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Telomer Research Program (TRP) Update

Presented to
U.S. EPA - OPPT
25 November 2002

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TRP Presentation Outline

- Introductions, Agenda, Timeline Review
- Telomer Production Mass Balance - Draft
- 8-2 Alcohol Studies : Toxicology, Environmental Fate & Effects
- PFOA Potential Consumer Exposure Route Industry Study
- Conclusions, Discussion & Questions

Telomer Research Program (TRP) : 2002 Key Events

- *January 2002* : METI
- *April 18-19, 2002* : TRP Meeting, Wilmington
- *May 9, 2002* : U.K. DEFRA
- *June 13, 2002* : Environment & Health Canada
- *July 2002* : Joint FMG-TRP Meeting
- *Sept. 2002* : TRP Meeting, Tokyo
- *Oct. 2002* : TRP-EFE Work Team Meeting, Frankfurt
- *Nov. 2002* : U.S. EPA

Telomer Production Mass Balance - Draft

- Global Telomer A equivalents produced in 2000-2002
 - approximately 5- 6.5 Million kg/yr
- Regional Product Distribution :

North America	- 40%
Europe	- 30%
Asia Pacific	- 30%
- Polymers : 80% of total product manufacture
- Preliminary Data Analysis

	C4	C6	C8	C ≥ 10	Total
% of Telomer Production	4%	16%	46%	33%	100%
Polymer	99%	45%	85%	88%	80%
Non-Polymer	1%	55%	15%	12%	20%



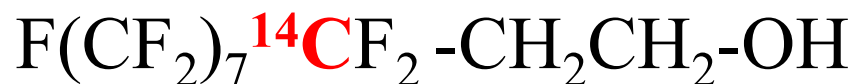
8-2 Alcohol Studies

- Rationale
- Radiolabel Study Material Update
- Toxicology & Descriptive Biology
 - Overall Plan & Timeline
 - 90 Day Subchronic Oral Study results
 - Developmental Study Plan
 - Pharmacokinetics Study Plans and Timeline
 - Reproduction
- Environmental Fate & Effects
 - P-C Properties (8-2 TBA)
 - Effects Studies
 - Fate Studies
 - Environmental Risk Assessment - EUSES Modeling
 - Broader Research Plan Overview

$\text{n-C}_8\text{F}_{17}\text{CH}_2\text{CH}_2\text{OH}$ Selection Rationale

- Selection Rationale Included: Simple, Single, Pure, Representative, and Readily Characterized
- Most Common and Representative from Each of the 4 Major Producers – Includes Both Type and Chain Length
- Telomer 8-2 Alcohol Was Chosen To
 - Be Able to Characterize a Single Compound versus a Complex Product Mixture
 - Enable the Research Team to Study Metabolites in the Pharmacokinetics Work (ADME)
 - Study the Degradation Products and Locations in the Environmental Fate Studies
 - Enable the Team to Measure Critical Physical Property Data
 - Enable the Team to Radio-label a Single Key Compound for the Toxicology and Environmental Fate Studies

Radiolabeled 8-2 Telomer B Alcohol



Needed for Pharmacokinetics & Environmental Fate Studies
Critical Marker

Status

- Synthesis successfully demonstrated : Delivery December 2002
 - Confirming all is in place for safe handling & use
-



Status

- Synthetic Route Demonstrated
- Synthesis complete
- Delivery pending specific packaging instructions
- For Adsorption-Desorption Studies

Telomers Research Program

Toxicology and Descriptive Biology Studies: Timeline*

Telomer 8-2 Alcohol = $\text{F}(\text{CF}_2)_8 \text{CH}_2\text{CH}_2\text{OH}$

		2001				2002				2003			
Test Material	Work	1Q	2Q	3Q	4Q	1Q	2Q	3Q	4Q	1Q	2Q	3Q	4Q
8-2 Alcohol <i>TRP Work</i>	Acute Oral	■	■	■									
	Range-Finding Oral Toxicity		■	■	■								
	Subchronic 90 Day Gavage (Rat) w/ recovery					■	■	■	■				
	Multigeneration Reproduction (Rat)										■	■	■
	Developmental Toxicity (Rat)									■	■	■	
	Bacterial Reverse Mutation			■	■	■							
	Bone Marrow Erythrocyte Micronucleus Test (Rat)			■	■	■							
		■ Work Complete				■ Work Underway				■ Proposed Work			

* This is a proposed timeline and subject to change.

8-2 Telomer B Alcohol

Acute Oral Toxicity – Fixed Dose Method

- Dosing: 5 Male/5 Female rats, 2,000 mg/kg
- Results
 - No clinical signs
 - No mortality
 - Lethal dose >2,000 mg/kg
- Conclusion:
 - Does not present a significant acute toxic risk

8-2 Telomer B Alcohol Genetic Toxicology Testing

- *In vivo* rat micronucleus assay
 - (Covance 22900-0-454 OECD, 1/25/02)
- Dosing: Single dose, male rats, 500, 1000, 2000 mg/kg
- Results
 - No clinical signs of toxicity
 - Not cytotoxic to bone marrow
 - No increase in micronucleated PCE's
- Conclusion: Negative results in test system

