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Exhibit 1489 State of Minnesota v. 3M Co., Court File No. 27-CV-10-28862

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Toxicology Contribution to White Paper

Prepared by:

John L. Butenhoff, Ph.D., DABT, CIH

February 28, 1998

3M sells products which contain the series of chemical compounds built from the parent molecule, perfluorooctanesulfonyl fluoride (POSF), as either intentional components or residual contaminants. These chemicals include, in order of increasing molecular size, Perfluorooctane Sulfonate (PFOS), N-Ethyl Perfluorooctane Sulfonamide (N-Et FOSamide), N-Ethyl Perfluorooctane Sulfonamidoethanol (N-Et FOSE), and the mixture of Mono-, Di- and Tri[N-Ethyl Perfluorooctane Sulfonamidoethyl] Phosphates (Monoester, Diester, and Triester, respectively). All of these molecules incorporate the PFOS structure, which is not known to degrade metabolically.

Risk is related to exposure and bioavailability as well as toxicity. The data suggest that, with the exception of diester and triester, all of these molecules are appreciably absorbed form the digestive system. Specific absorption studies show that absorption from the digestive system decreases with molecular weight. In other words, PFOS is > 95% absorbed, N-Et FOSE is > 75% absorbed, Monoester is approximately 40% absorbed, and Diester and Triester do not have appreciable absorption. While we have no specific data n the N-Et FOSE milde, its significant sub-chronic oral toxicity suggests that it is well absorbed.

After absorption of N-Et FOSE or N-Et FOSamide, PFOS can be found in various tissues, with the largest relative amounts found in liver and blood. Based on an intravenous injection study using PFOS, it appears that 25 % of the dose can be found in the liver after 89 days, and 3 % in the plasma. There is little concentration in fat. Evidence suggests that PFOS is highly protein bound, and it has a high affinity for fatty acid carrier proteins. Other evidence suggests that it can incorporate into membranes and increase membrane fluidity.

All of these molecules could be expected to degrade metabolically in some proportion to the PFOS structure as an end-stage metabolite. Other metabolites are known, such as the N-Ethyl Perfluorooctane Sulfonamido Acetate (for example). We do know that the N-Et FOSE, Monoester and the N-Et FOSamide will form PFOS metabolically. There is also evidence to suggest that N-Et FOSE and Monoester will form the N-Et FOSEmide as well as other metabolites.

PFOS is very effective at ion pairing with proteins, and has a high affinity for fatty acid carrier proteins such as albumin and L-FABP. PFOS also has an amphoteric nature which would suggest an affinity for incorporation in membranes. Because of these properties, it is not surprising that PFOS is slowly eliminated from the body, once absorbed. In rats, approximately 60 % of a given dose was still present after 89 days. With good absorption (> 95 %) and slow clearance from the body, chronic ingestion can significantly contribute to observed biological effects due to accumulation of PFOS.

With the exception of the Monoester, Diester, and Triester, which have not been studied as pure compounds, these molecules appear to share the similar toxic effect of severe weight loss and anorexia. In the case of PFOS, N-Et FOSE, N-Et FOSamide and Monoester, there is potential for cumulative toxicity over time. The similar values of the product of dose x time with respect to total dose (mg/kg/d x days) would be expected to and does appear to lead to a similar degree of toxicity. The primary toxic effect appears to be metabolic stimulation or metabolic wasting. This is hypothesized to be due to an effect on fatty acid metabolism, membrane function, protein synthesis and/or mitochondrial bioenergetics. These compounds lack genotoxicity but have NOAELs or LOAELS generally in the range of 0.1-1 mg/kg/d. Cumulative toxicity and toxic endpoint will certainly affect the value of the LOAEL or NOAEL.

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Overview Assessment of Information Adequacy

Prepared by:

John L. Butenhoff, Ph.D., DABT, CIH February 28, 1998 At the direction of Larry Zobel, MD

Note bene: This table should not be construed to suggest that all areas not noted as adequate should require specific studies in those areas. For example, a better understanding of monoester metabolism may preclude specific studies on monoester, if studies are adequate for known metabolites. This table is meant as a framework for the prioritization process.

