The acute dietary assessment concludes that for tomatoes, the acute dietary risk estimates are below the Agency's level of concern at the 95th exposure percentile for the U.S. population (total) and all population subgroups. The most highly exposed population subgroup in the acute dietary analysis is children 1-2 years of age (29% of acute population adjusted dose or aPAD).

Using the exposure assumptions discussed above, the acute dietary exposure from food to fosthiazate will occupy 12 % of the aPAD for the U.S. population, 10% of the aPAD for females 13-49 years of age, 11 % of the aPAD for all infants <1 year of age and 29 % of the aPAD for children 1-2 years of age. In addition, there is potential for acute dietary exposure to fosthiazate in drinking water. After calculating DWLOCs and comparing them to the EECs for surface and ground water, EPA does not expect the aggregate exposure to exceed 100% of the aPAD, as shown in the following table:

Table 4.–Aggregate Risk Assessment for Acute Dietary Exposure to fosthiazate

Population Subgroup	aPAD (mg/kg)	% aPAD (Food)	Surface Water EEC (ppb)	Ground Water EEC (ppb)	Acute DWLOC (ppb)
U.S. Population	0.0004	12	2.1	2.4	12
Infants <1 year	0.0004	11	2.1	2.4	4
Children 1-2 yrs	0.0004	29	2.1	2.4	3
Females 13-49	0.0004	10	2.1	2.4	11

Chronic Dietary Risk Assessment

The chronic dietary assessment also concludes that the chronic dietary risk estimates are below the Agency's level of concern for the U.S. population (total) and all population subgroups. The most highly exposed population subgroup in the chronic dietary exposure analysis is also children 1-2 years of age (15% cPAD).

Using the exposure assumptions described above for chronic exposure, EPA has concluded that exposure to fosthiazate from food will utilize 7% of the cPAD for the U.S. population, 4 % of the cPAD for all infants < 1 year, 15 % of the cPAD for children 1-2 years, and 6% of the cPAD for females 13-49 years. In addition, there is potential for chronic dietary exposure to fosthiazate in drinking water. After calculating DWLOCs and comparing them to the EECs for surface and ground water, it is noted that the DWLOCs are slightly exceeded by the estimated ground water EECs for two population subgroups. However, these concentrations were modeled under the most conservative scenarios and likely exceed the actual level of contamination in the environment. SCI-GROW, used to model ground water exposures, is a Tier 1 unrefined assessment and therefore, highly conservative. Importantly, pesticide-specific aspects to this use of fosthiazate are likely to significantly exaggerate the conservativeness of the SCI-GROW estimates. SCI–GROW assumes the pesticide is applied above ground without cover and a subsequent and heavy amount of water (~140% of yearly average amount of rainfall) leaches some of the pesticide down to ground water. However, with the proposed registration using the drip irrigation method, a small amount of water is slowly dripped into soils precisely where it is needed, thus lessening the amount of water containing pesticide residues flowing down through the soil past the root zone where it cannot be used by the crop. This is expected to reduce the potential for the chemical to reach into ground water systems, and the actual ground water EECs would be less than what SCI-GROW predicted. Further, fosthiazate is required to be applied in fields using plastic mulch which significantly decreases the effect of rainfall on pesticide leaching. Finally, terrestrial field dissipation studies submitted to the Agency indicate no leaching of fosthiazate residues below the top (0-15 cm) soil layer. Therefore, EPA does not expect the aggregate exposure to exceed 100% of the cPAD, as shown in the following table:

Table 5. Aggregate Risk Assessment for Chronic Dietary (Non-Cancer) Exposure to Fosthiazate

Population Subgroup	cPAD mg/kg/day	% cPAD (Food)	Surface Water EEC (ppb)	Ground Water EEC (ppb)	Chronic DWLOC (ppb)
U.S. Population	0.00017	7	0.6	2.4	6
Infants < 1 year	0.00017	4	0.6	2.4	2
Children 1-2 years	0.00017	15	0.6	2.4	2
Females 13-49 years	0.00017	6	0.6	2.4	5

Occupational Risk

Based on the proposed use pattern, short-term (1 to 30 days) and intermediate-term (1 to 6 months) dermal and inhalation exposures are expected for pesticide handlers and postapplication workers. Since fosthiazate may be applied only one time per year, long-term (longer than 6 months) exposures to pesticide handlers or postapplication workers are not expected from the proposed use pattern.

Characterization of Occupational Risk

The Agency has determined that there are potential exposures to mixers, loaders, applicators, and other handlers associated with the preplant or pre-transplant use of fosthiazate on tomatoes applied by drip irrigation under the tarp. Based on this use pattern, one major occupational exposure scenario was identified for fosthiazate: Mixing/loading/applying liquids using chemigation systems.

Although there is data on risk to handlers while mixing/loading, at this time the Agency has no data to assess exposures during chemigation applications while handlers are laying pesticide-contaminated driplines or laying tarps over a just-treated field. Exposures to handlers during chemigation applications were estimated by using data for mixing/loading only. Therefore, the Agency believes that estimates of handler risks for the dripline irrigation scenario underestimates likely risks for chemigation scenarios.

The handler exposure and risk assessments are based on selected data from five fosthiazate-specific studies and the Pesticide Handler Exposure Database (PHED) Version 1.1 (August 1998). Based on the proposed use pattern, the following data sources were used to estimate fosthiazate handlers' exposure and risk:

- open mixing/loading liquids for chemigation application using data from PHED;
- open mixing/loading liquids for chemigation application using data from fosthiazate-specific studies; and
- closed mixing/loading liquids for chemigation application using data from PHED.