8-2 Telomer B Alcohol Genetic Toxicology Testing

- *Salmonella/E. coli* Reverse Mutation Assay
 - (Covance 22900-0-409 OECD, 2/11/02)
- Strains: *S. typhimurium*, TA98, TA100, TA1535, TA1537, *E. coli*, WP2uvrA
 - With and without S9 activation
- Results
 - No toxicity to 5,000 µg/plate
 - No increase in revertants
- Conclusion: Negative results in test system

8-2 Telomer B Alcohol

Oral Range-Finder Study : Summary

- Male rats at 125 mg/kg/day
 - Test Day 81
 - Decreased final body weight (86% of control)
 - Increased relative liver weight (149% of control)
 - Increased incidence of striated teeth (70%)
 - Test Day 159 (Day 75 of recovery)
 - Increased relative kidney weight (114% of control)

8-2 Telomer B Alcohol Range-Finder Study Summary

- Female rats at 125 mg/kg/day
 - Test Day 81
 - Increased incidence of striated teeth (70%)
 - Test Day 159 (Day 75 of recovery)
 - Increased absolute kidney weight (123% of control)
 - Increased relative kidney weight (111% of control)
 - Increased relative liver weight (113% of control)

8-2 Telomer B Alcohol Range-Finder Study

- Substances Identified in Blood Plasma
 - $\text{C}_8\text{F}_{17}\text{CH}_2\text{CH}_2\text{OH}$ = Test Substance
 - $\text{C}_7\text{F}_{15}\text{COOH}$
 - $\text{C}_8\text{F}_{17}\text{COOH}$
 - $\text{C}_8\text{F}_{17}\text{CH}_2\text{COOH}$
- **Note:** These are the only species which were looked for.
Total fluorine analysis shows that these do not account for all fluorinated species in plasma. Radiolabel pharmacokinetic studies are expected to identify and quantitate all species.

8-2 Telomer B Alcohol

90-Day Subchronic Study w/Recovery

Study Overview

- Start : February 2002; In-life complete : 8/21/02
- Control + 4 dose groups (1, 5, 25, 125 mg/kg/day)
 - Parameters:
 - In-life (body weights, clinical signs, etc.), clinical pathology (hematology, clinical chemistry, urinalysis), neurotox (extended clinical observations, FOBs, and motor activity), hepatic β -oxidation, and pathology (gross and histopathology), 90-day recovery
 - Kinetics subset - 5/sex/group
 - Blood, liver & fat (day 175 only)
- Report Issue date - March 2003

8-2 Telomer B Alcohol

90-Day Subchronic Study w/Recovery

Study Findings

- 125 mg/kg/day
 - Body weight gain decreased (M), liver & kidney weight increased (M&F)
 - Degeneration/disorganization of tooth enamel ameloblasts in male rats (not reversible)
 - Focal hepatic necrosis in males (not reversible)
 - Hepatocellular hypertrophy in males (reversible)
 - Renal tubular hypertrophy in males (reversible)
 - Chronic progressive nephropathy in females (not reversible)
 - Increased B-oxidation
- 25 mg/kg/day
 - Liver & kidney weight increased (M&F)
 - Focal hepatic necrosis in males (reversible)
 - Hepatic necrosis in males
 - No effects in females
- 5 mg/kg/day and 1 mg/kg/day
 - No adverse effects observed in males or females

90-Day Subchronic Study w/Recovery
**8-2 Telomer B Alcohol vs. DuPont Telomer B
Alcohol Product**

Observed in Both Studies

- Teeth effects
- At High Doses (>100mg/kg/day)
 - Increased hepatic β -oxidation
 - Increased liver weight
 - Increased kidney weight
- Increased plasma and urine fluoride

Only Observed for

8-2 Telomer B Alcohol

- Increased incidence of focal liver necrosis at 25 and 125 mg/kg/day
- Increased incidence of chronic progressive nephropathy in 125 mg/kg/day females

Developmental Toxicity Study DuPont Telomer B Alcohol Mixture

- Maternal findings
 - Decreased body weight at 500 mg/kg/day
- Fetal findings
 - Increased fetal variations at 500 mg/kg/day
- Maternal and Developmental NOEL = 200 mg/kg/day

8-2 Telomer B Alcohol

Developmental Toxicity Study

- Developmental Toxicity in Rodents (25/sex/dose; 4 groups)
 - Dosing: oral gavage (OPPTS 870.3800)
 - Days 6-20 of gestation
 - Proposed dose levels of 25, 125, and 250 mg/kg/day
 - Parameters
 - In-life (body weights, clinical signs, etc.)
 - Dams at euthanasia: visceral evaluation, uterine weight, CL counts, implantation sites
 - Pups: sex, numbers, weight, visceral & skeletal evaluations, etc.
- Tentative start date – February 2003
- Tentative issue date ~10 months from study start

Radiolabeled 8-2 Telomer B Alcohol Pharmacokinetics Studies

- Radiolabeled Test Substance
 - [3-¹⁴C]8-2 Telomer B Alcohol : $\text{F}(\text{CF}_2)_7^{14}\text{CF}_2\text{CH}_2\text{CH}_2\text{OH}$
- Exposure routes: oral and dermal
 - IV dosing for bioavailability
- Dose levels: 5 and 125 mg/kg
 - Match 90-day oral subchronic toxicity study