Information	Information	Adequacy by Molec	ule (Adequate me	ans no additional v	vork warranted)
	7977	লগ্রন্থার এর জিলার জন্ম		12010	Mono-ue:
GI Absorption	Good	Good	Fair (toxic)	Fair (toxic)	Fair (impurity)
Distribution	Good	Good	None	Poor	Good
Metabolism	Good	Fair	None	Fai-	Fair
Excretion	Good	Good	None	Unknown	Good
Acute Toxicity	Adequate	Adequate	Good	Adequate	Poor
Sub-Chronic	Adequate	Adequate	None	Adequate	None or Poor (to extent that monoester is a component of FC-807)
Chronic	None or Poor (to extent that arnide is metabolite of N-EtFose)	Fair (impurity)	None	None or Poor (to extent that amide is metabolite of N-EtFose)	None
Reproductive	None	None	None	Adequate	None
Developmental	Adequate	Adequate	None	Adequate	None
Genotoxicity	Adequate	Adequate	Adequate	Adequate	None
Immunotox.	None	None	None	Unknown	None
Protein Bind.	Good	Good	None	Good	None
Bioenergetics	Good	Good	None	Good	None
Peroxis. Prolif.	Good	None	None	None	None
Food Transfer	Poor	Adequate	Poor to Good	Poor	Poor
Milk Transfer	Poor	Poor	None	Poor	None
Placental Trans	None	None	None	None	None

Other areas of investigation to be considered:

- Additional mechanistic work
- Sources of exposure other than Scotchban
- Preferential partitioning, distribution, metabolism based on branched vs. linear isomer structure
- Multisource risk assessment

Facts/Obscrvations	Significance/Possible Interpretation 201 1481121 Questions/Knowledge: Gaps V	With Questions/Knowledge/Gaps	Approactics/Recommendations
PI:OS is basis for large number of cliemistrics and applications	Potential for human and environmental exposure, direct or indirect, is high		
PFOS is persistent in the environment	Docs not degrade; may gradually accumulate, either in dispersed fashion or through concentration	 PFOS bioconcen Jation; 2) environmental fate; 3) current prevalence in environment 	
PFOS is readily absorbed form the GI and is toxic with cumulative toxicity higher than acute toxicity and subchronic cumulative toxicity dosc-response curve is quite stoep: 90-day oral studies in rats and monkeys resulted in deaths at 6 mg/kg/d in rats via feed and 4.5 mg/kg/d in monkeys via water, however rats survived 1.8 mg/kg/d and monkeys survived 1.5 mg/kg/d :: All pregnant f. rats died within five days after 20 mg/kg/d for 10 days (days 6-15 of gestation); however, they survived less than 10 mg/kg/d under same circumstances (1 and 5 mg/kg/d) with NOAEL at 1.0 mg/kg/d	Cumulative tox coupled with lack of climination presents a true concern for lifetime cumulative doscrbody burden; 2) good interspecies comparison on subchronic basis with regard to lethality, suggesting common mechanism of action; 3) seldom see aub-chronic study dose response curves as steep; 4) a critical threshold body burden appears to be reached over time	 Biological exposure guideline is necded; 2) what are the biologicaly relevant endpoints which determine the critical toxic response; 3) what is the threshold body burden 	 Develop biological exposure guideline; investigale plasma concentration vs. liver concentration; 3) do an acute and subchronic study to look at lethal body burdens; 4) study blood concentrations in workers; 5) discover primary mechanism of toxicity
PFOS is accumulative in mammals and is concentrated in the liver (10 x other tissues) and is not climinated	 potential for drug interactions and other competitive effects; 2) may provide clue to mechanism; 3) potential for reaching critical toxic body burden is ligh; 3) may be resorbed in proximal tubule; 4) may undergo enterohepatic circulation; 5) may bioaccumulate 	 what is bioaccumulation potential; 2) are there potential drug interactions; 3) what is the potential for dermal absorption (may have been answered); 4) why is accumulation in liver preferential over other tissues; 5) excretion mechanisms 	 bioaccumulation study; 2) protein binding in plasma; 3) membrane accumulation; 4) L-FABP; 5) impaired transport; 6) differential accumulation in tissue; 7) dermal absorption; 8) ADME with specific reference to enterohepatic circulation, carrier protein and renal clearance
Biochemical effects/interactions: 1) docreased body weights, all species: a) male mice (m.m) 0.05% of dict, 5 days; b) male rats (m.r.) 0.02% of dict, 7-14 days; c) monkeys 1.5 mg/kg/d 90 days; d) rats 1.8 mg/kg/d 90 days; f. rats 10 mg/kg/d 10 days	Scycre metabolic effect		
2) increased liver weights in (rats and (ni.m. but not monkeys)	Species differences, rodent to primate, possibly due to lack of primate responsiveness to PP effect; however, very similar toxic response with respect to tethality; therefore, PP may be secondary to prime toxic mechanism		

