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September 24, 2001

AR 226
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Karen Lannon
U.S. EPA, OPPTS
Document Control Center
401M Street, S.W. (TS-7407)
Washington, DC 20460

Reference: AR266

Dear Ms. Lannon:

I have once again prepared authentic sanitized copies of the two presentations we gave on February 21, 2001. A paper copy of each presentation is enclosed for the public record.

These presentations are as follows:

"DuPont Research Program Update and Status Report" - February 21, 2001

and

"Telomer Research Program Update and Status Report" - February 21, 2001.

Each of these reports has been company sanitized. They do not contain TSCA CBI. Each and every chart that has had CBI removed has been marked with the following note: "CBI Information has been redacted."

Please let me know if you have any additional questions on these two documents. You can reach me via phone on (302)992-3672 or fax on (302)892-1135. My email address is stephen.h.korzeniowski@usa.dupont.com.

With regards,

Steve

Stephen H. Korzeniowski
Market & Business Manager

SHK/klo
Attachment

Company Sanitized

Telomer Research Program Update and Status Report

Presented to U.S. EPA, OPPT

21 February, 2001

Company Sanitized

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TRP Member Companies

- Asahi Glass
- Atofina
- Clariant
- Daikin
- DuPont

Agenda

- TRP
- Toxicology & Descriptive Biology
- Pharmacokinetics
- Radiolabel
- Environmental Fate
- Environmental Effects
- TRP Database
- Summary

Telomer Research Program (TRP)

- Key Events Timeline
  - *June 20, 2000* : Formal Organization Proposal
  - *July 7, 2000* : Met with U.S. EPA
  - *July 11, 2000* : Met with METI
  - *August 14-15, 2000* : First Meeting as Formal Consortium, Toxicology Planning
  - *October 23, 2000* : Present Update to U.S. EPA
  - *October 30, 2000* : Present Update to METI
  - *January 9, 2001* : Environmental Fate & Effects Research Team Meeting
  - *February 21, 2001* : Next U.S. EPA Meeting
  - *March 2, 2001* : Next METI Meeting
  - *March 20-22, 2001* : TRP Meeting

TRP Review with U.S. EPA : 23 Oct. 2000

- TRP Members, Principles, Structure, Processes
- Chemical to be tested : n-$C_8F_{17}CH_2CH_2OH$
  - Toxicology and Descriptive Biology Studies : Protocol Review
  - Pharmacokinetics Studies : Protocol Review
  - Radiolabel Work
  - Environmental Fate Outline
  - Overall Timeline
- Path Forward Items

U.S. EPA Comments & Feedback : 23 Oct 2000

- Develop communication plan : Deliver the same message to other Global Regulatory Agencies (OECD, MITI, UK DETR, Environment Canada, etc.)
- Program is very well designed. Like Pharmacokinetics focus.
- 8-2 Telomer Alcohol as study compound accepted.
- TRP should consider multiple species (≥ 2) for developmental toxicology work.
- Biodegradation studies are an important area; use radiolabeled material.
- Environmental Fate & Effects work is critical. Start soon even if phased in. Want to review program when methods are complete. Feb 2001 target.

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TRP Chemical to be Tested

- Telomer 8-2 Alcohol:
  $n\text{-}C_8F_{17}CH_2CH_2OH$

- Purity >99%, and characterized
- Sample made, 20 kg

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n-$C_8F_{17}CH_2CH_2OH$ Analysis Profile

- Purity > 99% by G.C.
  - 99.2% n-$C_8F_{17}CH_2CH_2OH$
  - no other $C_nF_{2n+1}CH_2CH_2OH$ species
  - 0.8% impurity

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TRP Toxicology and Descriptive Biology Studies : Timeline

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TRP Toxicology and Descriptive Biology Studies

- Acute Oral Toxicity - Fixed Dose Method

  -Objective: to assess acute oral toxicity from administration of compound to rats by oral gavage

- Repeated-Dose Oral Toxicity Gavage Range-Finding Study in Rats

  -Objective: to determine appropriate dose levels for use in a 90-day oral subchronic study

TRP Toxicology and Descriptive Biology Studies

- Subchronic Toxicity: 90-Day Gavage Study in Rats with Recovery

  -Objective: to evaluate the potential subchronic toxicity and reversibility of toxicity and concentration of parent compound and metabolites in the blood when 8-2 alcohol is administered to male and female rats.