Radiolabeled 8-2 Telomer B Alcohol

Pharmacokinetics Studies

- Outline of Experiments
 - Analytical Methods & Material Handling (underway)
 - Pilot Studies (Start date February 2003)
 - Main Studies
 - Absorption experiments (non-radiolabeled)
 - Distribution experiments at plasma $T_{\max}$ and $T_{\max}/2$ (radiolabeled)
 - Elimination and metabolism experiments (radiolabeled)
 - Supplemental Experiments
 - Biliary elimination experiments (radiolabeled), if >20% of dose is eliminated in feces following oral dosing
 - *In vitro* metabolism experiments using rat microsomes and hepatocytes

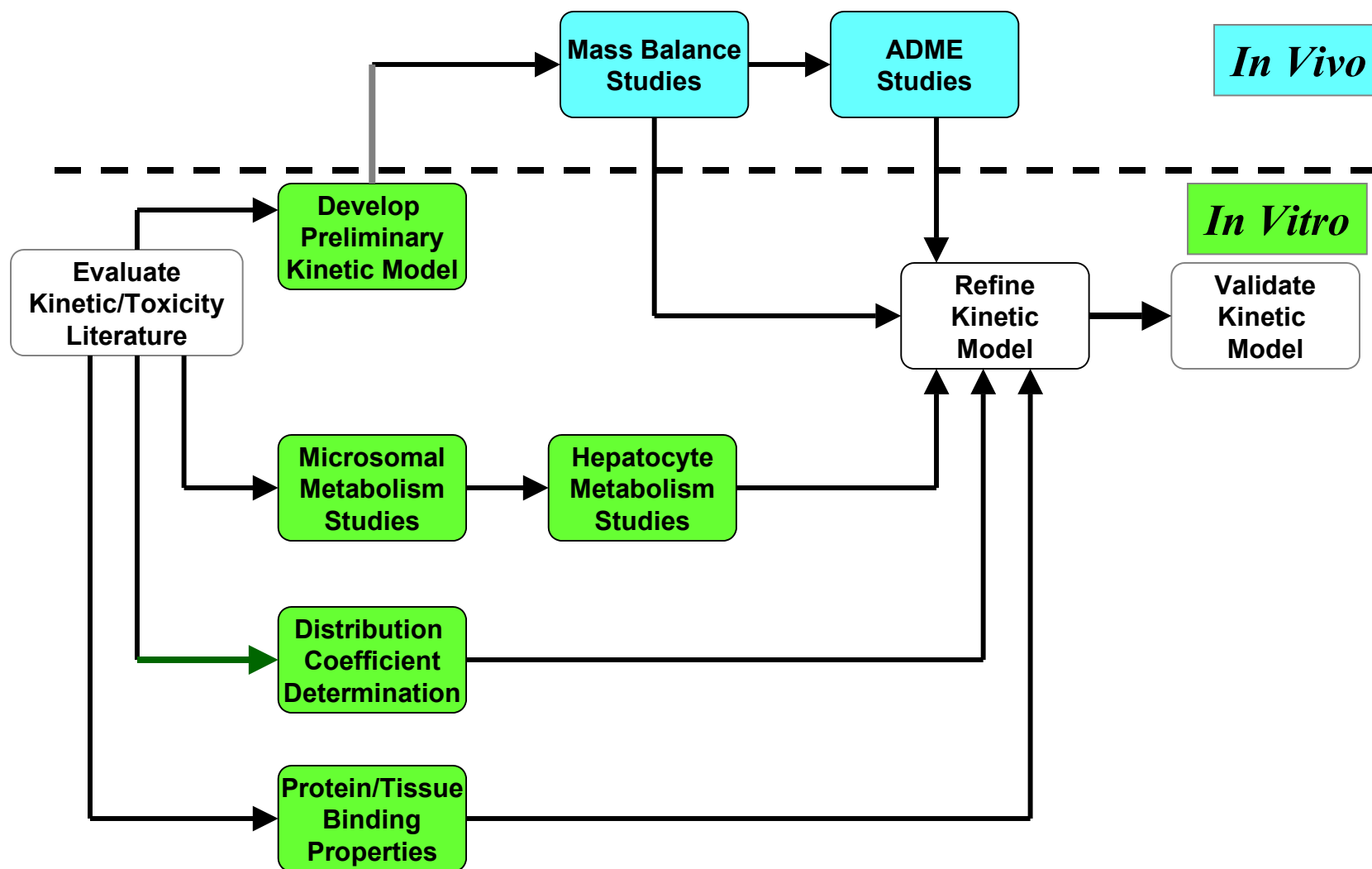
Telomer B Alcohol Kinetic Studies Timeline

Radiolabeled Telomer 8-2 Alcohol = $\text{F}(\text{CF}_2)_7^{14}\text{CF}_2\text{CH}_2\text{CH}_2\text{OH}$

	2002	2003												2004											
	D	J	F	M	A	M	J	J	A	S	O	N	D	J	F	M	A	M	J	J	A	S	O	N	D
Method Development & Material Handling																									
Issue Protocol																									
Pilot Experiments																									
Review Pilot Data with Sponsors																									
Main Study : Absorption																									
Main Study : Distribution																									
Main Study : Excretion																									
Supplemental Experiment, Biliary Elimination (if required)																									
Supplemental Experiment, <i>in-vitro</i> metabolism (if required)																									
DRAFT REPORT																									

