- RESTRICTED -

HEALTH HAZARD SUMMARIES AND PROPOSED TESTING PROGRAM FOR SEVERAL 3M FLUOROCHEMICALS

3M FLUOROCHEMICAL TECHNICAL ADVISORY COMMITTEE

SEPTEMBER 6, 1994

HUMAN STUDIES - 3M PRODUCTION WORKERS

Medical Surveillance Testing Program

* Blood Testing
* Chemistry Battery
* Complete blood count (CBC)
* Urinalysis
* Spirometry - respiratory testing
* Chest X-ray
* EKG
* Questionnaire

Allows for:

* Morbidity (disease) assessment - to determine if there is a relationship of fluorine serum levels to disease states
* Hormone & immune function - to determine if there is an imbalance in hormone or immune function
* Liver function tests (no effects seen over 6-7 years)
* Reproductive/sperm effects (monitored through surveys)
* Immunologic effects - abnormalities monitored as part of blood survey

ANALYSIS OF BLOOD BANK SAMPLES

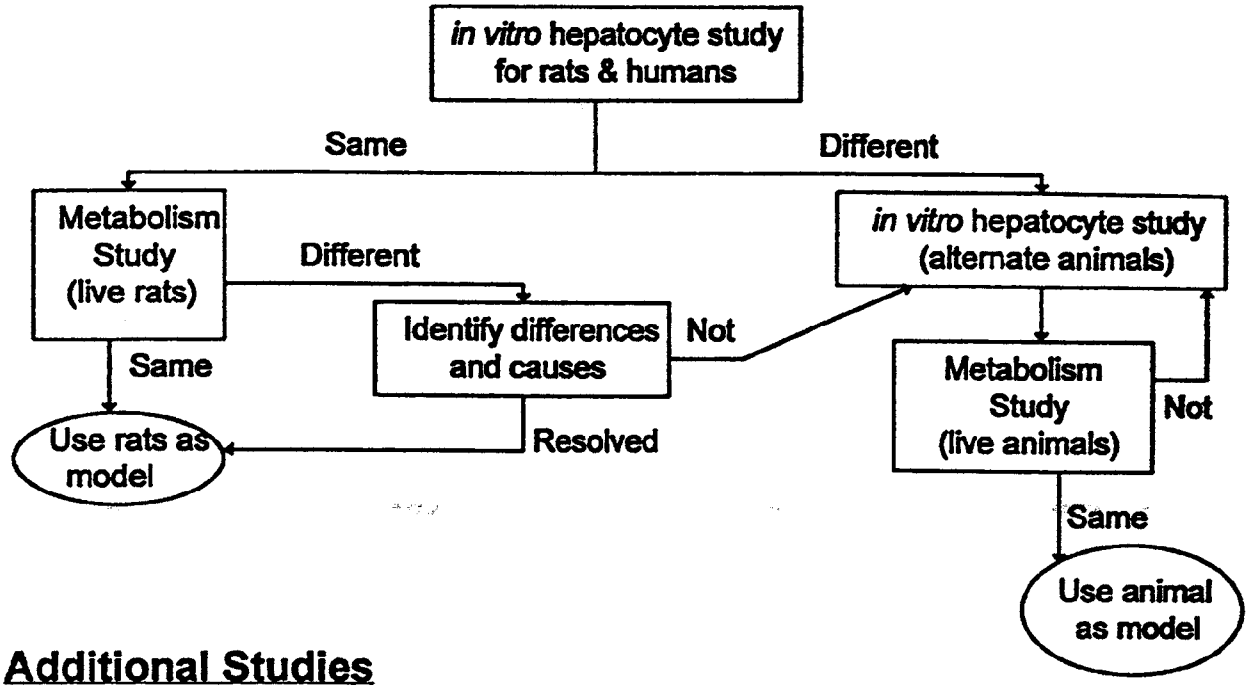
Procedure:

* Obtain samples from blood banks around the world
* Determine
  - Total fluorine
  - Total organic fluorine
  - $C_8F_{17}SO_3^-$ level
  - $C_7F_{15}CO_2^-$ level

Considerations:

1. Data would provide a base line for future reference.
2. Data would provide a basis for comparison to levels in workers.
3. Others have the capability of making such measurements.
4. Data would allow for a correlation of levels with known distribution of 3M products.
5. Findings may require an EPA sec. 8(e) sustantial risk submission.