  The oral route of administration was selected because it provides a controlled and effective means of compound delivery.

TRP Toxicology and Descriptive Biology Studies

- Developmental Toxicity Study in Rats

  -The purpose of this study is to evaluate the developmental toxicity of Telomer 8-2 alcohol, administered by gavage, to pregnant rats from the time of implantation to the end of gestation.

TRP Toxicology and Descriptive Biology Studies

- Multigeneration Reproduction Study in Rats

  -The objective of this study is to evaluate the effect of Telomer 8-2 alcohol on the gonadal function, conception, parturition, and the growth and development of offspring of male and female Crl:CD®(SD)IGS BR rats over two generations involving the production of at least one set of litters in each generation

TRP Toxicology and Descriptive Biology Studies

- Bacterial Reverse Mutation Test with an Independent Repeat Assay

  -The purpose of this study is to evaluate the mutagenic potential of the test substance by measuring its ability to induce reverse mutations at selected loci of several strains of *Salmonella typhimurium* and at the tryptophan locus of *Escherichia coli* WP2 uvrA in the presence and absence of S9 activation.

- *In Vitro* Mammalian Chromosome Aberration Test

  -The purpose of this study is to evaluate the clastogenic potential of a test substance based upon its ability to induce chromosome aberrations in human peripheral blood lymphocytes (HPBL).

TRP Toxicology and Descriptive Biology Studies

- Rat Bone Marrow Erythrocyte Micronucleus Test

  -The purpose of this study is to evaluate the clastogenic potential of the test substance as measured by its ability to induce micronucleated polychromatic erythrocytes in rat bone marrow. The micronucleus test is also able to detect chemicals that induce whole chromosome loss (aneuploidy) in the absence of clastogenic activity.

TRP Pharmacokinetics Studies : Timeline

CBI Information has been redacted

TRP Pharmacokinetics Study

- *In Vitro* Microsomal Metabolism Study

  -The objective of this study type is to determine the rate of metabolism of a test compound in microsomes prepared from livers of a number of species (normally rat, rabbit, dog, monkey, and human) and to identify the metabolites produced in each species.

- Metabolism of Telomer 8-2 Alcohol by Mammalian Hepatocytes

TRP Pharmacokinetics Study

- Toxicokinetics of Telomer 8-2 Alcohol in the Rat

  -The objectives of this study are to determine the Absorption, Distribution, Metabolism and Excretion (ADME) of Telomer 8-2 Alcohol in male and female rats following oral and dermal dosing.

Radiolabeled 8-2 Telomer B Alcohol

$$F(CF_2)_7\,{}^{14}CF_2\text{-}CH_2CH_2\text{-}OH$$

Needed for Pharmacokinetics & Environmental Fate Studies

CBI Information has been redacted

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Radiolabeled 8-2 Telomer B Alcohol : Synthesis Route "A"

CBI Information has been redacted

$C_7F_{15}\,{}^{14}CF_2\text{-}CH_2CH_2\text{-}OH$: *Timeline*

CBI Information has been redacted

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TRP Environmental Fate & Effects Studies

- Focus on :
  - Physical - Chemical Properties
  - Environmental Fate
  - Environmental Effects
  - Bioconcentration

Physical - Chemical Properties

$n\text{-}C_8F_{17}CH_2CH_2OH$

- Molecular Weight
- Boiling, Melting Point
- Vapor Pressure
- Water Solubility
- Log K_{ow} (Octanol - Water Partition)
- UV / Visible Absorption Spectrum
- Henry's Law Constant
- Adsorption/desorption onto glassware

CBI Information has been redacted

Environmental Fate & Effects Work Plan

$n\text{-}C_8F_{17}CH_2CH_2OH$

Physical Properties

- UV/Visible Spectrum
- Water Solubility
- Adsorption to Glass
- Air-Water Partition Coefficient

Environmental Fate : Abiotic

- Hydrolysis
- Adsorption / Desorption
- Indirect Photolysis in Air

Environmental Fate : Biotic

- Anaerobic Biodegradation*
- Aerobic Biodegradation*

(* ***Radiolabeled Material***)

Environmental Effects

- Bioconcentration Factor
- 90 Day Early Life Stage Study – Rainbow Trout
- 21 Day Invertebrate Daphnia Study