* metabolism included in main study line items

8-2 Telomer B Alcohol Pharmacokinetic Studies Flowchart



Telomers Research Program

Environmental Fate & Effects Work Plan

Telomer 8-2 Alcohol = $\text{F}(\text{CF}_2)_8\text{CH}_2\text{CH}_2\text{OH}$

Tier I	Water Solubility X	Sorption X	UV/Vis X	Vapor Pressure X	Volatility HLC, K _{OA} ✓	Hydrolysis X
Tier II	Aerobic Biodeg. Act. Sludge ¹⁴ C ✓	Anaerobic Biodeg. Act. Sludge ¹⁴ C ✓	Indirect Photolysis in Air ✓		Acute Ecotox Studies Fish, Daphnia X	Chronic Nematode Ecotox ✓
	Aging / Sequester ¹⁴ C ✓	Adsorption/Desorption ¹⁴ C ✓	Radiolabel Study Material ✓		OECD 207 Acute Ecotox Earthworm ✓	OECD 208 Acute Ecotox Plant Seedling ✓
Tier III	Water-Sediment Biodeg. ¹⁴ C	OECD 303 WWTP Simulation	Chronic Ecotox Daphnia ✓		Bioconcen. Factor - Fish X	Chronic Ecotox Algae X
	Incineration		Sediment Repro C. ripanus		Chronic Ecotox Fish	
			Sediment Repro L. variegatus BSAF			

X = Work Complete ; ✓ = Work Ongoing / Underway

Fate

Effects

Physical Properties

Physical - Chemical Properties

$\text{n-C}_8\text{F}_{17}\text{CH}_2\text{CH}_2\text{OH}$

- UV / Visible Spectrum - Complete
- Vapor Pressure - Complete
- Sorption - Still Learning
- Water Solubility - Complete
- Henry's Law Constant (K_H) - pursuing T dependent determination

8-2 Telomer B Alcohol Physical-Chemical Properties

Analytical Challenges

- The unique characteristics of the 8-2 Telomer B Alcohol (taken in total) make it challenging to work in complex environmental fate test systems.
- Taken separately, each aspect can be dealt with using simple controls. When all physical aspects are considered, it is difficult to design a system in which analytical measurements can be reliably performed.
- *Considerations :*
 - Solubility
 - Sorption
 - Volatility
 - Transformation and Mass Balance

8-2 Telomer B Alcohol

Acute Tests Results In Saturated Aqueous Solution

- Acute tests for fish, daphnia and algae carried out in saturated aqueous solution are complete
- Details on guidelines and test organisms
 - OECD 203, Danio rerio (30 fish according US EPA in test and control)
 - OECD 202, Daphnia magna Strauss
 - OECD 201, Scenedesmus subspicatus
- Ecotoxicity results in saturated aqueous solution

Organism	Fish	Daphnia	Algae
Exposure	96h	48 h	72h
Result type	NOEC & LC0	NOEC	NOEC _b & NOEC _r
Result	0,18 mg/L	0,16 mg/L	0,20 mg/L
No toxicity observed at the limit of water solubility			

8-2 Telomer B Alcohol

Activated Sludge Respiration Inhibition Test

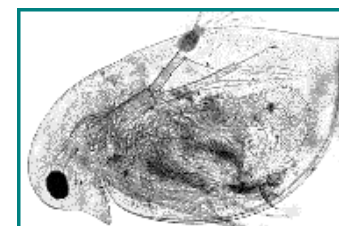
- An Activated Sludge, Respiration Inhibition Test according OECD 209 was carried out
 - with mostly municipal sewage sludge (minor industrial input)
 - at different concentrations, highest nominal concentration was 1000 mg/L
 - no respiration inhibition was observed at highest concentration

Organism	Activated Sludge / Bacteria
Exposure	3h
Result type	NOEC
Result	1000 mg/L
No inhibition observed	

8-2 Telomer B Alcohol

21 Day Daphnia Chronic Test

- 8-2 Telomer B Alcohol Test Substance
- Test type
 - flow through test at solubility limit approx. 150 ppb
 - 4 replicates with 5 animals
- Time schedule
 - working through test details, especially water concentration measurements
 - study to begin when details are worked out (est. 1Q2003)



8-2 Telomer B Alcohol

Earthworm, Nematode & Plant Studies

- Spiking of Sediment & Soil
 - dissolve 8-2 Telomer B Alcohol in a solvent (MTBE), mix with primary substrate (quartz sand); evaporation of MTBE in a ventilated hood; 24 Hr. equilibration
- Potential test substance loss due to evaporation was not observed; recovery was 96% when test substance was re-extracted
- Potential substance loss during the earthworm and plant tests (test period 14 & 21d) will be monitored by a total fluorine analysis at the highest concentration of 1000 mg/kg dw
- Range Finding tests were carried out to decide whether limit or dose response tests are necessary in the definitive tests
- Definitive Studies to begin Nov. 2002 with preliminary reports Jan. 2003

8-2 Telomer B Alcohol

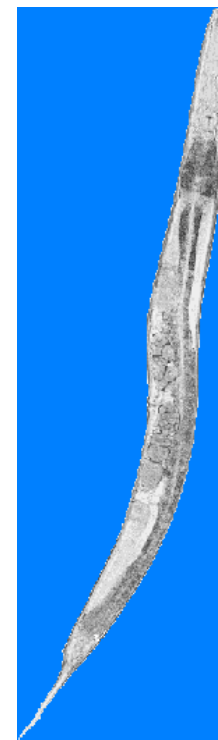
OECD 207 : Acute Earthworm Study

- Tested concentration in Pre-test
 - 10, 100 & 1000 mg/kg dw
- Pre-test Results
 - **mortality**
 - at 10 & 100 mg/kg dw no mortality was observed
 - at 1000 mg/kg dw some mortality was found
 - **loss of body weight of surviving worms was**
 - effects observed at 100 mg/kg dw. (statistically relevant)
 - **pathological effects were observed at**
 - 100 and 1000 mg/kg dw
- Definitive test
 - **5 concentration dose response**
 - **from 10, 32, 100, 320, 1000 mg/kg dw.**