FC-95 or PFOS

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1) increased anticocharacteristic for an V		Warnhometry	
	Discretes of DD		
4) Increased beta onioalion (m.m. or I.n.)	DIOINALKCT OL PP		
5) increased catalase in mitochondria and	Biomarker of oxidative stress which could	1) is SOD activity clevaled; 2) are other	
cytosol (m.m.)	reflect uncoupling of oxidative	antioxidant pathways impaired	
	phosphorylation with concommitant		
	increase in superoxide and peroxyradicals		
	or impairment of other antioxidant		
	mochanisms		
6) increased glutathione transferase			
(m.m.)			
7) increased cpoxide hydrolase (m.m.)			
8) increased DT-diaphorase (m.m.)			
9) increased omega- & omega-1-	1) microsomal FA oxidation pathway		
hydroxylation (m.m.)	stimulated; 2) leads to increased		
	dicarboxylates which stimulate PP		
10) increased liver triacylghycerol (m.r.)			
11) increased liver free cholesterol (m.r.)	Could represent increase in mitochondrial		
	FA oxidation leading to decrease in	•	
	phosphatidate phosphohydralase activity,		
	thus stimulating CTP:phosphocholine		
	cytidyltransferase leading to increased		
	phospholipid and docreased triglyceride		
	which could affect formation of		
	cholesterol esters		
12) decreased liver cholesterol esters	d.o. above		
(m.r.)			
13) decreased scrum cholesterol (rats &	d.o. above		
monkeys)			
14) decreased scrum triacylglycerols	d.o. above		
(n.r.)			
15) decreased synthesis of cholesterol	Cholesterol biosynthetic pathway is		
from pyruvate, acctate & 3-hydroxy-3-	impaired prior to mevalonate and may		
methyl-glutarate but not mevalonate (1.h.)	relied low activity of HMU COA		

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Troos is not climitated a dot And there meaningful assays the chanism of testicular alrophy Are there meaningful assays the chronic dosing data; Are there meaningful assays the chronic dosing data; Are there build the chronic dosing data;	previously recommended	reversible testicular atrophy; however,		
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 Previously We don't have chronic dosing data; Are there better surrogates however, there is no evident direct gemotoxicity: would expect tumors in rats related to PP (liver, paacreas, testes); a 2-year swudy of cumulative body burden and tox would help establish biological EG tox and tox and 	recommended			
however, there is no evident direct genotoxicity; would expect tumors in rats related to PP (liver, paacreas, testes); a 2- year swudy of cumulative body burden and tox would help establish biological EG tox and relopmental effects	A 2-ycar bioassay was proviously	We don't have chronic dosing data;	Are there better surrogates	Await results of incclumistic studies
genotoxicity: would expect timors in rais related to PP (liver, paacreas, testes); a 2- year swudy of cumulative body burden and tox would help estublish biological EG tox and velopmental effects	recommended	however, there is no evident direct		and/or design chronic cumulative tox
related to PY (inver, paacreas, textes); a 2- year swurdy of cumulative body burden and tox would help estublish biological tox and velopmental effects		genoloxicity; would exped tumors in rais		study and incorporate mechanistic
tox and velopmental effects		related to PP (liver, pancras, testes); a 2-		endpoints in two species
tox and vetopmental effects		year swiudy of cumulative body burden and tox would help establish biological		
NOAEL for maternal tox and cmbro/fetotox and developmental effects is 1.0 mg/kg/d in rats		EG		
embro/fetotox and developmental effects is 1.0 mg/kg/d in rats	NOAEL for maternal tox and			
	cmbro/fctotox and dcvctopmental effects is 1.0 mg/kg/d in rats			