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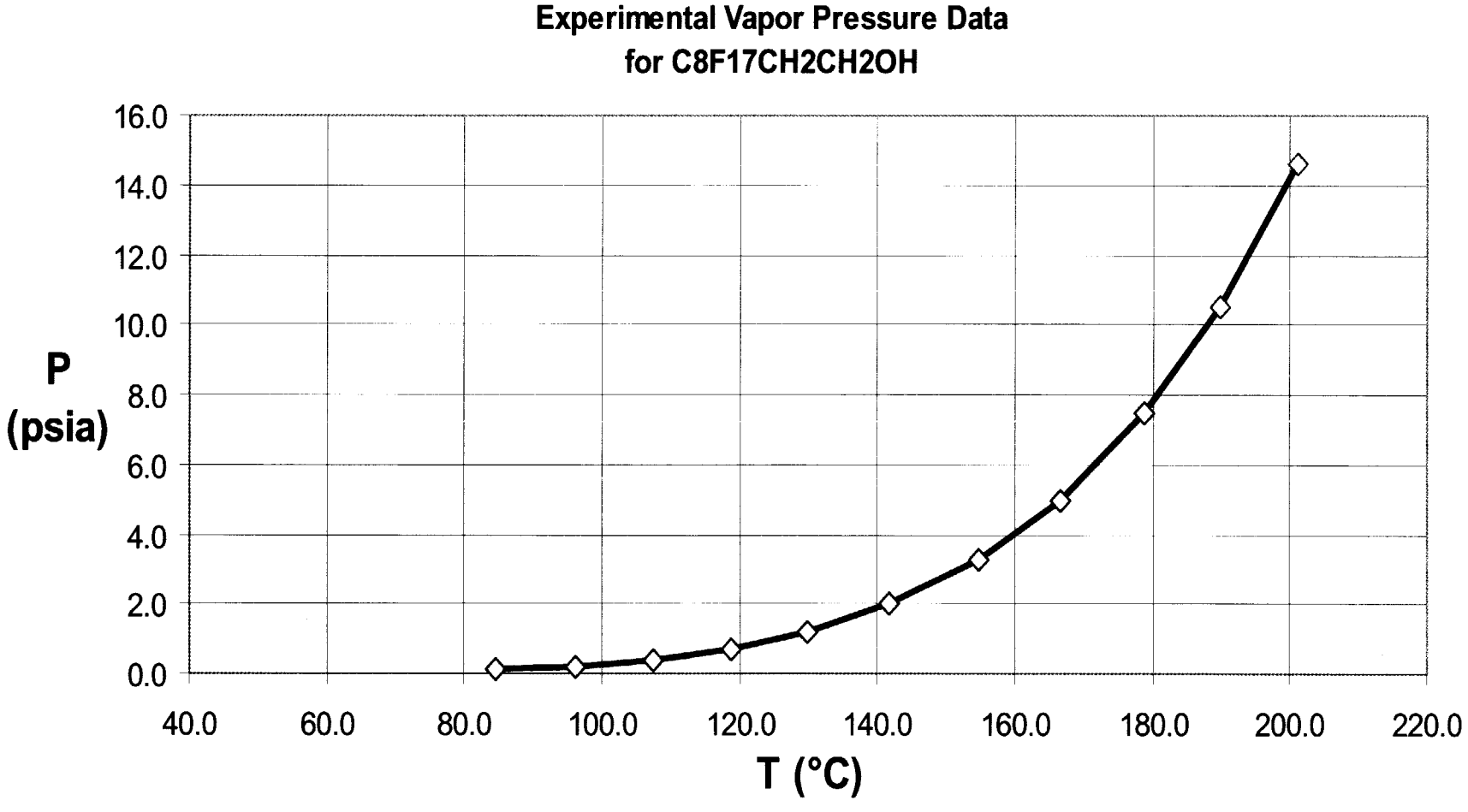
Physical - Chemical Properties : Vapor Pressure