The maximum application rate of 1.5 pounds active ingredient per acre was assessed for dripline irrigation applications to tomatoes, in order to reflect the possible rate reduction when the application is applied in banded areas only and not broadcast evenly across the treated area. The assessment for dripline chemigation for tomatoes uses the standard value of 350 acres per day as well as the 25 acres per day proposed by the applicant.

Since both the dermal and inhalation toxicological endpoints of concern are based on inhibition of cholinesterase, dermal and inhalation MOE values were aggregated for both short- and intermediate-term exposures. The MOEs presented below represent the aggregated MOEs for each handler scenario.

The short- and intermediate-term handler risks for dripline chemigation applications to tomatoes at 1.5 pounds active ingredient and a maximum of 25 acres treated per day per handler are not of concern, based on EPA's level of concern for margin of exposure (MOE $\geq$100). Using PHED data for mixing/loading liquid formulations with closed systems as a surrogate for closed-system dripline chemigation applications, MOEs are 120 for short-term and 110 for intermediate-term exposures. Using fosthiazate-specific data for mixing/loading liquid formulations with maximum dermal personal protective equipment (but not a respirator) as a surrogate for dripline chemigation applications, the MOEs are 250 for short-term and 240 for intermediate-term exposures.

The proposed label submitted by the registrant in support of fosthiazate registration requires mixers/loaders and applicators to use engineering controls, including closed mixing/loading systems. As mandated in the Worker Protection Standard for Agricultural Pesticides (WPS), the proposed label also permits handlers to wear reduced personal protective equipment when engineering controls are used.

In order to minimize risk to workers, pesticide labeling directions limit dripline irrigation application to closed mixing/loading systems (engineering controls) and limit the application to 25-acres per day per handler and to a maximum application rate of 1.5 pounds active ingredient per acre, applied in bands.

Fosthiazate is applied directly to the soil before or at planting and postapplication exposure to fosthiazate may result from contact with treated soil. In particular, the Agency is concerned about transplanting tomatoes soon after a fosthiazate application. However, at this time, no postapplication assessment was performed, since there are no data on the soil residue dissipation of fosthiazate and no exposure data for activities resulting in contact with treated soil. Based on information provided by the registrant (i.e., the proposed label requires workers to wear gloves and boots when transplanting tomatoes within 7 days following applications to certain soil types) and fosthiazate-specific data indicating a relatively lengthy half-life in soils, a 7-day restricted-entry interval (REI) following fosthiazate applications is required. The Worker Protection Standard for Agricultural Pesticides (WPS) prohibits workers from performing routine early entry tasks while wearing personal protective equipment. Instead, the WPS requires that EPA establish a restricted-entry interval for the length of time following application until risks are not of concern for workers entering treated areas and performing tasks requiring contact with the treated surface without the use of personal protective equipment. A worker exposure study done concurrently with a fosthiazate soil residue dissipation study is needed as

confirmatory support for the registration on tomatoes. The following postapplication exposure monitoring data are required as a condition of registration of fosthiazate on tomatoes: GLN 875.2200, Soil Residue Dissipation and GLN 875.2400, Postapplication Dermal Exposure.

The WPS prohibits routine entry to perform hand labor tasks during the REI and requires PPE to be worn for other early-entry tasks that require contact with treated surfaces. Based on the acute toxicity of fosthiazate active ingredient (i.e., toxicity category II for dermal toxicity and for eye irritation potential and classified as a skin sensitizer) and using the default early entry personal protective equipment (PPE) established by the WPS, the following early entry PPE is required: long-sleeved coveralls over short-sleeved shirt and short pants, chemical-resistant gloves, chemical-resistant footwear plus socks, and protective eyewear.

Summary of Occupational Risk

For **dripline irrigation applications to tomatoes** (using data for mixing/loading liquid formulations) at a maximum area treated per day of **25 acres** per handler, the MOEs are:

- **120** for short-term and **110** for intermediate-term exposures for mixer/loaders using PHED data for mixing/loading liquid formulations using closed systems and a maximum application rate of 1.5 pounds active ingredient per acre;

- **250** for short-term and **240** for intermediate-term exposures for mixer/loaders using fosthiazate-specific data for maximum dermal personal protective equipment (but no respirator) and a maximum application rate of 1.5 pounds active ingredient per acre;

- **51** for short-term and **43** for intermediate-term exposures for mixer/loaders using PHED data for maximum dermal personal protective equipment (but no respirator) and a maximum application rate of 1.5 pounds active ingredient per acre without closed systems.

The Agency concludes that pesticide labeling directions must limit dripline irrigation applications to closed mixing/loading systems (engineering controls) and limit the applications to 25-acres per day per handler and to a maximum application rate of 1.5 pounds active ingredient per acre.

Residential Exposure and Risk Assessment

Not applicable since there are no residential uses of fosthiazate.

5. ENVIRONMENTAL EXPOSURE AND RISK

Environmental Fate Characteristics

Fosthiazate is expected to degrade slowly in the environment, with the major routes of dissipation being aerobic soil and anaerobic aquatic soil metabolisms (half-life in aerobic soil of

45 days and anaerobic water-sediment of 37 days). Under alkaline conditions, fosthiazate may also dissipate quite rapidly via hydrolysis (half-life of less than a week). Photodegradation in water is not significant. Soil photolysis study was waived, as incorporation of the chemical into soil is required immediately after application.

Although mobile in all soils tested under laboratory conditions, in the field fosthiazate residues were seen to remain mostly on the surface soils. Insignificant amounts of residues (<10% of total applied) were found in the deeper 15-30 cm soil layers, and no residues in soil below the 30 cm layer. The half-lives of fosthiazate in the terrestrial field dissipation studies are between 10 - 17 days.