8-2 Telomer B Alcohol Acute Nematode Study

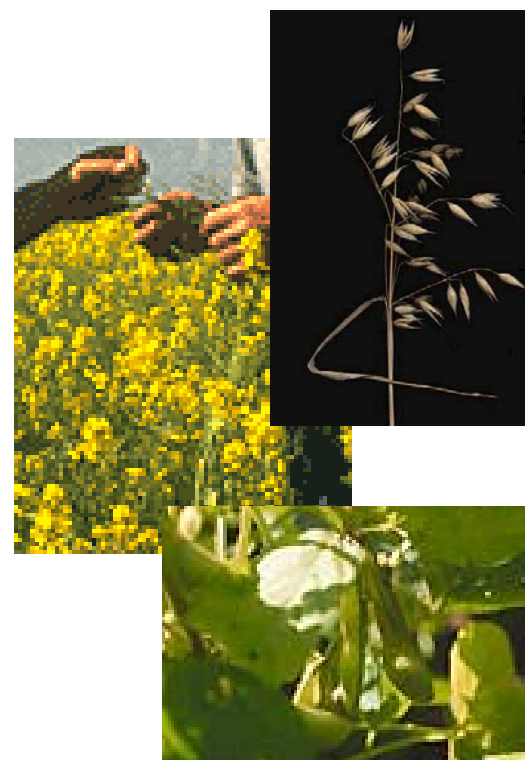
- 3d Reproduction Test
 - carried out according Hoess et al.
- Pre-Test concentration
 - 10, 100 & 1000 mg/kd dw
- Results of the Pre-test
 - body length & egg production
 - no statistically relevant differences to the control group was observed
- Definitive test
 - Limit test at 1000 mg/kg dw



8-2 Telomer B Alcohol

OECD 208 : Plant Seedling Emergence

- species : oat, rape & soybean
- Tested concentration in Pre-test
 - 10, 100 & 1000 mg/kg dw
- Pre-test Results
 - **phytotoxicity**
 - no phytotoxicity at 10, 100 & 1000 mg/kg dw.
 - **rate of emergence**
 - not reduce at 10, 100 & 1000 mg/kg dw.
 - **Inhibition of Biomass Growth**
 - no inhibition for oat and soybean
 - inhibition observed for rape
- Definitive Test
 - **5 concentration dose response**
 - **Oat & Soybean : from 10 mg/kg dw. to 1000 mg/kg dw. (geometric factor $\sqrt[5]{10}$)**
 - **Rape : 6.25, 12.5, 25, 50, 100 mg/kg dw**



8-2 Telomer B Alcohol Bioconcentration Factor

Conducted by METI, Japan on 98% Telomer 8-2 Alcohol

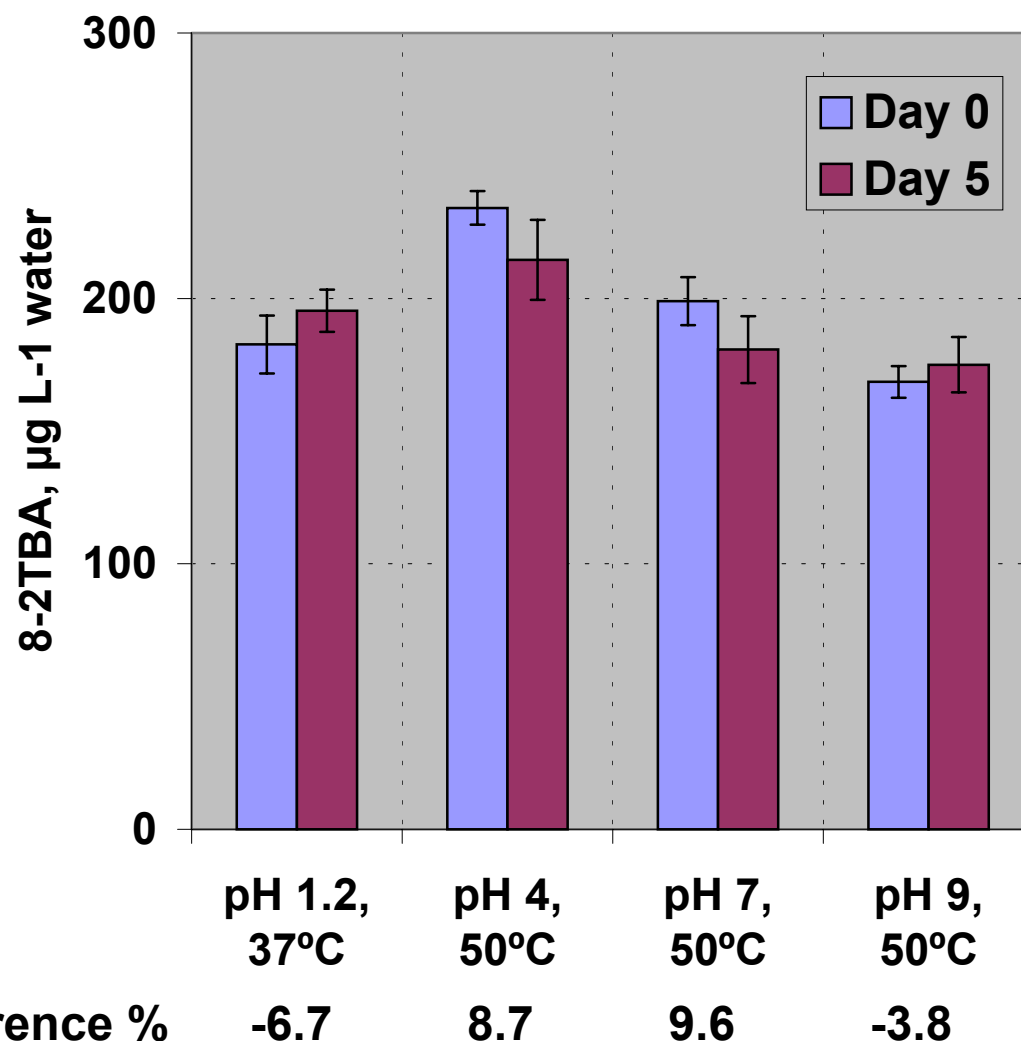
- Acute Study
 - Orange-red killifish (*Oryzias Latipes*)
 - 96Hr LC₅₀ >125 mg/L
- Bioconcentration Study
 - Carp (*Cyprinus Carpio*)
 - 60 Days, Continuous Flow, GC/MS Analysis
 - Report being reviewed by TRP experts