$n\text{-}C_8F_{17}CH_2CH_2OH$



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Environmental Compartments

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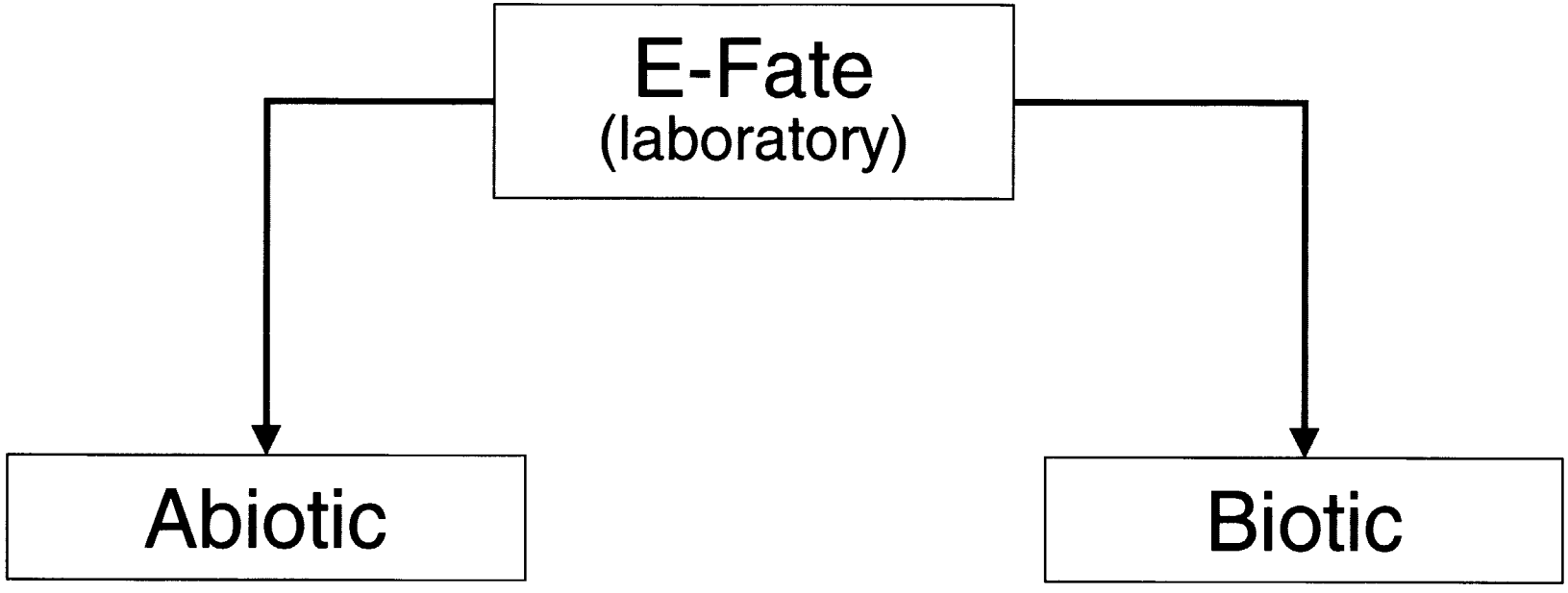
- **Based on Emissions, Applications/Uses, and Physical-Chemical Property Information :**
  - *Water and Soil are the major compartments*
  - Air is a minor compartment

Routes to E-Fate

Goal:

Identify environmental transformations relevant to toxicity and chemical cycling



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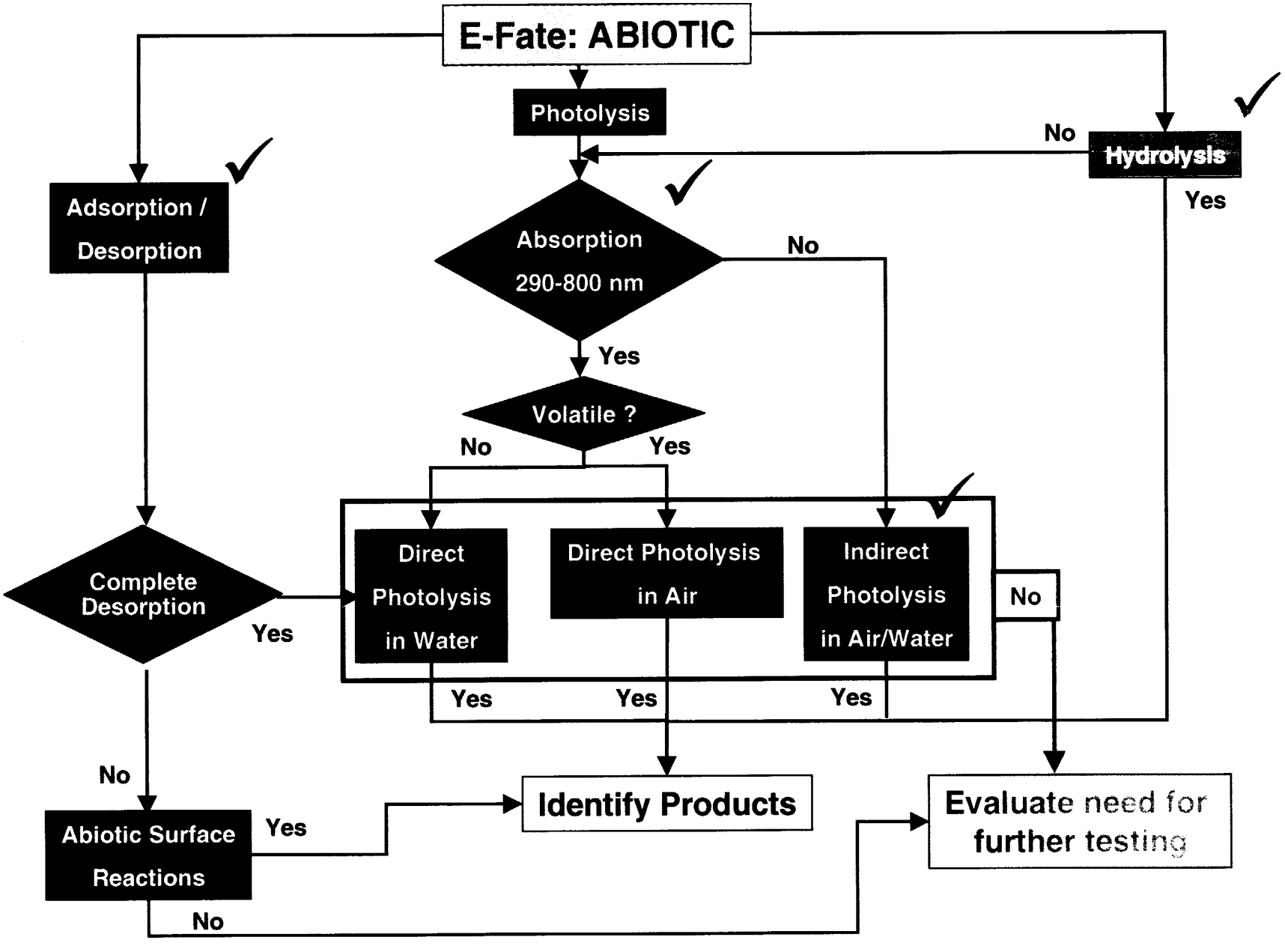

E-Fate: ABIOTIC
Photolysis
Hydrolysis
No
Yes
Adsorption / Desorption
Absorption 290-800 nm
No
Yes
Volatile ?
No
Yes
Complete Desorption
Yes
Direct Photolysis in Water
Direct Photolysis in Air
Indirect Photolysis in Air/Water
No
Yes
Yes
Yes
No
Abiotic Surface Reactions
Yes
No
Identify Products
Evaluate need for further testing

E-Fate: Abiotic Degradation Studies

- **Hydrolysis**
  - **Transformation of a test chemical by reaction with water into new chemicals**
- **Adsorption/Desorption Studies**
  - **Evaluate the migratory tendency of a test chemical into the air, water, and soil or sediment compartments of the environment**
- **Indirect Photolysis**
  - **Assess the reaction of a test chemical that is a result of chemical or electronic excitation transfer in air**