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Gaps Approaches/Recommendations Ifonamide Approaches/Recommendations ersion; what		rial	
Significanco/Possible Interpretation 14 14:10 Questions/Knowledge Gaps EtPFOSulfonamide toxicity may be in part, to PFOSulfonamide and/or OS; PFOSulfonamidoethanol and OSulfonamidoacctate may be readily is half-life of elimination creted <i>in vivo</i> ; current ADME data is omplete and does not form adequate is on which to assess risk		nt What is basis for male/fcmale difference in sensitivity to branched material	
Significanco/Possible Interpretation N-EtPFOSulfonamide toxicity may be duc, in part, to PFOSulfonamide and/or PFOS; PFOSulfonamidoocthanol and PFOSulfonamidoacctate may be readily excreted <i>in vivo</i> ; current ADME data is incomplete and does not form adequate basis on whith to assess risk	May be primary mechanism of toxicity which could be common to other members of PFOSulfonsmide class	Branched and linear may have different tox patterns, with branched being nore toxic, particularily to male rats	
Facts/Observations PFOS and PFOSulfonamide are found as products of metabolism and formation of PFOSulfonamide is known to occur readily <i>In vitro</i> , also find PFOSulfonamidoacthanol and PFOSulfonamidoacetate as metabolites; prior studies of ADME failed to quantitate PFOSulfonamidocthanol or PFOSulfonamidocthanol or PFOSulfonamidocthanol or PFOSulfonamidocetate, since they looked primarity at ^{1,4} C tabeled ethyl mocity.	The metabolite, PFOSulfonamide, uncouples oxidative phosphorylation in isolated kidney proximal tubules and cortical mitochondria	Acute loxicity is low and has some dependence on isomeric mixture and sex (wide range LD50 rat < 5g/kg (7/10) and NOAEL of 500 mg/kg rat in cottenscod oil; narrow range NOAEL rat 5g/kg aqueous solution; 72.2% linear LD50 rat 2549 mg/kg male 1580 mg/kg female; 31.7 % linear LD50 rat 772 male 1571 female)	Sub-chronic dermal toxicity is low (3- week dermal in rabbits resulted in 8/10 dead at 1000 mg/kg/d and NOAEL of 100 mg/kg/d, males and females) with emaciation, decreased food consumption and body weight, testicular atropy, kidney and ovary weight increases, and effects on G1 lune liwer testes)

FX-12 or N-Ethyl PFOSulfonamide

What were clinical chemistry changes	Common intermediate metabolite	Purity of products			
Possible sign of uncoupling of oxidative phosphorylation	May be able to approach toxicity of entire class al structure activity level	Perhaps a primary toxic form			
Siub-chronic oral tox more serious (female raits survived 17 mg/kg/d for ten days with NOAEL of %.5 mg/kg/d for 8 weeks with no change in food consumption but a 7% change in body weight; NOAEL for 90- day fooding study in male and female raits was approx. 1 mg/kg/d with deaths at approx. 9 mg/kg/d (10/30) and emaciation, weight loss, decreased food consumption, increased liver weight, decreased spleen, lung, heart and kidney weights, hematological and serum chemistry changes (huhat?77), morphologic changes in liver, Gl, lung, testet, histopath changes in liver and kidney, no effect on sperm number or motility - NOAEL 0.6 mg/kg/d - NOAEL of 25 mg/kg/d females and 8 mg/kg/d males, signs of weight loss, testicular atrophy, decreased sperm number and motility, shown in a later study to be reversible	ne fits common in other members of	EtPFOSulfonamide is residual in many applications	Maternal and fetal NOAEL in rats = 1 and 4 mg/kg/d, respectively, maternal and fetal NOAEL in rabbits = 0.1 and 1.5 mg/kg/d, respectively		