	<u>conc.</u>	<u>BCF</u>
High Exposure	10 µg/L	200 -1100
Low Exposure	1 µg/L	87 - 310

8-2 Telomer B Alcohol Aqueous Stability

Hydrolytic reactions are one of the most common means of non-biological degradation of substances in the environment.

- 150 μg 8-2TBA L^{-1} , sterile conditions
- pH 4, 7, 9 @ 50°C
- pH 1.2 @ 37°C
- Sealed glass vials with Al-foil liners
- 4 replicates at 0 and 5 days
 - Extracted with MTBE
 - Analyzed with GC/MS



8-2 Telomer B Alcohol

Aqueous Stability: Summary

- 8-2 Telomer B Alcohol is hydrolytically (abiotically) stable
 - <10% change in concentration after 5 days compared to day 0

8-2 Telomer B Alcohol **Adsorption-Desorption**

Study Objective:

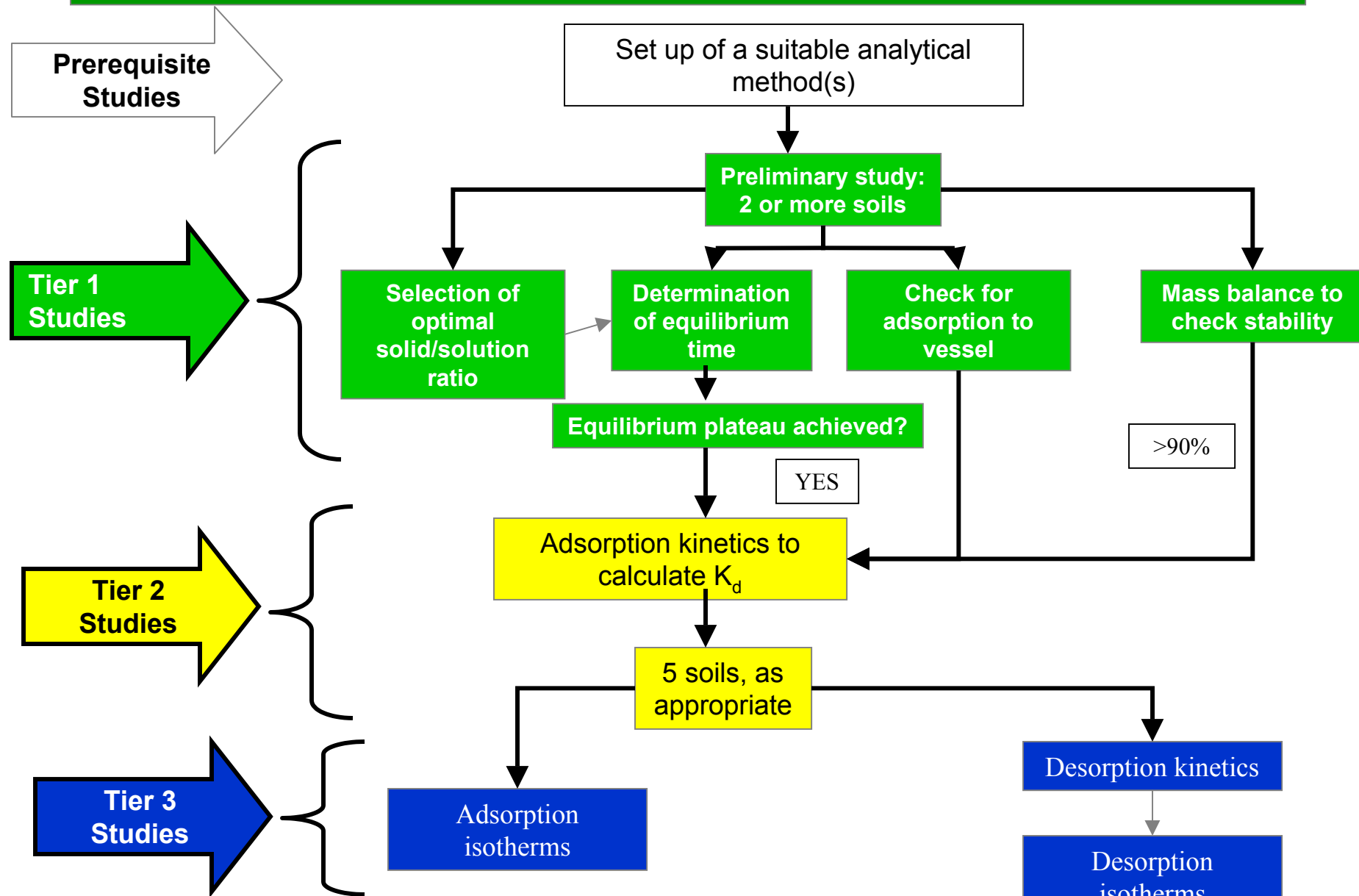
- Provide data for determining the leaching and runoff potential of the test substance in soil and determine the Freundlich adsorption isotherm
- 8-2 TBA