The major laboratory soil degradates, MBS (methyl sec-butyl sulfone) and BSA (2-butanesulfonic acid) were found in the field at concentrations less than 5% of total applied and in the surface soil layer only. Laboratory studies are not available to determine either the persistence and mobility of these degradates in the environment or their level of toxicological concern to the environment.

Fate data suggests that fosthiazate degradates would pose minimal risk to non target organisms with the proposed use pattern.

Table 6 - Environmental Chemistry for Fosthiazate

Study Type; MRID #	Half Life/Other
Solubility (water);	9800 mg/L
Hydrolysis; 41347637	104 days
Photolysis in Water; 43916831	Stable to aqueous photolysis
Photolysis on Soil;	Not required since incorporation is needed immediately after application
Aerobic Soil Metabolism; 43916832	45.89 and 41.75days
Anaerobic Aquatic Soil Metabolism; 43916833	37 days
Aerobic Aquatic Metabolism	Not required
Leaching and Adsorption/Desorption in Soils; 42825701, 41347639	0.43, 1.22, and 1.71 mL/g
Volatility from Soil (Laboratory and Field, respectively)	Not required. The vapor pressure of fosthiazate does not trigger this data requirement
Terrestrial Field Dissipation (Short Term); 43952001, 43952102, 43952103, 43952104	10-17 days
Aquatic Field Dissipation	Reserved, if aquatic crop uses are proposed in the future. The proposed use is on terrestrial crops.
Chemical Application Method	soil applied, linearly decreasing with depth
Depth of incorporation	4 inches (10 cm)

Ecological Effects and Risk

Terrestrial

1. Acute, sub-acute, and chronic toxicity; birds

Fosthiazate technical is categorized as highly toxic to birds as determined from acute oral and subacute dietary studies. The bobwhite quail LD50 and LC50 were 16.6 mg/kg and 85 ppm respectively. Both the mallard duck and bobwhite quail avian reproduction studies had the same NOAEC (21.7 ppm) and LOAEC (42.6 ppm). Significant effects on male and female weight gain, decreased eggshell thickness and increased cracked eggs were observed in the bobwhite quail. MRID #s 43916818, 43916819, 43916820, 43916821, 43916824, 43916825.

2. Acute and chronic toxicity; mammals

Wild mammal testing was not performed for fosthiazate. Studies conducted on laboratory rats were substituted. An acute oral study produced an LD_{50} of 51 mg/kg for females and 73 mg/kg for males indicating fosthiazate is moderately toxic to mammals. A 2 generation rat study yielded a reproductive NOAEL of 10 ppm (or 0.91 and 0.91 mg/kg/day for males and females respectively) and a LOAEL of 30 ppm (equivalent to 2.09 and 2.60 mg/kg/day males and females, respectively) based on decreased viability index, litter size and pup weight for the f_1 generation.

3. Toxicity to insects

The acute contact honey bee LD50 is 0.247 *u*g/bee. Since the LD50 is less than 2 *ug* per bee fosthiazate TGAI is categorized as highly toxic to pollinators on an acute contact basis. MRID # 41347636.

4. Toxicity to terrestrial plants

An extensive battery of Tier I and Tier II tests were performed on technical fosthiazate in which dicots appear to be more sensitive than monocots. Because the Tier I seedling emergence test at 6.0 lbs ai/A produced a >25% response with cucumber and pepper, a Tier II test was conducted on technical fosthiazate. The NOAEC and EC25 for mustard are 0.8 and 1.0 lb ai/A respectively. Although the Tier I test results showed peppers were more sensitive (27 %) than mustard (<25 %) no test was conducted with peppers. The Tier I vegetative vigor test at 6.0 lbs ai/A produced a >25% response with sorghum, cucumber, radish, soybeans, mustard, buckwheat and pepper; therefore a Tier II test was conducted. For Tier II vegetative vigor, the most sensitive terrestrial plant is the dicot buckwheat (NOAEC.= 0.8 lbs ai/A and the EC25 = 3.3 lbs ai/A). Sorghum was the only monocot tested (NOAEC = 3.0 lbs ai/A and the EC 50 = > 6.0 lbs ai/A). MRID #s 43916836, 43916837, 43916839, 43916940.

Aquatic

A. Toxicity to aquatic organisms

1. Acute and chronic toxicity; freshwater fish

Fosthiazate technical is categorized as practically non toxic to freshwater fish on an acute basis. The LC50 for both bluegill sunfish and rainbow trout are 157 and 111 ppm respectively. Data were submitted for the freshwater fish early life stage using the fathead minnow (*Pimephales promelas*). Effects seen in the study included reduced dry weight and length of young fish (NOAEC = 2.32 ppm, LOAEC 4.48 ppm). MRID #s 43916826, 43916827.

2. Acute and chronic toxicity; freshwater invertebrates

Fosthiazate technical is categorized as acutely highly toxic to freshwater invertebrates. The lowest *Daphnia magna* EC50 for the technical grade is 0.26 ppm. The freshwater invertebrate life-cycle study determined an NOAEC of 0.061 ppm and an LOAEC of 0.128 ppm based on reduced number of offspring produced and parental mortality. MRID #s 43916828, 43916829.

3. Acute and chronic toxicity; estuarine/marine organisms

Technical Fosthiazate is classified acutely as slightly toxic to estuarine fish - sheepshead minnow LC50 is 46.5 ppm; highly toxic to Molluscs - eastern oyster EC50 = 14.1 ppm; and very highly toxic to Crustacea - mysid EC50 = 0.429 ppm. MRID #s 45540401, 45540402, 45540403.

