STRUCTURE ACTIVITY TEAM REPORT	ver. 04/98 [redacted]		
Case #:	P-08-0088	**DCN:**	
SAT Date:	11/27/2007	**SAT Chair:**	[redacted]

Submitter: [redacted]

Chemical Name:

[redacted]

CAS RN:	**Trade Name:**
[redacted]	[redacted]

Structure

[redacted]

Molecular Formula:	[redacted]		
Molecular Wt.	[redacted]	**WT%<500:**	**WT%<1000:**
MP:	[redacted]	**BP:** [redacted]	**Eq. Wt:**
H2O Sol (g/L):	Dispersible	**V.P.**	<0.045
Max. Prod. Volume (kg/yr):	[redacted]	**Physical State:**	[redacted]

USE:

Emulsifier [redacted]

Related Case Numbers	Case Role	Related Case Numbers	Case Role
[redacted]			

Focus Date: 12/03/07 Results: Standard Review-Health, 5e Category-P

STRUCTURE ACTIVITY TEAM REPORT

CASE NUMBER: **P08-0088**

RELATED CASES: [redacted]

CONCLUSIONS/DISCUSSIONS

TYPE OF CONCERN:	HEALTH	ECOTOX
LEVEL OF CONCERN:	3	3

KEYWORDS:

BLOOD
LIVER
KIDNEY
MUTA
ONCO
IMMUNO
DEVEL
REPRO
LUNG
AQUATOX-A,C

SUMMARY OF ASSESSMENT

FATE: Estimations for covalent ion pair, sodium salt.
[redacted]
log Kow = 0.24 (E);
S = 2.9 g/L/dispersible at 25 °C (E)
VP < 1.0E-6 / < 0.045 torr at 25 °C (E)
BP > 400 °C (E)
H =1.82E-6 (E)
log Koc = 1.05 (E)
log Fish BCF = 0.50 (E)
POTW removal (%) = [redacted] OECD 301C(MITI): 0% (HPLC)/28d NRB
Time for complete ultimate aerobic biodeg > mo
Sorption to soils/sediments = low
Volatilization half-life from a standard river = 931 hrs
Volatilization half-life from a standard lake = 288 da
PBT Potential: P3B2T3
*CEB FATE: Migration to ground water = rapid

HEALTH: Absorption is nil through the skin as the neat material and poor through the skin when in solution based on physical/chemical properties. Expect good absorption through the lungs and GI tract based on analogs. There is concern for liver, kidney, and blood effects and mutagenicity based on the submitted toxicity data and concern for lung effects if inhaled based on the surfactant properties of the PMN compound. There is also concern for developmental toxicity, reproductive effects, immunosuppression and oncogenicity by analogy to perfluoroctanoic

acid (PFOA). In the assessment conducted by the state of West Virginia with input from EPA, the RfD for oral exposure was determined to be 0.004 mg/kg/day and the RfC for inhalation exposure was determined to be 1 ug/m3. Some of the key findings for noncancer assessment are for PFOA and/or its salts:
90-day dietary study in male rats - NOAEL = 0.47 mg/kg/day based on liver effects at 1.44 mg/kg/day. The benchmark dose was 1.3 mg/kg/day;
two-generation reproduction study in rats, gavage - LOAEL = 1 mg/kg/day based on increased liver and kidney weights in P and F1 generations;
2-year dietary study in rats - NOAEL = 1.3 mg/kg/day in males based on increased liver weight, hepatic cystoid degeneration, increased ALT enzyme activity, testicular vascular mineralization and LOAEL = 1.6 mg/kg/day in females based on an increase in the incidence of ovarian stromal tubular hyperplasia; the benchmark dose was 0.73 mg/kg/day based on liver effects in males;
26-week oral study in cynomolgus monkeys - LOAEL is from 3 to 10 mg/kg/day based on 30% increased absolute liver weight with no NOAEL;
2-week dermal study in rats - increased liver weight and liver pathology;
2-week inhalation study in male rats - liver effects at 7.6 mg/m3; severe toxicity including the death of one animal at 84 mg/m3, increased lung and testes weight at 84 mg/m3;
inhalation developmental toxicity study in rats - maternal deaths, reduced maternal weights, reduced fetal weights at 25 mg/m3;
oral developmental toxicity in rabbits - increase in skeletal variations at 50 mg/kg. The concern for PFOS is for liver toxicity, liver cancer, thymus effects, reproductive toxicity and developmental toxicity.
*CEB HEALTH: High concern (Inhalation, dermal, and drinking water).