Methods:

- OECD 106: Adsorption - Desorption using a Batch Equilibrium Method;
- Developing analytical capability to extract and quantify test substance
- Non-GLP

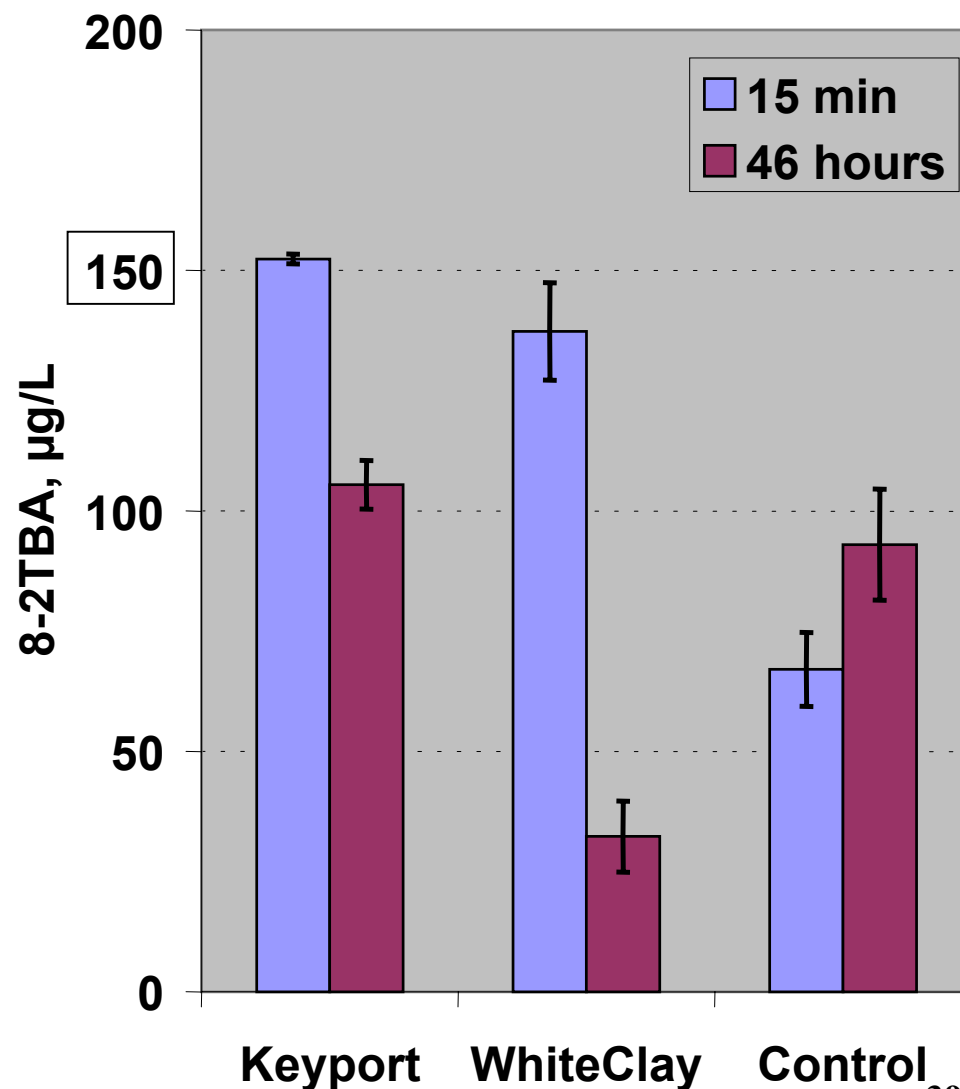
Start Date : Aug 02 End Date: Feb. 03

OECD 106: Adsorption/Desorption using a Batch Equilibrium Method



8-2 Telomer B Alcohol Soil/Water Partitioning Studies

- “Cold” study material for method development
- Two materials
 - Keyport silt loam
 - Sand 17%, Silt 62%, Clay 21%, pH 5.3, OM 4.0%
 - White Clay Creek sand
 - Sand 98%, Silt 2%, pH 7.2, OM 0.4%
- Mix for 15 m and 46 h, separate phases
- Extracted with hexane from solid and water phases, SPE to clean, analyzed
- Low recoveries - need radiolabel study material