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Approaches/Recommendations Assign research into non-food-packaging	1) Assign team of toxicology, lab, and PRL to review adequacy of transfer data and determine what additional work may be needed; 2) verify ADI based on FDA current FDA approach; 3) have ENVIRON review issue; 4) await results on metabolism and risk assessment as issue may be tied to review of FC-95 and EIFOSE remoductive and chronic review	 Complete SRU/ABS in vitro comparative metabolism study; 2) verify results in vivo; 3) identify suitable human surrogate species 	Refer to approaches above	See above			Complete comparative ADME studies
Current uses other than food packaging; Current and protected muchterian volumes	Adequacy of food transfer data for PO ₄ esters, amides and other components; 2) adequacy of current information on FC-807 be considered adequate by current FDA review practior; 3) are mechanistic, segment II, 90-day dog, reprodev and 2-year feeding studies necessary	Knowledge of the overall ADME characteristics of FC-807 as a complex mixture	Whether or not there is a concern for cumulative toxicity based on food transfer data and ADME data	See above			Full understanding of ADME
Significance/Possible Interpretation 1 2010 Cuestions/Knowledge Gaps Widespread exposure and regulatory Current uses other than food packag sentiny	Food use risk from EtFOSE exposure well understood; however, dietary exposure to other components less clearly understood	Doubts concerning ADME characteristics of components of FC-807	Definite species differences (rat to dog); initial response is that this is not a concern; however, if cumulative (see above) it may be a concern	Possible metabolic effect Low contact hazard	Supports low genotoxicity potential	Supports low contact hazard	Potential mathuman metabolic differences may support observation of rat/dog toxicity differences
Facts/Observations Used in high volume for indirect food contact	Thorough risk analysis on dictary cyposure to EtFOSE residues completed by ENVIRON and 1M	ADME data contradictory, old, and based on radiolabel of perfluorinated chain	Differences observed in feeding studies based on species and length of study: 1) 33-day rat NOEL was 60 mg/kg/d; 2) 90- day rat LOEL was 30 mg/kg/d; 3) 90-day dog NOEL was 125 mg/kg/d (high dose)	Corneal opacity observed in PEI study Irritation/sensitization potential is low	Genotoxicity studies are negative (Ames and Yeast, with and without activation, and mouse micronucleus)	Dermal absoption/persistence shows no transport	Limited evidence from comparative metabolism shows extensive metabolism in rat and potential rat/human difference