4. Toxicity to aquatic plants

At this time there is no guideline (122-2) requirement for this use. However, the Tier I Aquatic Plant Growth study contained the results on a Tier I test with the green algae *Selenastrum capricornatum*. No adverse effects at a concentration equal to 4.5 ppm (equal to 6.0 lbs ai/A placed directly into a 1 acre pond 6 inches deep.). MRID # 43916821.

Risk to Terrestrial and Aquatic Organisms

Fosthiazate when applied as a broadcast or banded spray may pose acute risk to birds, mammals, and pollinators such as honey bees as well as chronic risk to mammals. But, when applied by chemigation under plastic, fosthiazate poses minimal acute or chronic risk to endangered or non endangered non target animals and plants. All ecotoxicity requirements are fulfilled for the use of fosthiazate on tomatoes.

6. FOSTHIAZATE AS A METHYL BROMIDE ALTERNATIVE ON TOMATOES

The United States Department of Agriculture's Interregional Research Project No. 4 has identified fosthiazate as a viable alternative to the use of methyl bromide for control of nematodes infesting tomato fields. Methyl bromide has been identified as a chemical that depletes the earth's ozone layer, and thus its use is being phased out. The United States is in the process of implementing a methyl bromide use reduction strategy leading to a complete ban for soil fumigation uses by the year 2005. Fosthiazate will provide growers with a pest management tool for use against nematode pest pressure.

Fosthiazate has also been identified as a methyl bromide alternative in the 2002 Report of the Methyl Bromide Technical Options Committee, which was established by the United Nations Environmental Programme's Parties to the Montreal Protocol on Substances that Deplete the Ozone Layer to identify existing and potential alternatives to methyl bromide. This Committee addresses the technical feasibility of chemical and non-chemical alternatives for the current uses of methyl bromide, and has identified fosthiazate as one of the non-fumigant, non-volatile pesticides which kills target pests by systemic action, providing a broad spectrum control of nematode pests, replacing use of methyl bromide for this purpose.

7. SUMMARY OF REGULATORY POSITION AND RATIONALE

Available data provide adequate information to support the conditional registration of fosthiazate technical and end-use products for use on tomatoes.

Labeling Restrictions

Manufacturing Use Products

Precautionary Statements/Environmental Hazards:

- This pesticide is toxic to birds, mammals, and aquatic invertebrates. Do not discharge effluent containing this product into lakes, streams, ponds, estuaries, oceans or other waters unless in accordance with the requirements of a National Pollutant Discharge Elimination System (NPDES) permit and the permitting authority has been notified in writing prior to discharge. Do not discharge effluent containing this product to sewer systems without previously notifying the local sewage treatment plant authority. For guidance contact your State Water Board or Regional Office of the EPA.

8. SUMMARY OF DATA GAPS

Residue Chemistry

- The final report of the 3 year storage stability data for tomato must be submitted and reviewed.
- Data are required depicting the frozen storage stability of fosthiazate and ASC-67131 in a representative foliage commodity. The Agency notes that a tobacco storage stability study will be submitted.
- Analytical grade reference standards for the fosthiazate metabolite ASC-67131 must be submitted to the EPA standards repository.
- Additional data are required to characterize insoluble residues in 30-DAT rotated wheat commodities.
- Storage stability data are required to support the additional analyses required on the 30-DAT wheat forage, straw, and grain.
- Based upon the petitioner's data to support the proposed plantback intervals (PBIs) for rotated crops (30 days for cereal grains and root and tuber vegetables, and 90 days for leafy vegetables and cucurbits), extensive field rotational crop trials and rotational crop tolerances will be required for leafy vegetables, root and tuber vegetables, and cereal grains.
- If the petitioner amends the proposed label to specify a 90-day PBI for root and tuber vegetables, fruiting vegetables, or cucurbits, extensive field rotational crop trials and rotational crop tolerances may only be required for leafy vegetables and forages of cereal grains. Rotation to crops other than root and tuber vegetables, fruiting vegetables, or cucurbits is prohibited.

Toxicology

- A 28-day inhalation study in rats with fosthiazate is required, as there is concern for toxicity by the inhalation route following exposure on multiple days in a commercial setting. Registrants are recommended to follow the protocol provided in OPPTS Guideline 870.3465 (90-day inhalation study) but cease exposure at 28 days.

- A DNT study in rats with comparative ChE measurements in adults and pups is also required. The protocol has been submitted and reviewed.

Occupational

- A worker exposure study for activities involving contact with treated soil conducted concurrently with a soil residue dissipation study is needed to assess postapplication risk. These data requirements are 875.2200 and 875.2400 in Group B-Postapplication Exposure Monitoring Test Guidelines in the Series 875-Occupational and Residential Exposure Test Guidelines.

9. CONTACT PERSON AT EPA

Rita Kumar, Senior Regulatory Specialist
Insecticide-Rodenticide Branch
Registration Division (7505C)
Office of Pesticide Programs
Environmental Protection Agency
Ariel Rios Building
1200 Pennsylvania Avenue, N.W.
Washington, DC 20460

Office Location and Telephone Number

Room 215, Crystal Mall Building #2
1921 Jefferson Davis Highway
Arlington, VA 22202
(703) 308-8291
E-mail: kumar.rita@epa.gov

DISCLAIMER: The information presented in this Pesticide Fact Sheet is for informational purposes only and may not be used to fulfill data requirements for pesticide registration and reregistration.