TOXICITY DATA: negative in Salmonella and E coli
uncertain positive for chromosome aberrations in CHL cells, positive results seen at the threshold of or beyond the point of cytotoxicity
28-day oral study in rats - NOEL = 5 mg/kg; hematological findings and changes in blood chemistry at 100 mg/kg; effects on the liver , kidneys, and forestomach at 100 mg/kg; increased kidney weights at 25 and 100 mg/kg
pharmacokinetic study in rats, iv administration - systemic exposure was 7 times higher in males than females; serum half-life = 9.4 hours in females and 5.4 hours in males
pharmacokinetic study in monkeys, iv administration - pharmacokinetic parameters in serum were similar between genders; males appeared to have a higher exposure and longer half-life than females
acute oral study in rats - LD50 = 500 mg/kg

test data for [redacted] were:
rat acute oral LD100 = 2.0 g/kg with systemic toxic signs, with

NOEL = 300 mg/kg
moderate skin irritation in rabbits
severe eye irritation in rabbits
Ames test was negative
E. coli test was negative
no skin sensitization in mice up to 50% ai (LLNA)

test data for a [redacted] analog, [redacted] were:
liver toxicity in rats during an acute toxicity test at 0.600 mg/kg
liver toxicity at 4 mg/kg during a dog acute toxicity test

concern for another analog, [redacted], [redacted], were:
rat 90-d NOEL 0.030 mg/kg/d based on liver toxicity and effects to the lungs

ECOTOX: Measured toxicity values for the PMN substance:

fish (OM) 96-h LC50	>	100.0	M SR,M
fish (OM) 96-h LC50	>	500.0	M SR,M
daphnid 48-h LC50	>	100.0	M S,M
algal 72-h EC50 c	>	100.0	M S,N
algal 72-h EC50 a	>	100.0	M S,N
algal 72-h EC50 r	>	100.0	M S,N
fish ChV	>	50.0	P F96/ACR10
daphnid ChV	>	10.0	P D48/ACR10
algal 72-h ChV	>	10.0	P

Predicted (P) and measured (M) toxicity values in mg/L (ppm) FOR [redacted]

fish (FHM) 96-h LC50
fish (FHM) 96-h LC50
fish (FHM) 96-h LC50
fish (FHM) 96-h LC50
fish (FHM) 96-h LC50
fish (FHM) 96-h LC50
fish (FHM) 96-h LC50
fish (FHM) 96-h LC50
fish (FHM) 96-h LC50
fish (FHM) 96-h LC50
fish (FHM) 96-h LC50
fish (BG) 96-h LC50
daphnid 48-h LC50
daphnid 48-h LC50
daphnid 48-h LC50
daphnid 48-h LC50
daphnid 48-h LC50
daphnid 48-h LC50
daphnid 48-h LC50
daphnid 48-h LC50
daphnid 48-h LC50
green algal 96-h EC50
green algal 96-h EC50
green algal 96-h EC50
green algal 96-h EC50
green algal 96-h EC50
green algal 96-h EC50
green algal 96-h EC50
green algal 14-h EC50
green algal 14-h EC50
ss 0.5-h EC50 O2
fish chronic value
daphnid ChV
algal ChV a
algal ChV a

[redacted]

Predictions are based on SAR-test data for PFOA; SAR chemical class = PFOA; pH7; effective concentrations based on 100% active ingredients and mean measured concentrations; DW hardness < 150.0 mg/L as CaCO3; and DW TOC <2.0 mg/L;

moderate concern for aquatic toxicity;
high concern for reproductive toxicity to birds and wild mammals due to chronic toxicity observed in mammals;
assessment factor = 10.0
concern concentration = 1.0 mg/L (ppm)
*CEB ECOTOX: All releases to the environment with CC = 1000 ppb

[redacted] [redacted]

GTOX Report

PMN No.
P-08-0088

CAS No. [redacted]

Rcvd:
11/14/07

OECD
Incomplet

ID: Rec# 6 : 552

S/A
S

Name of Analog

Reviewer
JVR

		with activation	without activation	Positive Strains
Salmonella Assay:		N	N	
Chromosomal Aberration	**CHO:**			
	CHL:	P	P	
	V79:			
E. coli Reverse Mutation:		N	N	
Mouse Micronucleus Assay:	Route:			
Rat Hepatocytes Unscheduled DNA Synthesis:				