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Facts/Observations	Significance/Possible Interpretation	Contractions/Knowledge Gaps Contraction	Approaches/Recommendations
Henatocellular adenouua in Ione-lerm	"Cancer" implication is most likely not	Is it possible to revert ACGIH opinion	Support through EPA guidclines for
feeding studies in its which can be	valid for humans; however, with respect	based on mechanistic data	cancer risk assessment, and/or have
explained to relate more specifically to rat			consultant make casc; c.g., Mel Anderson
model based on PP mechanism	presenting human cancer risk based on		or Joe Rodricks
	FDA interpretive policy re contaminants		
	of products in contact with food; ACGIH	-	
	lists as A3 carcinogen;		
Main use of FC-14.3 is as enulsifier for	Potential food and device exposure;	What are residues in applications for	Ask DuPont for information on uses and
TEFLON	exposure in numerous compounding and	TEFLON, particularily, food and device	residues; have PRL investigate current
	processing operations	applications; what is extent of exposure	production volumes
		based on compounding	
In rats, dose dependent clevation in	Possible "cancer" effect which could	Does aroinatase induction occur in higher	Mechanistic studies and consultation
Leydig cell adenoma, explained by	relate to humans if E2 elevated; however,	species; are there other possible	
clevation of E2 by induction of aromatase	workers with > 30 ppm in plasma have	mechanisms; can we argue that a 10%	
	only 10% increase in E2, which	increase in E2 within normal range is	
	represents a threshold	insignificant, especially since we do not	
	-	obsere an increase in testicular cancer	
Evoced workers have 10% F7 increase if	Annear to be at a threshold of response in	Of high dose workers, how long exposed	Analyze work histories on these
I also FC-141 > 10 mm	these workers which compares well to rat	and what is risk of exceeding threshold	employees and estblish EG based on
			places level rather than air concentration
	FC-143 is a threshold); if FC-143		
	accumulates in humant, not much margin		
	of safety		
FC-143 is being re-engineered/phased out	May disappear as product	What is current/future value	Assign to PKL to gamer data
Some antivalence between where rat,	Can relate human serum levels closely to		
monkey and huntan serum PFOA levels	other species data		
are associated with elevation of E2			
Female rats exercte PFOA 10 X more	Is renal climination controlled by E2 in		
rapidly than males rats, but no sex	rat		
difference is seen in mice, rabbits, dogs,			
monkcys			Develop DRDK model rat. human
Humans have very long climination half-		Does Durbont have more data on diministion in humine: need ADMF data:	
life	between rais and numbers	mential for cumulative effect in humans;	
		do we have all data relative to tissue	
		concentration and dose: are there specific	
		carrier proteins for PFOA	
and eveneed underst have significantly	May be PFOA related, since PP reduce		
I ness cardiovoscular discase			
	CoA reductase		

FC-143 or PFOA

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T ain I can	Pancreatic acinar cell tumors in rats	ors in rats	May be relevant to humans if cholestasis	Is this relevant to humans, what is mechanism; what are responses of pancreas; duodenal synthesis and exerction of CCK; bile acids; P450 induction	
Spec.	Dose me/re/d ppm PFOA E2	DOM PFOA	32		
Ĩ	0.64	: ??			
E	1.94	101	+		
ē	6.50	159	+	-	
montecy	3.0	2	2		
monkey		67			
monkey		115	2		
human		>30			

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Facts/Observations	Significance/Possible Interpretation $\mathbb{N} \in \mathbb{R}$	Significance/Possible Interpretation 1: 69 100 100 Occations/Knowledge: Cape 1: 1: 1: Approaches/Recommendations	Approaches/Recommendations
High to extreme acute oral toxicity	High acute toxicity risk	Unsure about dosing and symptoms in study	Have toxicologist: 1) correct summary; 2) check symptoms relative to morbidity and time in study; 3) check reference to cholinesterase inhibition; 4) check preparation of sample and dosing
Lower production volume and fewer use applications are assumed	Limits potential risk	Current production volumes and applications and do these justify recommendations for: 1) acute inhalation; 2) PP; 3) 90-day feeding study	Assign PRL to collect data on current production volumes and use applications and have toxicologist review
Estimated acute dermal toxicity is >250 mg/rg with one death at 14 days with GI symptoms prevalent	Skin is significant route for systemic exposure	What were results of dermal absorption/persistence	Assign toxicologist to find out
Negative genotoxicity assays (Ames c & c/o activation and mouse micronucleus)	Low risk of genotoxicity		
Minimal contact irritation, eyes and stin Ha recommended Seg II and 90-day feeding study			