Appendix I

GLOSSARY OF TERMS AND ABBREVIATIONS

ADNT	Acute delayed neurotoxicity
a.i.	Active Ingredient
aPAD	Acute Population Adjusted Dose
BCF	Bioconcentration Factor
CAS	Chemical Abstracts Service
ChE	Cholinesterase
ChEI	Cholinesterase inhibition
cPAD	Chronic Population Adjusted Dose
%CT	Percent crop treated
DAT	Days after treatment
DEEM-FCID	Dietary Exposure Evaluation Model - Food Consumption Intake Database
DNA	Deoxyribonucleic acid
DNT	Developmental neurotoxicity
DWLOC	Drinking Water Level of Comparison.
EC	Emulsifiable Concentrate Formulation
EEC	Estimated Environmental Concentration. The estimated pesticide concentration in an environment, such as a terrestrial ecosystem.
EPA	U.S. Environmental Protection Agency
FQPA	Food Quality Protection Act
GLC	Gas Liquid Chromatography
GLN	Guideline Number
LC_{50}	Median Lethal Concentration. A statistically derived concentration of a substance that can be expected to cause death in 50% of test animals. It is usually expressed as the weight of substance per weight or volume of water, air or feed, e.g., mg/l, mg/kg or ppm.
LD_{50}	Median Lethal Dose. A statistically derived single dose that can be expected to cause death in 50% of the test animals when administered by the route indicated (oral, dermal, inhalation). It is expressed as a weight of substance per unit weight of animal, e.g., mg/kg.
LOAEL	Lowest Observed Adverse Effect Level
LOAEC	Lowest Observed Adverse Effect Concentration
LOC	Level of Concern
LOD	Limit of Detection
LOQ	Limit of quantitation
mg/kg/day	Milligram Per Kilogram Per Day
mg/L	Milligrams Per Liter
MOE	Margin of Exposure
MRID	Master Record Identification (number), EPA's system of recording and tracking studies submitted
MTD	Maximum tolerated dose
NA	Not Applicable
NOEC	No Observable Effect Concentration
NOEL	No Observed Effect Level
NOAEL	No Observed Adverse Effect Level

GLOSSARY OF TERMS AND ABBREVIATIONS (Continued)

NOAEC	No Observed Adverse Effect Concentration
NPDES	National Pollutant Discharge Elimination System
OP	Organophosphate
OPP	EPA Office of Pesticide Programs
OPPTS	EPA Office of Prevention, Pesticides and Toxic Substances
PAD	Population Adjusted Dose
PAG	Pesticide Assessment Guideline
PAM	Pesticide Analytical Method
PHED	Pesticide Handler's Exposure Data
PHI	Preharvest Interval
ppb	Parts Per Billion
PPE	Personal Protective Equipment
ppm	Parts Per Million
PRZM/ EXAMS	Tier II Surface Water Computer Model
RAC	Raw Agriculture Commodity
RBC	Red Blood Cell
RED	Reregistration Eligibility Decision
REI	Restricted Entry Interval
RfD	Reference Dose
SCI-GROW	Tier I Ground Water Computer Model
SF	Safety Factor
TGAI	Technical Grade Active Ingredient
UF	Uncertainty Factor
µg	micrograms
µg/L	Micrograms Per Liter
µL/g	Microliter per gram
USDA	United States Department of Agriculture
WPS	Worker Protection Standard

Appendix II

Citations Considered to be Part of the Data Base Supporting the Registration of Fosthiazate

MRID	CITATION
41347606	Koyanagi, T.; Miyaji, M.; Shindo, T.; et al. (1989) Physical and Chemical Characteristics: "IKI-1145 Technical". Unpublished study prepared by Ishihara Sangyo Kaisha, Ltd., Toray Research Center, Inc., and others. 257 p.
41347622	Cummins, H. (1989) Acute Oral Toxicity Study in the Rat: IKI-1145 Technical: Lab Project Number: 89/ISK093/0846. Unpublished study prepared by Life Science Research Limited. 54 p.
41347625	Cummins, H. (1989) Acute Dermal Toxicity Study in the Rat: IKI-1145 Technical: Lab Project Number: 89/ISK094/0847. Unpublished study prepared by Life Science Research Limited. 60 p.
41347626	Hino, Y. (1989) Acute Inhalation Toxicity Test of IKI-1145 Technical in Rats: Lab Project Number: D-1695E. Unpublished study prepared by Hita Research Laboratories. 48 p.
41347627	Cummins, H. (1989) Primary Eye Irritation Study in the Rabbit: IKI-1145 Technical: Lab Project Number: 89/ISK097a/0848. Un- published study prepared by Life Science Research Limited. 26 p.
41347628	Cummins, H. (1989) Primary Eye Irritation Study in the Rabbit (Eye Washing Study): IKI-1145 Technical: Lab Project Number: 89/ISK097b/0848. Unpublished study prepared by Life Sciences Research Limited. 23 p.
41347629	Cummins, H. (1989) Primary Dermal Irritation Study in the Rabbit: IKI-1145 Technical: Lab Project Number: 89/ISK107/0851. Unpublished study prepared by Life Science Research Limited. 20 p.
41347630	Smith, K. (1989) Dermal Sensitization Study in the Guinea Pig: IKI-1145 Technical: Lab Project Number: 89/ISK108/0852. Unpublished study prepared by Life Science Research Limited. 34 p.
41347633	Watanabe, K. (1989) IKI-1145 Technical: Reverse Mutation Test: Lab Project Number: IET 89-0054. Unpublished study prepared by Institute of Environmental Toxicology. 24 p.
41347637	Kato, Y. (1987) IKI-1145: Hydrolysis in Buffer Solutions at PH 5, 7, and 9: Lab Project Number: I-221. Unpublished study prepared by Ishihara Sangyo Kaisha Ltd. 34 p.