Other GTOX Results

Comments

Biodeg OECD301C

ECOTOX: X

Fate:

WS/Log P: **WS: Soluble in water (MSDS; pg. 23)**

Toxicology Report

PMN No.	CAS No.	Rcvd:	OECD	ID: Rec# 6 : 558
P-08-0088	[redacted]	11/14/2007	Incomplete	

S/A	Name of Analog	Reviewer	Study#:
S		JVR	558

Study Type	Species	Sex	Route
STOXRPDS	RATS	MF	GAVG

Test Substance Description

[redacted]

Test Conditions

Study duration: 6 weeks; Strain: Crl:CD(SD); Wt/Life Stage: 132.7- 365.6 g/5 weeks ; No Groups/No. per group: 6/10 ; Controls: purified water (vehicle and recovery control); Dose range: 0 (vehicle), 5, 25 or 100 mg/kg/day; Test conditions (dose regimen): The test substance was administered daily to rats by oral gavage for 28 days followed by a 14-day recovery period. Observations were made on clinical signs, sensorimotor functions, body weight, food intake, hematology, blood chemistry, urinalysis and pathology. Doses were based on results from a previously conducted 14-day repeated oral dose toxicity study in rats at 50, 250, 500 or 1000 mg/kg/day.

Results

Hematological findings in the 100 mg/kg group included decreased RBC and Ht in males and females, increased Reticulo in females and prolonged PT in males. Changes in blood chemistry included increased ALT and A/G ratio and decreased T-Cho in males of the 100 mg/kg group. Absolute and relative kidney weights were increased in males treated with 25 mg/kg or more and absolute and relative liver weights were increased in males in the 100 mg/kg. At necropsy, observations of the high dose group included an elevation in and hyperplasia of (squamous epithelium) the limiting ridge in the forestomach in males and females and enlargement of the liver in males. Diffuse hypertrophy of hepatocytes with granular degeneration in males and focal necrosis of hepatocytes in females were observed in the 100 mg/kg group. In the recovery test, all observed changes were completely reversible. NOEL = 5 mg/kg/day.

Toxicology Report

PMN No.	CAS No.	Rcvd:	OECD	ID: Rec# 6 : 559
P-08-0088	[redacted]	11/14/2007	Incomplete	

S/A	Name of Analog	Reviewer	Study#:
S		JVR	559

Study Type	Species	Sex	Route
OTHR	RATS	MF	OTHR

Test Substance Description

[redacted]

Test Conditions

Study duration: 5 days; Strain: CrlCD(SD); Wt/Life Stage: 157-248 g/ 7 weeks ; No Groups/No. per group: 1/18 and 1/6 ; Controls: N/S; Dose Level: 10 mg/kg; Test conditions (dose regimen): Pharmacokinetic study; The test substance (0.5 mL) was administered intravenously once to a pharmacokinetic (blood collection) group and an excretion group. Following treatment, observations were made up to 48 hours at which time animals were euthanized. Parameters evaluated included clinical observations, body weights, food consumption, toxicokinetics, pharmacokinetic profile (blood chemistry) and excretion profile (urinalysis).

Results

Systemic exposure was 7 times higher in males than in females, the test substance remaining mostly in the circulation of male rats but having extensive tissue distribution in female rats. The terminal elimination phase in serum had a half-life of 9.4 and 5.4 hours for female and male rats, respectively. The half-life in urine was 1.8 and 5.4 hours for females and males, respectively. Overall, elimination in the urine of both sexes was 65% and most of the test substance was eliminated over 12 hours post-dosing in both sexes. The elimination of the test substance in the urine appeared to be mono-exponential for male rats and was not log-linear for females.

Toxicology Report

PMN No.	CAS No.	Rcvd:	OECD	ID: Rec# 6 : 560
P-08-0088	[redacted]	11/14/2007	Incomplete	

S/A	Name of Analog	Reviewer	Study#:
S		JVR	560

Study Type	Species	Sex	Route
OTHR	MONK	MF	OTHR

Test Substance Description

[redacted]

Test Conditions

Study duration: 20 days; Strain: cynomolgus; Wt/Life Stage: 2003- 2751g/2.5-3.5 years; No Groups/No. per group: 1/6; Controls: N/S; Dose Level: 10 mg/kg; Test conditions (dose regimen): Pharmacokinetic study; Following a 13-day acclimation/pretest period (at which time physical examinations were performed), the test substance (5 mL/kg) was administered intravenously once to one group of monkeys. Observations were made up to 7 days post-dosing. Parameters evaluated included clinical observations, body weights, toxicokinetics, excretion profile (urinalysis) and pharmacokinetic profile (blood chemistry).