METABOLISM STUDIES (FC-10, FX-12, FC-807)



Additional Studies

⇒ *in vitro* metabolism studies using isolated human and rat hepatocytes (conducted by contract laboratory or 3M Pharmaceuticals metabolism group).

⇒ Metabolism study in live rats and/or monkeys will be needed to confirm results

Potential Value

⇒ Determine metabolic route in rats and humans. (Verify that FC-10, FX-12, and FC-807 metabolize to $C_8F_{17}SO_3^-$)

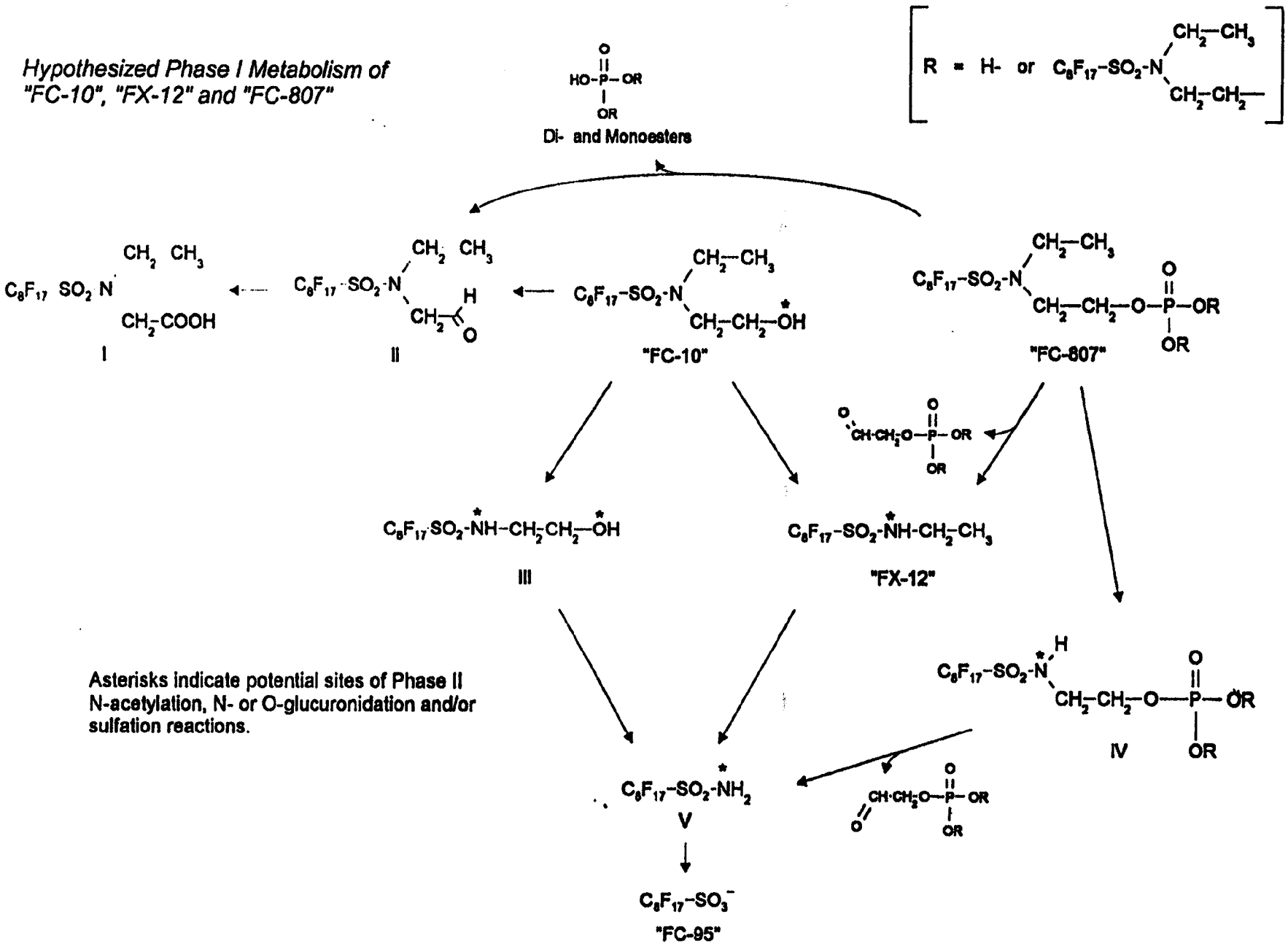
⇒ Determine suitable animal model for other testing.