MRID	CITATION
41347639	Kato, Y. (1988) IKI-1145: Adsorption and Desorption in Soils: Lab Project Number: I-231. Unpublished study prepared by Ishihara Sangyo Kaisha Ltd. 33 p.
41347642	Fackler, P. (1989) IKI-1145: Bioconcentration and Elimination of ?Carbon 14|-residues by Bluegill (Lepomis macrochirus): Lab Project Number: 89-11-3157. Unpublished study prepared by Spring- born Laboratories, Inc. 38 p.
41381105	Cameron, D.; Norman, A. (1989) The Acute Oral Toxicity (LD50) of IKI-1145 Technical to the Bobwhite Quail: Lab Project No: ISK 36/891276. Unpublished study prepared by Huntingdon Research Centre Ltd. 45 p.
41381106	Cameron, D. ; Norman, A. (1989) The Dietary Toxicity (LC50) of IKI- 1145 Technical to the Bobwhite Quail: Lab Project Number: ISK 34/891274. Unpublished study prepared by Huntingdon Research Centre Ltd. 43 p.
41381107	Cameron, D. ; Norman, A. (1989) The Dietary Toxicity (LC50) of IKI- 1145 Technical to the Mallard Duck: Lab Project No: ISK 34/891275. Unpublished study prepared by Huntingdon Research Centre Ltd. 42 p.
41381108	Broadmeadow, A. (1989) IKI-1145 Technical: Toxicity Study by Oral (Capsule) Administration to Beagle Dogs for 13 Weeks: Lab Project No: 87/0219. Unpublished study prepared by Life Science Research Ltd. 258 p.
42347615	Handley, J.; Sewell, I.; Bartlett, A. (1989) IKI-1145 TGAI: Acute Toxicity to Rainbow Trout (Salmo gairdneri): Lab Project No. 203/9. Unpublished study prepared by Safepharm Laboratories Limited. 21 p.
42347616	Handley, J.; Sewell, I.; Bartlett, A. (1989) IKI-1145 TGAI: Acute Toxicity to Bluegill Sunfish (Lepomis macrochirus: Lab Project Number: 203/10. Unpublished study prepared by Safepharm Laboratories Limited. 21 p.
42347619	Handley, J.; Sewell, I.; Barlett, A. (1989) IKI-1145 TGAI: Acute Toxicity to Daphnia magna: Lab Project Number: 203/8. Unpublished study prepared by Safepharm Laboratories Limited. 20 p.

MRID	CITATION
42791101	Brewer, L. (1993) Residue Levels in Soil-Dwelling Invertebrates, Plants and Soil Following Treatment with Fosthiazate (ASC-66824) Experimental Organophosphorus Nematicide: Final Report: Lab Project Number: 19-92-600: 09201. Unpublished study prepared by Ecotoxicology & Biosystems Assocs., Inc. 125 p.
42825701	Arita, H.; Kato, Y. (1993) IKI-1145: Mobility of Parent Compound And its Degradation Products in Soil Columns: Report Amendment: Lab Project Number: I-228-01. Unpublished study prepared by Ishihara Sangyo Kaisha, Ltd. 110 p.
43534502	Serrone, D.M., Laveglia J.; (1994) Determination of a No Effect Level for Cholinesterase Inhibition in Rats with Fosthiazate (IKI-1145 Technical). Ricerca, Inc., Plainesville, OH. Study No. 94-0096. October 20, 1994. Unpublished.
43534503	Tauchi, K. (1991) Chronic Oral Toxicity Study on the Dog Treated with IKI-1145 Technical for 12-Months: Lab Project Number: 230. Unpublished study prepared by Imamichi Institute for Animal Reproduction. 462 p.
43534504	Aughton, P. (1990) IKI-1145: Carcinogenicity Study by Dietary Administration to CD-1 Mice for Up to 104 Weeks: Final Report: Lab Project Number: 89/0624: ISK/088/1145: 89/ISK088/0624. Unpublished study prepared by Life Science Research Ltd. 2238 p.
43534508	Lloyd, J. (1993) IKI-1145 Technical: Investigation of Mutagenic Activity in the TK+/- Mouse Lymphoma Cell Mutation System: Final Report: Lab Project Number: ISK/192: 92/ISK192/0841. Unpublished study prepared by Life Science Research Ltd. 44 p.
43534511	Magee, T., Marciniszyn J,. and Laveglia, J.; (1992) Study to Evaluate the Distribution and Excretion of ^{14}C(R)-IKI-1145 in Rats. Lab Project Number: 91-0198: IKI-1145: 3968-91-0198-AM-001. Unpublished study prepared by Ricerca, Inc.
43534513	Magee, T., Marciniszyn J., and Johnson, D.; (1993) Study to Evaluate the Distribution and Excretion of ^{14}C(R)-IKI-1145 in Rats Following Repeated Dosing:. Lab Project Number: 91-0429: IKI-1145: 5139-91-0429-AM-001. Unpublished study prepared by Ricerca, Inc.
43534515	Magee, T., Johnson, D., Laveglia, J.; (1993) Study to Measure the Pharmacokinetics of ^{14}C(R)-IKI-1145 in the Blood of Rats:. Lab Project Number: 91-0061: IKI-1145: 5217-92-0061-AM-001. Unpublished study prepared by Ricerca, Inc.