Results

All animals survived. Pharmacokinetic parameters in serum were similar between genders; male monkeys appeared to have a higher exposure and longer half-life than female monkeys. On average, about 60-65% of the administered dose was recovered in the urine during the 7 days post-dosing.

Toxicology Report

PMN No.	CAS No.	Rcvd:	OECD	ID: Rec# 6 : 561
P-08-0088	[redacted]	11/14/2007	Incomplete	

S/A	Name of Analog	Reviewer	Study#:
S		JVR	561

Study Type	Species	Sex	Route
ATOX	RATS	MF	GAVG

Test Substance Description

[redacted]

Test Conditions

Study duration: 12 hours; Strain: Sprague-Dawley CD (Crl:CD(SD) IGS BR); Wt/Life Stage: 203-294 g/ 8-12 weeks; No Groups/No. per group: 1/3 and 2/3; Controls: N/S; Dose Level: 300 or 2000 mg/kg; Test conditions (dose regimen): OECD TG 423 "Acute Oral Toxicity"; The test substance (10 mL/kg) was administered to the first group of three animals at the high dose level by oral gavage. Based on the effects, a second group was administered a lower dose in the same manner. Upon observation of no severe effects, another group was dosed in the same manner at the same low dose level. Observations were made up to 4 hours post-dosing, at which time they were euthanized.

Results

All animals treated at 2000 mg/kg died one of which was killed in extremis. No deaths were noted in animals treated at the 300 mg/kg dose level. Two high dose animals exhibited hunched posture, ataxia, lethargy, decreased respiratory rate, noisy respiration, dehydration and diuresis. Abnormalities noted at necropsy of the animals that died during the study were abnormally red lungs, dark liver, dark kidneys and clear liquid present in the stomach. LD50 = 500 mg/kg

NCSAB SAT REPORT		[redacted]?(Y/N):
PMN:	P-08-0088	CAS RN: [redacted]
Chemical Name: [redacted]		Analogs: [redacted]
		Production Volume: [redacted]

Structure:

2 Nov 2007

[redacted]

Use:
Emulsifier [redacted]

Formula:	[redacted]		Eq Wt:		
Mol Weight:	[redacted]	Wt%<500:		Wt%<1000	
MP:	[redacted]		BP:	>500	VP: <0.045
H2O Sol (g/L):	Dispersible	Physical State:	[redacted]	Log P:	

Endpoint (mg/L)	Est. Value	Meas. Value	Comments
Fish 96-h		>100 >500	
Daphnid 48-h		>100	
Algal 96-h		>100	
Fish ChV			
Daphnid ChV			
Algal ChV			
BCF			

CHEMICAL CLASS:				SAR: [redacted]	
ECOTOX CONCERN	H	M	L	CONCERN CONCENTRATION	
DATE				ASSESSOR:	

OPPT STRUCTURE ACTIVITY TEAM (SAT) MEETING DATE Nov. 27, 2007

ATTENDEES	SIGNATURE
CHEMISTRY	
___ Paul Bickart	
___ Diana Darling	
___ Rich Engler	
___ Greg Fritz	
___ Daniel Lin	
✓ Kathy Schechter	Kathy Schechter
ENVIRONMENTAL FATE	
___ Bob Boethling	
✓ Wen-Hsiung Lee	[illegible]
___ Laurence Libelo	
___ David Lynch	
___ Andy Mamantov	
HEALTH	
___ Katherine Anitole	
___ Michael Cimino	[illegible]
✓ Steve Cragg	Steve T Cragg
✓ Leonard Keifer	[illegible]
___ David Lai	
✓ Jim Murphy	[illegible]
___ Deborah Norris	
✓ Ronald Ward	[illegible]
✓ Yin Tak Woo	[illegible]
ENVIRONMENTAL EFFECTS	
✓ Gordon Cash	Gordon Cash
___ Vince Nabholz	
___ Maggie Wilson	
SAT CHAIR/OTHER	
✓ Rebecca Jones	Rebecca Jones
___ Leonard Keifer	
___ Vince Nabholz	
✓ Jim Kwiat	[illegible]