

- RESTRICTED -

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

3M FLUOROCHEMICAL TECHNICAL ADVISORY COMMITTEE

SEPTEMBER 6, 1994

**Exhibit
1421**

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

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

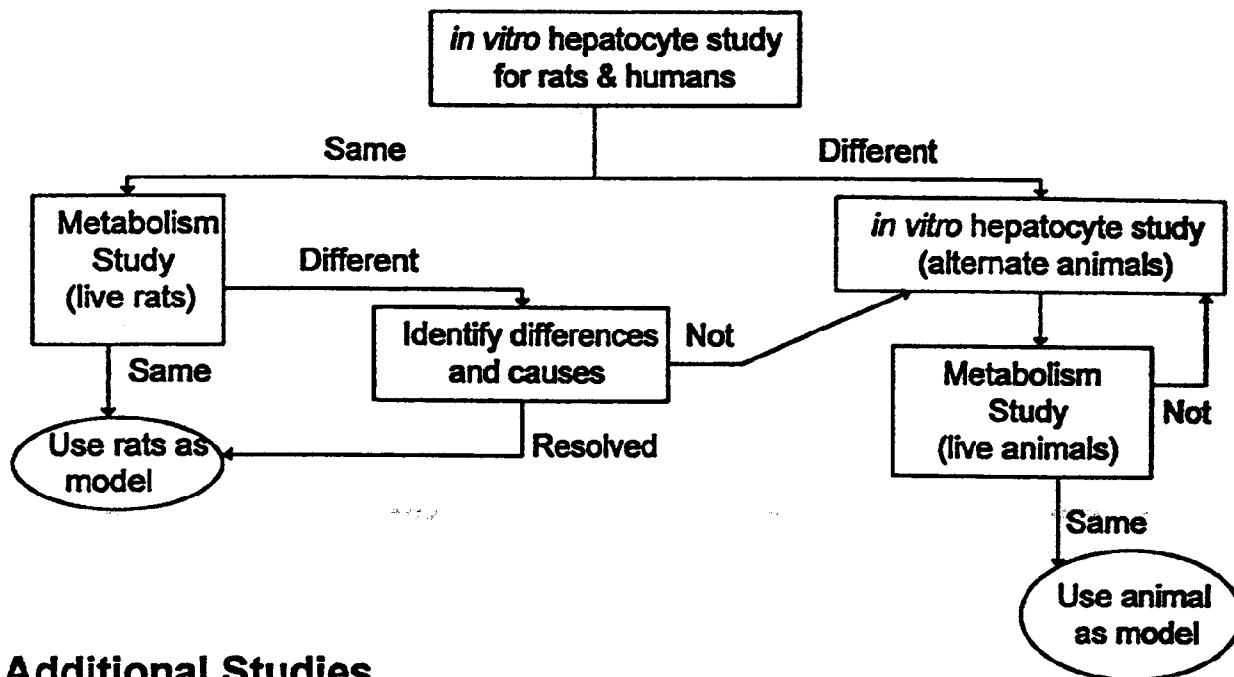
Procedure:

- * Obtain samples from blood banks around the world
- * Determine
 - Total fluorine
 - Total organic fluorine
 - $\text{C}_8\text{F}_{17}\text{SO}_3^-$ level
 - $\text{C}_7\text{F}_{15}\text{CO}_2^-$ 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) substantial risk submission.

