



# DuPont Comments

## Response to Petition to Expedite Consideration of PFOA under Proposition 65

Stanley W. Landfair  
November 16, 2006

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# DuPont Comments

## *Speakers*

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# DuPont Comments

## *Overview*

- Chemical Identity of PFOA and Its Uses (Boothe)
- Exposure/Risk Assessment (Boothe)
- Animal Testing Data and Epidemiological Data (Dr. Rickard)
- Reasons Why OEHHA Should Not Expedite Consideration of PFOA under Proposition 65 (Dr. Murray)



# DuPont Comments

## Chemical Identity of PFOA and its Uses

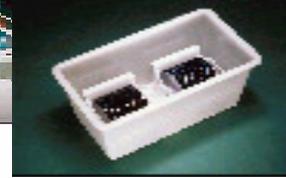
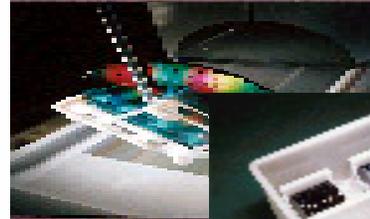
David W. Boothe  
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# Chemical Identity of PFOA and its Uses

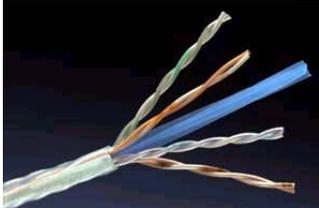
- What is PFOA?
  - PFOA is a surfactant used as an essential processing aid to produce fluoropolymer high-performance materials.
  - PFOA is not used to make fluorotelomers, but is found at trace levels in some fluorotelomer products as a byproduct of their synthesis.
  - PFOA also is an unintended byproduct of the manufacture of PFOS-based products
- PFOA is not **Teflon**<sup>®</sup>

# Fluoropolymer Uses -- Resins



**Semiconductor Manufacture**

**High Purity  
Liquid Handling**



**Telecomm  
Wire & Cabling**



**Chemical Processing  
Valves, Lined Piping, Tanks**



**Low Permeable  
Automotive Fuel Hose**



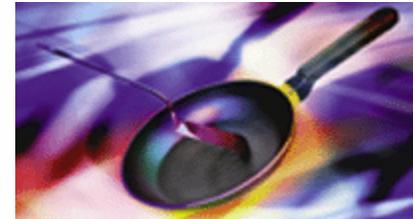
**Aerospace Materials  
Hydraulic Tubing  
Wire & Cabling Flares**

# Fluoropolymer Uses -- Dispersions



**Construction  
Architectural Fabric**

**Non-stick  
Coatings  
for  
Cookware and  
Small  
Electrical  
Appliances**



# Fluorotelomer Uses



**Industrial Fire Fighting**



**Architectural Coatings and Sealers**



**Carpet & Textiles**



**Health Care**



**Grease Resistant Packaging**



# DuPont Comments

## Exposure/Risk Assessment

David W. Boothe  
November 16, 2006

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# Exposure/Risk Assessment

- DuPont Exposure Assessment & Risk Characterization of Consumer Articles
  - Initiated in 2003 - part of DuPont's product stewardship program
  - Objective:
    - Estimate theoretical exposure to PFOA from consumer articles
    - Conduct risk characterizations
    - Provide risk context for analytical data on consumer articles
  - Conducted by ENVIRON
  - Peer-reviewed by independent scientific panel
  - Moderated by Dr. George Gray, former Executive Director of Harvard Center for Risk Analysis
  - *Environmental Science & Technology* 2005, 39(11), pp. 3904-3910

# Exposure/Risk Assessment

## Quantitative Evaluation of:

- Medical garments (nonwovens)
- Carpeting
- Carpet care products
- Textiles
- Cookware
- Thread sealant tape
- Membranes (apparel)
- Food contact paper

## Quantitative Evaluation (ingredients-basis) of:

- Stone, tile and wood sealants
- Industrial floor waxes and wax removers
- Latex paint
- Home and office cleaning products
- Textile treatments (upholstery, home, technical)

## Qualitative Evaluation:

- Cable, wire, hose & tubing
- Architectural membranes

# Exposure/Risk Assessment

- Results & Conclusions
  - PFOA was below detectable levels in coated cookware, non-woven medical garments and some textiles
  - Trace levels of PFOA detected in other end-use articles that were tested
  - Based on the exposure assessment and risk characterization:
    - Margins of Exposure (MOE; based on reasonable maximum exposure numbers) for all articles tested ranged from 30,000 to 9 billion
  - Use of these products will not result in measurable (0.5 ppb) levels of PFOA in blood