⇒ Determine the appropriate metabolites (compounds) for additional studies, as needed

⇒ Clarify differences in results obtained in earlier studies with FC-10 in different species.

⇒ *in vitro* model may also be useful in studying the mechanism of toxicity

Hypothesized Phase I Metabolism of "FC-10", "FX-12" and "FC-807"



Asterisks indicate potential sites of Phase II N-acetylation, N- or O-glucuronidation and/or sulfation reactions.

scg 7/7/94

FC-10

Structure: $C_8F_{17}SO_2N(CH_2CH_3)CH_2CH_2OH$

Quantity Manufactured: **~3.8M lbs./yr. (Decatur)**

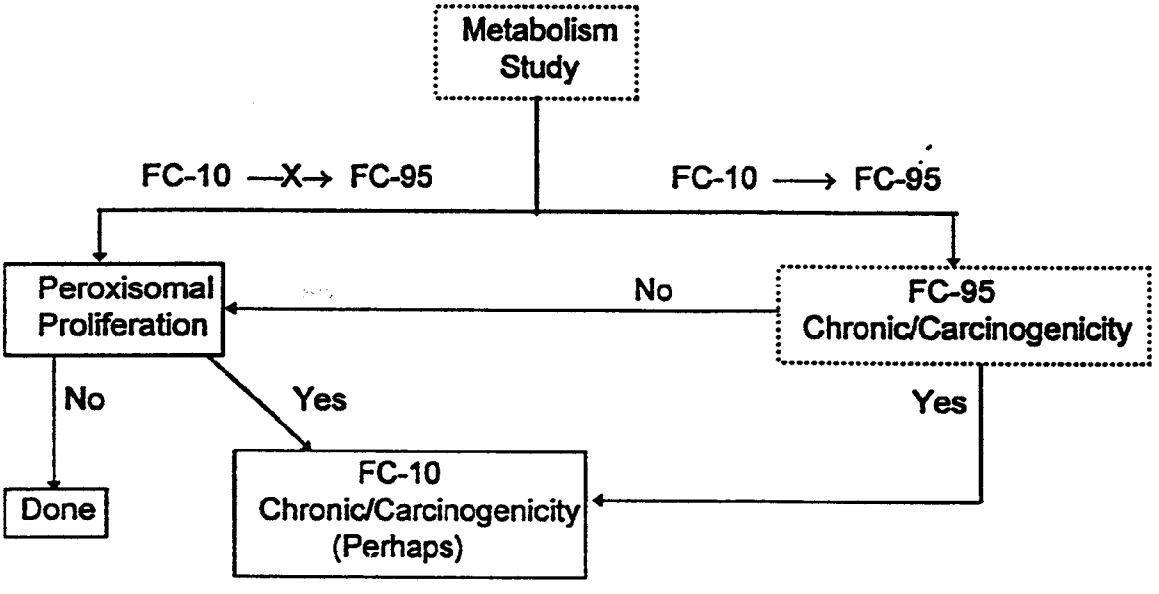
Uses: **Reactive intermediate in caulking sealant**

Exposed Population: **3M workers > Customer workers >> General Population**

Additional Studies

⇒ **Dermal absorption/persistence study (rabbits)**

⇒ ***in vivo* micronucleus assay (mice)** - to identify chromosomal damage, if any



Pending Results of FC-95 Studies

⇒ **Peroxisomal proliferation** - a screen to identify compounds that are more likely to be carcinogenic