8-2 Telomer B Alcohol

Soil/Water Partitioning Studies: Summary

- **At 15 min**
 - Good recovery (>90% of expected) of 8-2 TBA from both soils
 - Recovered primarily from solid phase, except for <4% in solution of White Clay
 - Poor recovery from control with no soil
 - Recovered from both solution and tube
- **At 46 hrs**
 - Poor recovery from both soils
 - White Clay <25% of expected
 - Keyport <75% of expected
 - Improved recovery from control with no soil
 - 62% vs. 45% after 15 m
- Need to improve recovery to achieve mass balance
- Test procedure and analytical method development continues
- Radiolabeled test material $\text{C}_8\text{F}_{17}^{14}\text{CH}_2^{14}\text{CH}_2\text{OH}$ studies to begin Dec. 2002

8-2 Telomer B Alcohol Biodegradation Studies

- 28 Day “Ready” Biodegradation Screening Study
 - Cold Test Material $\text{C}_8\text{F}_{17}\text{CH}_2\text{CH}_2\text{OH}$
 - Test Systems
 - Non-acclimated municipal sludge
 - Acclimated industrial sludge
 - No yeast for co-metabolism
 - Endpoints monitored : parent loss, fluoride
- Begin Dec. 2002

Telomer Research Program
Environmental Risk Assessment (ERA)
EUSES Evaluation

- TRP is utilizing EUSES and the inputs required for this model to help shape and guide its environmental research plans and data generation for 8-2 Telomer B Alcohol

EU ERA Approach with EUSES

- Parameters used in EUSES which influence results most
 - tonnage produced and used
 - release fractions during production & use
 - number of use days
 - elimination & distribution in stp (biodegradation, volatilisation, sorption to sewage sludge)
 - partitioning coefficients for all compartments (water/air, water/sludge, water/suspended solids, water/soil, water/sediment)
 - half-lives in water, sediment & soil

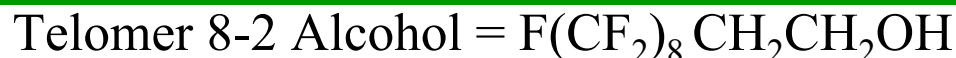
Telomer Research Program

Environmental Fate & Effects : Broader Research Plan

- Develop a Telomer industry view of the product trails for Textiles, Carpet and Paper and a mass balance for each
- Gather existing physical-chemical property and toxicology data from the Telomer Producers on :
 - 6-2 and 10-2 telomer alcohols $[F(CF_2)_nCH_2CH_2OH, n = 6, 10]$
 - telomer olefins $[F(CF_2)_nCH_2=CH_2, n = 6, 8, 10]$to determine whether and where additional data may be needed
- Develop a framework and test strategy to evaluate abiotic and biotic transformation of telomer-containing polymers

Telomers Research Program

Environmental Fate & Effects Studies : Timeline*



F = Fate Study ; E = Effects Study P = Physical Property Study		2001		2002				2003			
Work		3Q	4Q	1Q	2Q	3Q	4Q	1Q	2Q	3Q	4Q
F	Hydrolytic Stability										
F	Adsorption / Desorption (14C)										
F	Aging / Sequestration (14C)										
F	Aerobic Biodegradation (14C)										
F	Anaerobic Biodegradation (14C)										
F	Indirect Photolysis in Air			CNRS							
E	Acute Fish : Fathead Minnow			done							
E	Acute Invertebrate : Daphnia magna			done							
E	Biological Concentration Factor (BCF) (14C)			complete							
E	90 Day Rainbow Trout Chronic										
E	21 Day Daphnia Magna Chronic										
E	72 Hr Algae Acute & Chronic			done							
E	Acute Earthworm (14 Day)										
E	Acute Plant Seedling (21 Day)										
E	Chronic Nematode (3 Day)										
P	Water Solubility, UV/Vis, Vp, Sorption	done									
P	Temperature-Dependent Henry's Law Constant										

* This is a proposed timeline and subject to change.

Work Complete

Work Underway

Work Planned

PFOA Potential Consumer Exposure Study

- The TRP will focus in *two principal areas* in an effort to determine whether PFOA may arise from consumer articles treated with telomer-based products.
- **Consumer Articles** Treated with Telomer-based Products
 - Textile, Carpet, Paper
- **Telomer-based Products** used to “treat” the Consumer Articles
 - Acrylic Polymeric products are used most commonly in these applications
 - The “Telomer” functionality is introduced via an acrylic monomer bearing the Telomeric, $F(CF_2CF_2)_nCH_2CH_2-$, group
 - Other relevant Telomer product types are Urethane Polymers and Phosphates

PFOA Potential Consumer Exposure Study

Action Plan Overview

Samples :

- Actual Consumer Articles : representative textile, carpet and paper articles from **each** TRP member company
- Product : the actual products that were used to treat the above consumer articles

Analytical Methodology:

- A specific method will need to be developed for each substrate (textile, carpet, paper) and product matrix
- Method development will establish LOD and LOQ
- May need isotopically enriched (^{13}C) and other chemical standards
- Analysis to be done by third-party laboratories - will need to find and “qualify” labs

Timing:

- Goal is to have the majority of data analysis and interpretation by April 2003

Conclusions, Discussion, & Questions