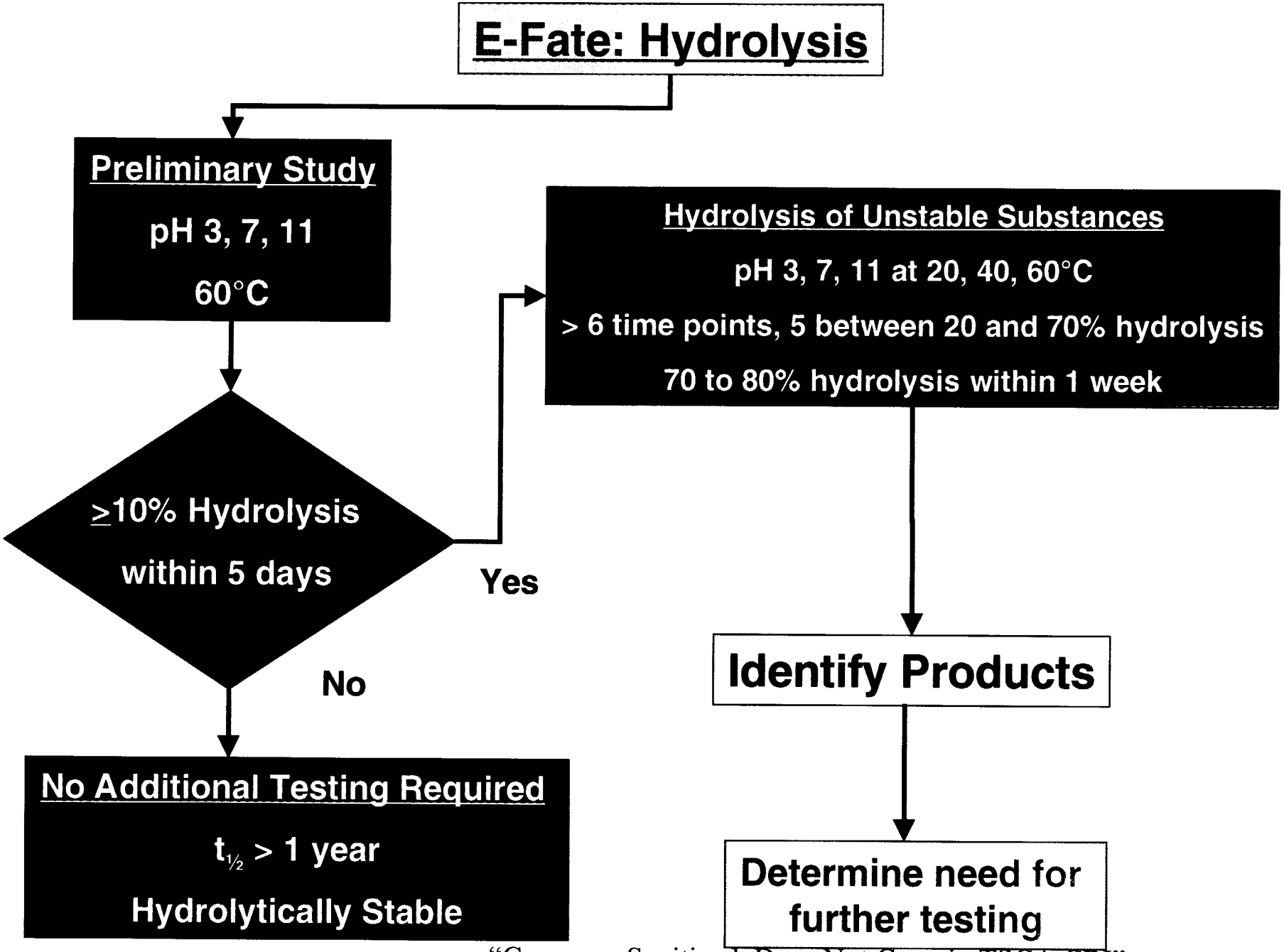
Hydrolysis

Objective: To assess hydrolysis, which represents the transformation of a chemical by reaction with water into new chemicals.

Methods:

- •OPPTS 835.2130/OECD 111
- •Test substance concentration is less than one-half its water-solubility and not greater than 10^{-3} M
- • Sterile glassware and aseptic conditions used in the preparation of all solutions and in performing experiments
- • pH 3, 7, and 11
- • Temp. 20, 40, and 60°C
- • Minimum of 7 time points

Results: - Rate of hydrolysis as a function of pH at a fixed temperature
- Rate of hydrolysis as a function of pH and temperature
- Rate of hydrolysis and the chemical half-life in the environment



Adsorption/Desorption Studies

Objective: To evaluate the migratory tendency of chemicals into the air, water, and soil or sediment compartments of the environment.

Method:

- •OPPTS 835.1220/OECD 106
- •Four initial concentrations up to one-half saturation but <5 mg/L
- • Minimum of nine adsorbants; 3 soils, 3 sediments, 3 sludges
- • Up to 4 time points
- • 3 adsorbant/solution ratios

Results: - Mass Balance
- Percent adsorption/desorption
- Adsorption/desorption Kinetics
- Adsorption/desorption Isotherms

Indirect Photolysis in Air

Objective: Assess the atmospheric degradation of n-$C_8F_{17}CH_2CH_2OH$ by hydroxyl radical in air.