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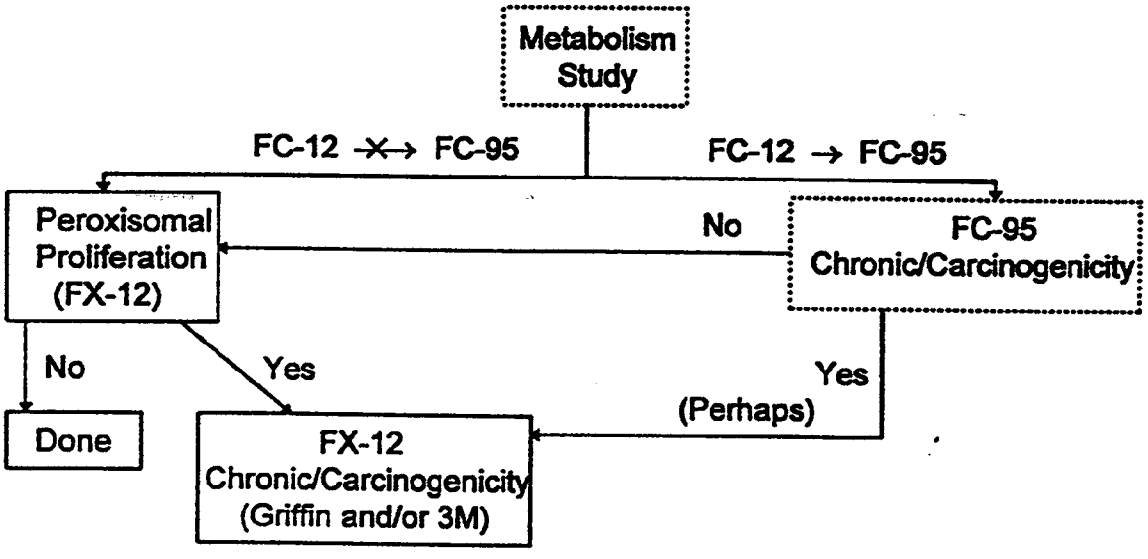
FX-12

Structure: $C_8F_{17}SO_2NHCH_2CH_3$

Quantity Manufactured: **~40M lbs./yr. (Decatur)**

Uses: **Branched component used in insecticide**
(Straight chain component present at 3-10% in FC-171, FX-1802, and FC-760)

Exposed Population: **3M workers = Customer workers > General Population**



Pending Results of FC-95 Studies

⇒ **Peroxisomal Proliferation** - a screen to identify compounds that are more likely to be carcinogenic

⇒ **Chronic/carcinogenicity**

Additional Studies

⇒ ***in vivo* micronucleus assay (mice)** - to identify chromosomal damage, it any

⇒ **Reproductive Studies, e.g., FDA Segment 1** - to identify effects on male and female reproduction in animal studies, if any. (May not be necessary if FX-12 is shown to metabolize to $C_8F_{17}SO_3^-$ and testing is done on $C_8F_{17}SO_3^-$)

FC-807

Structure: $[C_8F_{17}SO_2N(CH_2CH_3)CH_2CH_2O]_{n=1-3}P(O)(O^-NH_4^+)_{3-n}$

Quantity Manufactured: **~7MM lbs./yr. (~2.3 MM lbs. Solids)(Decatur, Antwerp)**

Uses: **Paper treatment**

Exposed Population: **3M workers = Customer workers > General Population**

Additional Studies

⇒ ***in vivo* micronucleus assay (mice)** - to identify chromosomal damage, if any

⇒ **Dermal absorption/persistence study (rabbits)** - (already included in separate program)

⇒ **Peroxisomal Proliferation** - a screen to identify compounds that are more likely to be carcinogenic

Pending Results of FC-95 Studies and Additional Studies

⇒ **Chronic/carcinogenicity**

FC-95

Structure: $C_8F_{17}SO_3^- K^+$

Quantity Manufactured: **10M lbs./yr. (Decatur, Cottage Grove)**

Uses: **Wetting and foaming agent**

Exposed Population: **3M workers > Customer workers >> General Population**

Additional Studies

⇒ **Dermal absorption/persistence study (rabbits)** - (already included in separate program) ✓

⇒ ***in vivo* micronucleus assay (mice)** - to identify chromosomal damage, if any done (-)

⇒ **Reproductive studies, e.g., FDA Segment 1** - to identify effects on male and female reproduction in animal studies, if any Not Done.

⇒ **Subchronic 90 day feeding study (monkeys)** - to clarify previous results and establish a NOAEL

⇒ **Chronic/carcinogenicity (rats)**

FC-143

Structure: $C_7F_{15}CO_2^-NH_4^+$

Quantity Manufactured: **~27M lbs./yr. (Cottage Grove)**

Uses: **Surfactant in polymer manufacture, e.g., PTFE**

Exposed Population: **3M workers = Customer workers >> General Population**

Additional Studies

⇒ **Dermal absorption/persistence study (rabbits)** - (already included in separate program) Done

⇒ ***in vivo* micronucleus assay (mice)** - promised to DuPont Done

⇒ **Additional chromosomal aberration studies** - promised to DuPont Being Done.