MRID	CITATION
43534519	Magee, T., Panthani, A., and Murray, M.; (1994) Study to Identify the Metabolites of ^{14}C(R)-IKI-1145 in the Urine of Rats. Lab Project Number: 91-0375:5096-91-0375-AM-001: IKI-1145. Unpublished study prepared by Ricerca, Inc.
43559701	Turck, P.; Laveglia, J. (1993) A 28-Day Feeding Study in Rats With 2-Butanesulfonic Acid: (Amended Report): Lab Project Numbers: 93-0020: 5598-93-0020-TX-002: 5598-93-0020-TX-000. Unpublished study prepared by Ricerca, Inc. 426 p.
43559702	Killeen, Jr., J.C. (1995) Histopathologic Reevaluation of the Adrenal Cortex from Subchronic and Chronic Toxicity Studies in the Dog with Technical Fosthiazate. Experimental Pathology Laboratory, Herndon, VA., and Ricerca, Inc., Painesville, OH. Laboratory Study Nos.: 156-088, 156-089, and 94-0249, January 10, 1995. Unpublished.
43559703	Aughton, P. (1990) IKI-1145: Combined Chronic Toxicity and Carcinogenicity Study by Dietary Administration to CD Rats for 104 Weeks: (Final Report): Lab Project Numbers: 89/0557: ISK/089/1145: 89/ISK089/0557. Unpublished study prepared by Life Science Research Ltd. 2256 p.
43559703	Aughton, P. (1990) IKI-1145: Combined Chronic Toxicity and Carcinogenicity Study by Dietary Administration to CD Rats for 104 Weeks: (Final Report): Lab Project Numbers: 89/0557: ISK/089/1145: 89/ISK089/0557. Unpublished study prepared by Life Science Research Ltd. 2256 p.
43916801	Hawkins, W.; Stalzer, W.; Jacobson, B. (1995) Technical Fosthiazate (IKI-1145) Product Identity and Disclosure of Ingredients: Lab Project Number: WR 2301-T: PC-1145-95-WAH-001. Unpublished study prepared by Ricerca, Inc. 33 p.
43916802	Hawkins, W. (1995) Technical Fosthiazate (IKI-1145) Preliminary Analysis and Certification of Limits: Lab Project Number: PC-1145-95-WAH-002: 95-0170: 95-0175. Unpublished study prepared by Ricerca, Inc. 159 p.
43916805	Killeen, Jr., J.C. (1995) Summary of the Pathology Working Group Peer Reviews of Histopathology of the Adrenal Cortex or Dogs from Studies with Technical Fosthiazate. Ricerca, Inc., Painesville, OH. Laboratory Study No.: 95-0221, October 25, 1995. Unpublished
43916806	Broadmeadow, A. (1989) IKI-1145 Technical: Twenty-One Day Dermal Toxicity Study in Rats: (Final Report): Lab Project Number: ISK/111/1145: 89/ISK111/0200: 89/0200. Unpublished study prepared by Life Science Research. 197 p.

MRID	CITATION
43916818	Turck, P.; Shults, S.; Laveglia, J. (1992) Acute Oral Toxicity (LD50) Study in Mallard Ducks with IKI-1145: Lab Project Number: 3917-91-0239-TX-004: 272-106: 91-0239. Unpublished study prepared by Ricerca, Inc. and Wildlife International Ltd. 140 p.
43916819	Turck, P.; Shults, S.; Laveglia, J. (1992) Acute Oral Toxicity (LD50) Study in Bobwhite Quail with IKI-1145: Lab Project Number: 3917-91-0240-TX-003: 272-105: 91-0240. Unpublished study prepared by Ricerca, Inc. and Wildlife International Ltd. 119 p.
43916820	Turck, P.; Shults, S.; Laveglia, J. (1992) Dietary (LC50) Study in Mallard Ducks with IKI-1145: Lab Project Number: 3917-91-0241-TX-003: 272-108: 91-0241. Unpublished study prepared by Ricerca, Inc. and Wildlife International Ltd. 113 p.
43916821	Turck, P.; Shults, S.; Laveglia, J. (1992) Dietary (LC50) Study in Bobwhite Quail with IKI-1145: Lab Project Number: 3917-91-0242-TX-003: 272-107: 91-0242. Unpublished study prepared by Ricerca, Inc. and Wildlife International Ltd. 127 p.
43916824	Turck, P.; Laveglia, J. (1993) Reproduction Study in Bobwhite Quail with IKI-1145: (Final Report): Lab Project Number: 3922-91-0259-TX-003: 272-111: 91-0259. Unpublished study prepared by Ricerca, Inc. and Wildlife International Ltd. 190 p.
43916825	Turck, P.; Laveglia, J. (1993) Reproduction Study in Mallard Ducks with IKI-1145: (Final Report): Lab Project Number: 3922-91-0258-TX-003: 272-112: 91-0258. Unpublished study prepared by Ricerca, Inc. and Wildlife International Ltd. 192 p.
43916826	Jenkins, C. (1991) IKI-1145 Technical: Acute Toxicity to Rainbow Trout: (Final Report): Lab Project Number: 91/ISK177/0015: ISK/177: 91-0015. Unpublished study prepared by Life Science Research Ltd. 26 p.
43916827	Jenkins, C. (1991) IKI-1145 Technical: Acute Toxicity to Bluegill Sunfish: (Final Report): Lab Project Number: 91/ISK178/0016: ISK/178: 91/0016. Unpublished study prepared by Life Science Research Ltd. 26 p.