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



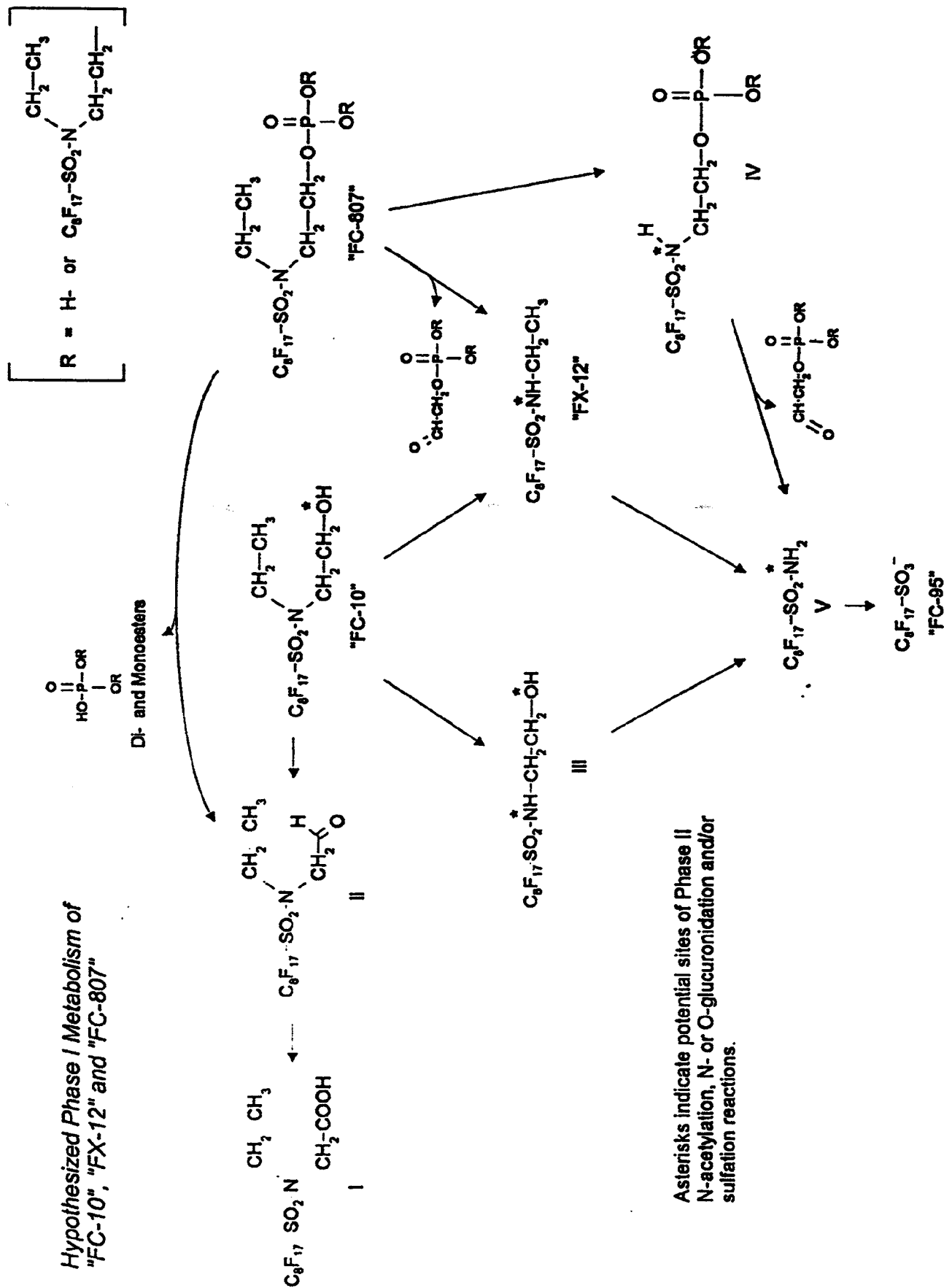
Additional Studies

- ⇒ *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"



scg 7/7/94

FC-10

Structure: $\text{C}_8\text{F}_{17}\text{SO}_2\text{N}(\text{CH}_2\text{CH}_3)\text{CH}_2\text{CH}_2\text{OH}$

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

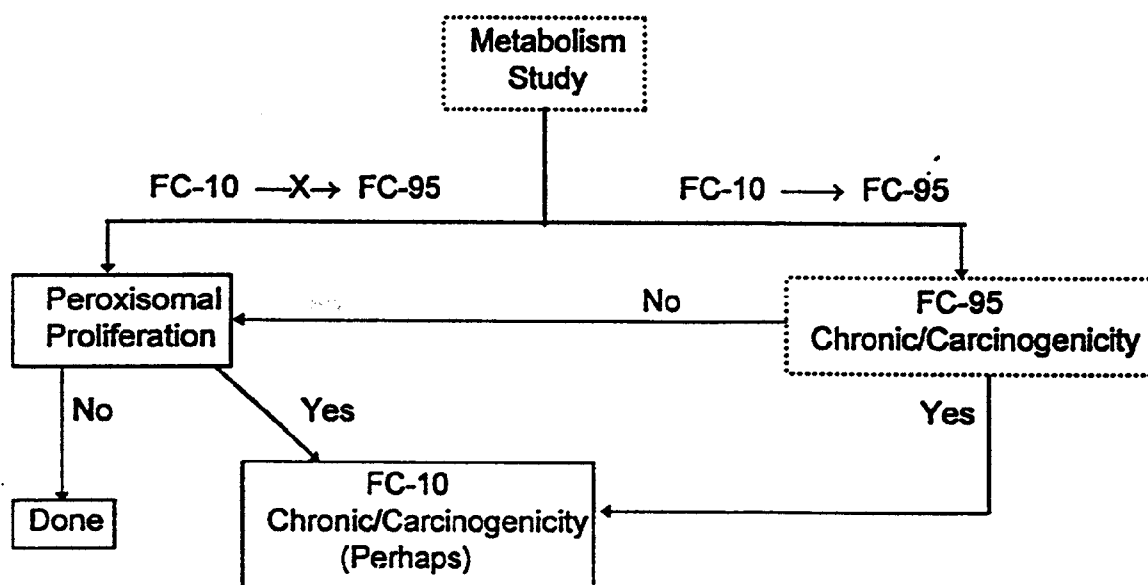
Uses: Reactive intermediate in caulking sealant