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		cance/Possible Interpretation in the interpretations/Knowledge/Gans	I Annoaches/Recommendations
McFOSE currently regulated based on	McFOSE is considered a carcinovenic	The extent to which MeEOSE can be	Summer the development of a constrate
EIFOSE data and MeFOSE is basis for	contaminant hy FDA Food Branch and is	concidence cimilarity toxic to BrEOCF	ruetoboli and foricity around for EtEOCE
			Inclabolic and lowering provide for Elevan
	exists on MeFOSE	Dased Oil. 1 J Incladdirc profile; 2) loxicity	
ElEOSE is an immediant intermediate in	Widemand automin to anotherize and		
		I) NIUWICUES UI CAITERIE PICUUCUON	
		VOIUTICS AND USCS OF ELFUSE; 2) What is	production volumes and uses of EIPUSE;
		contribution to exposure from metabolism	2) Support comparative ADME study to
		of FC-807 (see FC-807 review)	more thoroughly understand
			exposure/dose relationships
Wide-range and narrow-range EtFOSE	EIFOSE is comprised of a mixture of	Are there significant differences in	Support: 1) a scrics of comparative in
produced and degree of branching may	unique chemical components and isomers	toxicity based on "range" and branching	vitro studies lookine at specific toxic
	which could have individual influences on		endmints (e.g. culture cell amhiferation
			, comparing (e.g., cylotox, eeu promotatiou, associasme scoliferation asino-horded
			finding): 2) comparative ADME in vitro
Narrow range EIFOSE has always been	See above, and should there he more	See above and is wide range reflective of	See above
used to produce FC-807	concern to investigate narrow range	narmw range i e are there differences	
Tow data is sufit between a second		Continue and about and about date he	Control of the second s
I UX UNIO IS SPIIL DELWEEL FLATOW TANGE		SCC I WO TOWS ADOVE, AND SHOULD LATE DE	See two rows above and support. 1) two-
and whee range	conclusions regarding risk is similarity in	ocveroped on narrow range material to	year locaing study on narrow range
	between wide and narrow range is	support regulatory issues	EIFOSE
	assumed		
FDA considers EtFOSE a carcinogenic	1) EIFOSE exposure acceptable to FDA if	Does SCD want to spend resources to	Business must decide regulatory strategy,
contaminant of FC-807 and applies a risk	limited to 5 ug/day; 2) "cancer" label can	develop data to remove FDA "cancer"	and, if removing FDA "cancer" label is
factor of 5 ug/day	only be removed if supporting data is	label	considered desirable, SCD must commit
	developed		resources for two-year feeding study
Wide range EtFOSE contains	May be responsible for toxicity through	Do other materials contain carboxamides;	Assign Toxicology/PRL team to collect
carhoxamides	metabolism to acids we know to be PP	if so, how toxic are they and how are they	information and propose research plan to
		metabolized	study contribution of carboxamides to
			EIFOSE toxicity
Dcrmal absorption/persistence study was	May represent a significant route of	What was outcome	Assign toxicologist to discover outcome
recommended	cxposure		
Mouse inicronucleus was negative	Genotoxic potential is low	Was UDS done	Assign toxicologist to discover if UDS
Lincar sulfuramide, a possible metabolite	1) May be able to apply sulfuramide data	To what extent is EtFOSE metabolized to	1) support completion of comparative
of EtFOSE, produced decreased sperm	to EtFOSE if suffuramide is metabolite of	sulfuramide and is there a risk of	metabolism studics; 2) have toxicologist
count and motility in does and rats with	ELFOSE; 2) potential exists for	testicular effects	review suffuramide studies for testicular
cffoct being reversible in does based on	reproductive effects; 3) there has been a		effect and compare to available data on
Griffin study, and preliminary	past action against S. C. Johnson Wax by		Eurose
comparative metabolic data shows	EPA with repro effect potential at basis of		
conversion to sulfuramide (rat & man)	concern		
EIFOSE fetotoxic and equivocally	Cannot assess developmental effects risk	Dose representing NOEL for	Support Seg II reproduction study with
teratogenic in ruts without NOEL	without NOEL	fetotoxicity/tcratogenicity	appropriate species after clucinaung

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sex study inGP/Rbt							
Ovarcctomized rats & sex study inGP/Rbt							
Hormonal? PP? Sex diff other species?						. '	
Hormonal? PP7		·					
May explain species differences	·						u
Sex difference in hepatic response (rat)		·					

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