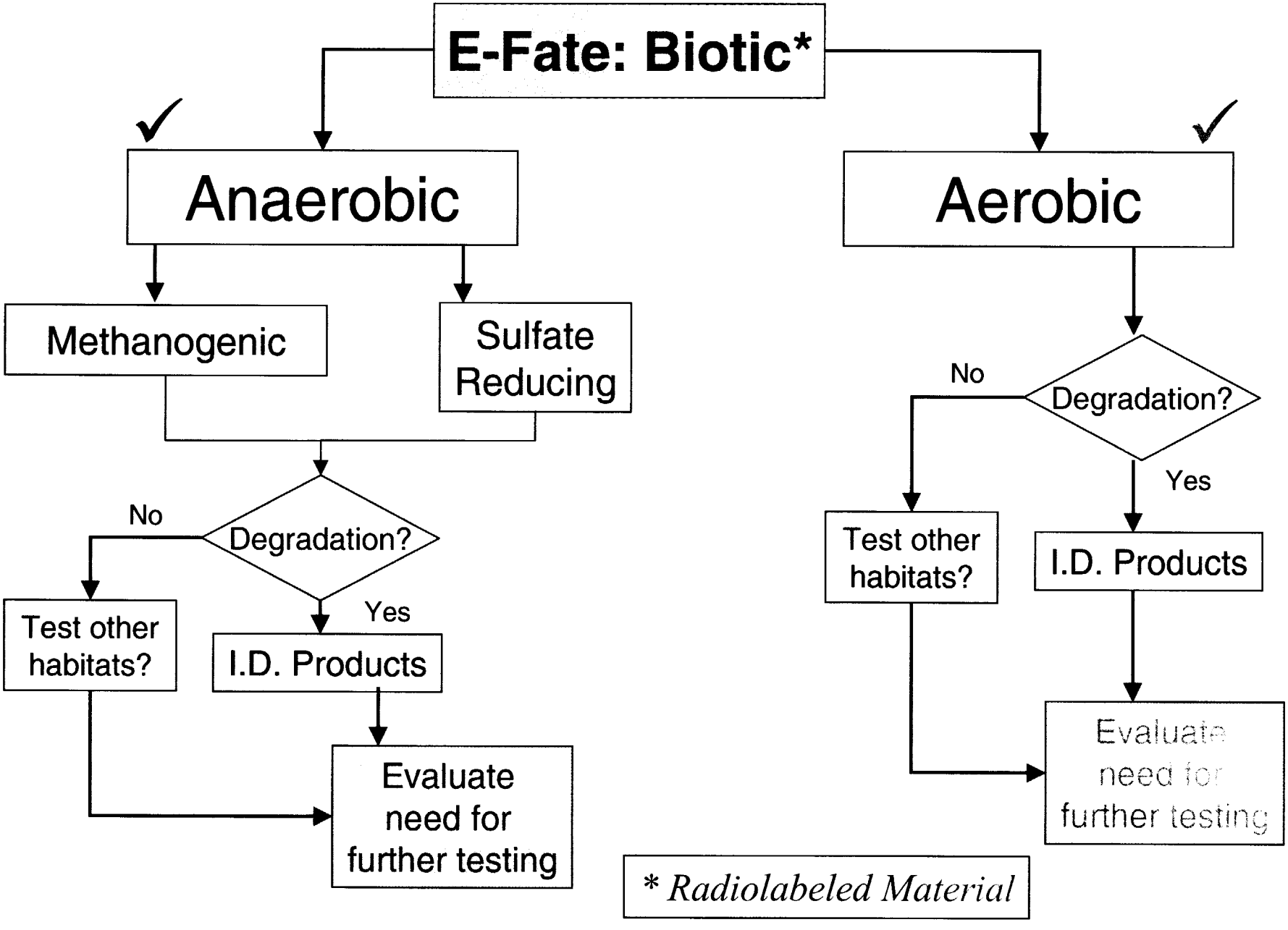
Method:

- Pulsed laser photolysis of H_2O_2
- Analysis of product(s) by FTIR, GC-MS
- Absence and presence of NO_x
- follow protocol described in cited reference

Results:

- Indirect photolysis rate constants
- Half-life of test chemical in air
- Major oxidation product(s) as well as their reactivity

Reference : Atmospheric Study of $C_4F_9CH=CH_2$ and $C_6F_{13}CH=CH_2$, J.Phys. Chem. **2000** 104, 8512-8520.