MRID	CITATION
43916828	Jenkins, C. (1991) IKI-1145 Technical: Acute Toxicity to Daphnia magna: (Final Report): Lab Project Number: 91/ISK179/0017: ISK/179: 91/0017. Unpublished study prepared by Life Science Research Ltd. 27 p.
43916829	Bogers, M. (1994) Daphnia magna Reproduction Test with IKI-1145 Technical: Lab Project Number: 123468. Unpublished study prepared by NOTOX B.V. 33 p.
43916831	Huhtanen, K.; Lentz, N. (1993) A Photolysis Study of Fosthiazate (IKI-1145) in Water at pH 5: Lab Project Number: 5287-92-0153-EF-001: 92-0153: 5287-92-0153-EF-000. Unpublished study prepared by Ricerca, Inc. 106 p.
43916832	Walsh, K.; Huhtanen, K. (1995) An Aerobic Soil Metabolism Study with IKI-1145 (Fosthiazate): Lab Project Number: 3378-89-0384-EF-001-001: 89-0384. Unpublished study prepared by Ricerca, Inc. 293 p.
43916833	Hatzenbeler, C. (1995) An Anaerobic Aquatic Soil Metabolism Study with ((carbon 14)-T)-IKI-1145 and ((carbon 14)-B)-IKI-1145: Lab Project Number: 5163-92-0023-EF-001: 92-0023: IKI-1145. Unpublished study prepared by Ricerca, Inc. 123 p.
43916836	Backus, P. (1993) Effect of IKI-1145 (Fosthiazate) on Seed Germination/Seedling Emergence (Tier I): Lab Project Number: 5691-93-0092-BE-001: 93-0092: 5691-93-0092-BE-000. Unpublished study prepared by Ricerca, Inc. 64 p.
43916837	Backus, P. (1993) Effect of IKI-1145 (Fosthiazate) on Vegetative Vigor of Plants (Tier I): Lab Project Number: 5691-93-0093-BE-001: 93-0093: 5691-93-0093-BE-000. Unpublished study prepared by Ricerca, Inc. 59 p.
43916839	Crosby, K. (1995) Effect of IKI 1145 on Seed Germination/Seedling Emergence (Tier II): Lab Project Number: 6362-95-0017-BE-001: 95-0017: 6362-95-0017-BE-000. Unpublished study prepared by Ricerca, Inc. 166 p.
43916840	Crosby, K. (1995) Effect of IKI 1145 on Vegetative Vigor of Plants (Tier II): Lab Project Number: 6362-95-0018-BE-001: 95-0018: 6362-95-0018-BE-000. Unpublished study prepared by Ricerca, Inc. 122 p.

MRID	CITATION
43952901	Jablonski, J. (1995) Terrestrial Dissipation of Fosthiazate Applied to Bare Ground Near Ridgefield, Washington: Lab Project Number: 92-0159: 5288-92-0159-CR-001: ISK-1992-501-00. Unpublished study prepared by Ricerca, Inc. 365 p.
43952902	Jablonski, J.; McFall, D. (1995) Terrestrial Dissipation of Fosthiazate Applied to Bare Ground Near Madera, California: Lab Project Number: ISK-1992-501-01: ISK-1992-501-00: 92119. Unpublished study prepared by Ricerca, Inc. 371p.
43952903	Jablonski, J. (1995) Terrestrial Dissipation of Fosthiazate Applied to Bare Ground Near Camilla, Georgia: Lab Project Number: 92-0159: ISK-1992-501-03: ISK-1992-501-00. Unpublished study prepared by Ricerca, Inc. 507 p.
43952904	Jablonski, J. (1995) Terrestrial Dissipation of Fosthiazate Applied to Bare Ground in Lucama, North Carolina: Lab Project Number: 92-0159: 5288-92-0159-CR-004: 5288-92-0159-CR-000. Unpublished study prepared by Ricerca, Inc. 407 p.
43971902	Aughton, P. (1989) IKI-1145 Technical: Preliminary Toxicity Study by Dietary Administration to CD-1 Mice for Four Weeks: Lab Project Number: 86/0307: 86/ISK070/307. Unpublished study prepared by Life Science Research Ltd. 239 p.
44269905	Broadmeadow, A. (1989) IKI-1145 Technical: Preliminary Toxicity Study in Dietary Administration to CD Rats for Four Weeks: (Final Report): Lab Project Number: 86/ISK071/0284: 86/0284: ISK/071/1145. Unpublished study prepared by Life Science Research Ltd. 271 p.
44269907	Serrone, D.; Lucas, F. (1997) An Acute Neurotoxicity Screening Study in Rats with Technical Fosthiazate (IKI-1145): Lab Project Number: 5609-95-0034-TX-003: 95-0034: 5609-95-0034-TX-000. Unpublished study prepared by Ricerca, Inc. and Pathology Associates International. 654 p.
44269908	Serrone, D.; Lucas, F. (1997) A 90-Day Neurotoxicity Study in Rats with Fosthiazate (IKI-1145 Technical): Lab Project Number: 5610-95-0035-TX-003: 95-0035: 5612-93-0023-TX-002. Unpublished study prepared by Ricerca, Inc. and Pathology Associates International. 742 p.
45540401	Boeri, R.; Ward, T. (2001) Technical IKI-1145: Flow-Through Mollusc Shell Deposition Test: Lab Project Number: 2118-SK. Unpublished study prepared by T.R. Wilbury Laboratories, Inc. 29 p. {OPPTS 850.1025}

MRID	CITATION
45540402	Boeri, R.; Ward, T. (2001) Technical IKI-1145: Acute Toxicity to the Mysid, Americamysis bahia: Lab Project Number: 2117-SK. Unpublished study prepared by T.R. Wilbury Laboratories, Inc. 29 p. {OPPTS 850.1035}
45540403	Boeri, R.; Ward, T. (2001) Technical IKI-1145: Acute Toxicity to the Sheepshead Minnow, Cyprinodon variegatus: Lab Project Number: 2119-SK. Unpublished study prepared by T.R. Wilbury Laboratories, Inc. 26 p. {OPPTS 850.1075}
45540404	Boeri, R.; Ward, T. (2001) Technical IKI-1145: Early Life Stage Toxicity to the Fathead minnow, Pimephales promelas: Lab Project Number: 2116-SK. Unpublished study prepared by T.R. Wilbury Laboratories, Inc. 51 p. {OPPTS 850.1400}