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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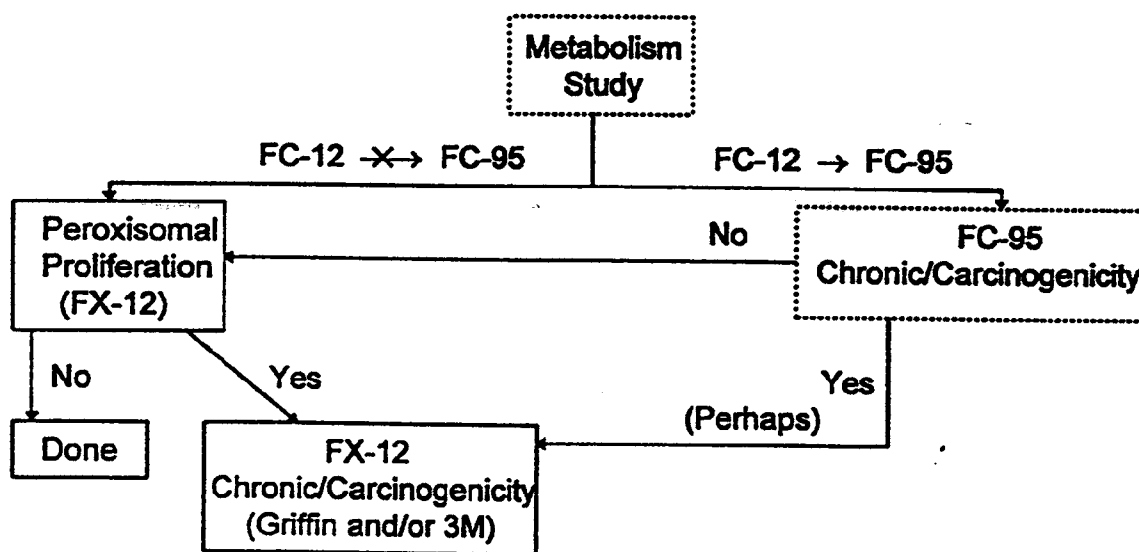
FX-12

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, if 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: $[\text{C}_8\text{F}_{17}\text{SO}_2\text{N}(\text{CH}_2\text{CH}_3)\text{CH}_2\text{CH}_2\text{O}]_{n-1-3}\text{P}(\text{O})(\text{O}^-\text{NH}_4^+)_{3-n}$

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: $C_7F_{15}CO_2NH_4^+$

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 Don
- ⇒ 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)

Quantity 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

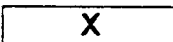
- ⇒ None at this time.
- ⇒ If other FC studies suggest concerns, they should be considered with respect to potential residuals in FC- 845/810.

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 assessment

 Additional testing

 Testing dependent on results of additional testing

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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

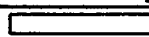
YEAR	COSTS (\$M)
1995	800
1996	290
1997	300*
1998	300*

* pending results of additional testing

TIMING

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PROCEDURE	1995	1996	1997	1998	1999
Global Blood Bank Samples					
- Metabolism Study					
- Metabolism Study (live)					
FC-10					
- Dermal absorption/persist					
- Micronucleus assay					
- Peroxisomal proliferation					
FX-12					
- Peroxisomal proliferation					
- Chronic/carcinogenicity					
- Micronucleus assay					
- Reproductive Study					
FC-95					
- Subchronic Tox(monkey)					
- Dermal absorption/persist					
- Micronucleus assay					
- Reproductive Study					
- Chronic/carcinogenicity					
FC-120					
- Dermal absorption/persist					
- Micronucleus assay					
- Peroxisomal proliferation					
- Acute Inhalation Toxicity					
- Ames Assay					
- Subchronic 90 day feeding					
FC-143					
- Dermal absorption/persist					
- Micronucleus assay					
- Chromosomal aberration					
- Peroxisomal proliferation					
- <i>in vitro</i> Immunotoxicity					
- Reproductive Study					
FC-807					
- Dermal absorption/persist					
- Micronucleus assay					
- Peroxisomal proliferation					
- Chronic/carcinogenicity					
FC- 845/810					
- Study of residuals					


 Potential value depends on results of earlier studies