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Environmental Fate - Biotic Studies

- **Aerobic Aquatic Biodegradation** - The purpose of this test is to examine biochemical transformation by aerobic ($+O_2$) microbes from exposed and unexposed habitats and to determine the decomposition kinetics and fate of the chemical of interest.

- **Anaerobic Biodegradation** - The purpose of this test is to examine biochemical transformation by anaerobic ($-O_2$) microbes from exposed and unexposed habitats and to determine the decomposition kinetics and fate of the chemical of interest.

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Aerobic Aquatic Biodegradation

Objective:

Determine biodegradation potential for Telomer BA 8_2 under aerobic conditions in aerobic sludge matrix.

Methods:

- Aerobic incubation of microbial communities from an exposed and unexposed habitat (based on OPPTS 835.3170 & .3100 with extended incubation)
- Microbial toxicity screen to determine high and low dose levels
- Follow parent/product transformations for up to a 1 year period
- Parameters - parent compound concentration, product identification, total heterotrophic microbial count, alcohol metabolic monitoring

Results:

- No observable adverse effect level for heterotrophic microbes
- Kinetics of aerobic decomposition
- Product identification

Anaerobic Biodegradation

Objective:

Determine biodegradation potential for Telomer BA 8_2 under anaerobic conditions in a saturated, landfilled sludge system

Methods:

- Anaerobic incubation of microbial communities from an exposed and unexposed habitat (based on OPPTS 835.5154)
- Microbial toxicity screen to determine high and low dose levels
- Follow parent/product transformations for up to 64 weeks under both sulfate reducing and methanogenic conditions
- Parameters - parent compound concentration, product identification, total counts: heterotrophs, sulfate reducers, & methanogens, alcohol metabolic monitoring

Results:

- Kinetics of anaerobic decomposition
- Product identification
- No observable adverse effect level for anaerobic microbes

Environmental Effects Studies

- **Acute Toxicity Tests -** The purpose of these tests is to determine the chemical concentration that effects (EC50) or is lethal (LC50) to 50% of the test organisms; the endpoints assess immediate, short-term adverse effects, e.g. immobility, survival.

- **Aquatic Chronic Toxicity Tests** - The purpose of these tests is to determine the chemical concentration that causes long-term, chronic effects on the test organism (survival, growth, reproduction).

Aquatic Chronic Toxicity Studies

Objective:

The purpose of these tests is to determine the chemical concentrations that are associated with long-term, chronic effects (NOEC, LOEC) on survival, growth, and reproduction of an aquatic invertebrate (e.g., *Daphnia)* and a fish (e.g., rainbow trout).

Methods: e.g. USEPA OPP 72-4; USEPA OTS 797.1000, 1330; OPPTS 850.1300, 1400; OECD TG 210, 211

- Includes acute limit test
- Dose response, analytical confirmation of test concentrations
- indications of cumulative or reproductive effects
- dose response, analytical confirmation of test concentrations

Results:

- assess effects on survival, growth (length, weight), reproduction

Aquatic Bioconcentration Study

Objective:

To determine the bioconcentration potential of a chemical (uptake and depuration potential), focus may be ecological and/or human health

Methods: e.g. USEPA OPP 72-6; USEPA OTS 797.1520
OPPTS 850.1730; OECD TG 305

- uptake (steady state) and depuration phases
- analytical confirmation of test concentrations and tissue residues

Results:

- BCF, uptake and depuration coefficients

TRP Environmental Fate & Effects Studies : Timeline

CBI Information has been redacted

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TRP Database

- Product Categories
  - Intermediates
  - Surfactants
  - Polymers
- Information Types
  - Toxicology
  - Environmental Fate & Effects
- Discussion & Analysis - March 2001

TRP Path Forward Items

- Toxicology & Descriptive Biology
- Pharmacokinetics
- Radiolabel
- Environmental Fate
- Environmental Effects
- TRP Database
- Analytical
- Summary

Next TRP Meeting : 20-22 March 2001

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