⇒ **Peroxisomal proliferation** - Being studied jointly (3M/DuPont) Being Done

⇒ **Immunotoxicity** - to determine effects on immune system and identify parts being effected

⇒ **Reproductive studies, e.g., FDA Segment 1** - to identify effects on male and female reproduction in animal studies, if any

FC-120

Structure: $C_{10}F_{21}SO_3^-NH_4^+$ (~90% of solids); $C_9F_{19}SO_3^-NH_4^+$ (~10% of solids)

Quantitiy Manufactured: ~50M lbs./yr. (Decatur, Cottage Grove)

Uses: Wetting and leveling agent, e.g., for floor wax, hair spray

Exposed Population: 3M workers > Customer workers = General Population

(NOTE: P&G should be consulted about testing they have conducted for the hair spray application.)

Additional Studies

⇒ **Acute inhalation toxicity** - due to hair spray application

⇒ **Ames Assay** - gene mutation

⇒ **Peroxisomal proliferation** - a screen to identify compounds that are more likely to be carcinogenic

⇒ ***in vivo* micronucleus assay (mice)** - to identify chromosomal damage, if any

⇒ **Dermal absorption/persistence study (rabbits)** - (already included in separate program)

⇒ **Subchronic 90 day feeding study** - for comparison with results from FC-95 study to identify any effects seen based on chain length

(NOTE: Where appropriate, use FC-120 solids)

FC-845/810

Structure: **Fluoroalkyl polymer**

Quantity Manufactured: **~1.25MM lbs./yr. (Decatur, Antwerp)**

Uses: **Paper protector for food packaging**

Considerations

* The product is manufactured as an emulsion with no misting.
* Worker exposure through inhalation is expected to be low.
* The large size of the polymer would appear to make absorption through the skin or from the digestive tract into the body insignificant.
* Some studies are being conducted in Europe, e.g., feeding study on Ethoquad surfactant

Additional Studies

⇒ None at this time.

⇒ If other FC studies suggest concerns, they should be considered with respect to potential residuals in FC- 845/810.

SUMMARY OF HEALTH HAZARD INFORMATION

ENDPOINTS	FC-10	FX-12	FC-95	FC-120	FC-143	FC-807	FC-845/ 810
Exposure							
3M Employees			A		A		
Customer Employees							
General Population			A		A		
Toxicokinetics							
Absorption					■		
Distribution	■	■	■		■	■	
Metabolism	A	A			■	A	
Excretion			■		■		
Biological half-life	■	■				■	
Acute Toxicity							
Oral	■		■	■	■	■	■
Dermal	A	■	■	■	■	A	
Inhalation	■	■	■	A	■		
Primary Irritation							
Ocular	■	■	■	■	■	■	■
Dermal	■	■	■	■	■	■	■
Respiratory							
Sensitization							
Dermal							■
Respiratory							
Genotoxicity							
Gene mutation (Ames)	■	■	■	A	■	■	■
Chromosomal effects	A	A	A	A	A	A	■
Other		■					
Subchronic Toxicity	■	■	A	A	■	■	
Peroxisomal Proliferation	X	X		A	A	A	
Chronic Toxicity & Carcinogenicity	■	X	A		■	X	
Reproductive Toxicity		X	A		A		
Developmental Toxicity		■	■		■		
Mechanistic Studies	A	A	A	X		A	
Human Health Data			A		A		

■ Adequate data exist for risk assissment

A Additional testing

X Testing dependent on results of additional testing

POTENTIAL COSTS ($M)

PRODUCT	ADDITIONAL STUDIES	STUDIES PENDING RESULTS
Global Blood Bank Study	20	
Metabolism Studies	110	
FC-10	43	10
FX-12	13	400
FC-95	493	
FC-120	116	
FC-143	143	
FC-807	53	300
FC-845-810	-	-
TOTAL	~$1MM	~$1.7MM

YEAR	COSTS ($M)
1995	800
1996	290
1997	300*
1998	300*

* pending results of additional testing

TIMING

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