# Exposure/Risk Assessment

- Cookware Testing
  - FDA approves fluoropolymer coatings for cookware
  - Issue raised: Is cookware a source of PFOA exposure?
  - DuPont extraction testing:
    - FDA protocol
    - Sensitive analytical techniques (LOD @ 100 picograms/cm<sup>2</sup>; ~ 10 ppt per aliquot)
    - PFOA not detected in cookware
  - Recent FDA experiment:
    - Extreme and abusive test methods – not reflective of consumer use
    - PFOA detected in minute quantities in cookware
    - Quantities of PFOA detected were too small to measure any migration of PFOA out of cookware into food
    - Begley, T., *et al.*, *Food Additives and Contaminants*, 22 (10), 2005

# Exposure/Risk Assessment

- Cookware Testing (*cont'd*)
  - Danish Technological Institute
    - No PFOA detected
    - PTFE-coated cookware
    - Testing for PFOA migration on heating to high temperatures (e.g., 300° C for 30 minutes)
  - Chinese State Testing Academy
    - No PFOA detected
    - Non-stick cookware products in Chinese market
    - 18 brands tested, strong scientific support, reviewed by experts in the area
  - European Food Safety Authority
    - Fluoropolymer-coated articles (e.g., cookware) manufactured at high temperatures
    - Determined exposure to PFOA is negligible

# Exposure/Risk Assessment

- Fluorotelomer Coated-Paper Studies
  - Published FDA research found trace migration of fluorotelomer products to food simulants but found PFOA to be below the level of quantification in the extracts (Begley, T., *et al.*, *Food Additives and Contaminants*, 22 (10), 2005)
  - FDA letter to DuPont stressed fluorotelomer exposure does not equate to PFOA exposure
  - DuPont fluorotelomer coatings shown to be highly stable to acidic and basic conditions even at elevated temperatures
  - FDA continues to state that these materials are safe for consumer use
  - FDA rejected allegations made by the Environmental Working Group
    - FDA letter to EWG describes claims as “irrelevant to the safety determination on the use of Zonyl RP and the company would not have been required to provide this information to FDA”
    - The letter also provides FDA’s estimate that consumers who use food contact paper made with DuPont materials are exposed to levels of the food contact substance that are “approximately 45 times lower than the 0.2 ppm (0.6 mg/day) concentration in the diet determined to be safe in 1967.”

# Exposure/Risk Assessment

– Dr. Paul Honigfort, Consumer Safety Officer, Office of Food Additive Safety in 16 November 2005 Letter to DuPont:

- “At this time, we have no reason to change our position that the use of both perfluorocarbon resin and telomer-based coatings are safe for use in contact with food as described in the applicable regulations or notifications.”
- Preliminary work cited in Begley, *et al.*, “...detected PFOA migration from microwave popcorn bags coated with telomer-based products only at a level below the standard of quantification...(<1 ppb in food).”
- “...fluorotelomer migration from coated paper, as reported in this article, occurs in the form of telomer-based compounds themselves and should not be equated to PFOA exposure.”



# DuPont Comments

## Animal Toxicology Data and Epidemiological Data

Robert W. Rickard, Ph.D.

November 16, 2006

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# Overview

- Carcinogenicity – Summary
  - Non-genotoxic in a battery of *in vitro* and *in vivo* studies
  - Carcinogenicity studies in animals
    - Benign tumors in male rats only
    - No effect on incidences of mammary gland tumors
    - Class effect of questionable relevance to humans
  - Human studies
    - No carcinogenic effects observed in worker studies

# Genotoxicity

## ***No genotoxicity in:***

- *S. typhimurium* strains TA1535, TA1537, TA1538, TA98, and TA100
- Chromosomal aberrations in CHO cells
- Chromosomal aberrations in human lymphocytes
- The *in vivo* mouse micronucleus assay
- C3H 10T1/2 cell transformation

# Animal Toxicology Data

- Tumor Incidence (Rats)

|                                    |   |     |     |
|------------------------------------|---|-----|-----|
| – Dose level (ppm in diet):        | 0 | 30  | 300 |
| – Dose level (estimated mg/kg-day) | 0 | 1.3 | 14  |

- 3M Study – Sibinski, *et al.* (1987)

|                       |      |      |        |
|-----------------------|------|------|--------|
| – Leydig cell adenoma | 0/44 | 2/44 | 7/48 * |
|-----------------------|------|------|--------|

- DuPont Study – Biegel, *et al.* (2001)

|                                  |      |  |         |
|----------------------------------|------|--|---------|
| – Hepatocellular adenoma         | 1/79 |  | 10/79 * |
| – Leydig cell adenoma            | 2/78 |  | 8/76 *  |
| – Pancreatic acinar cell adenoma | 1/79 |  | 7/76 *  |

\*increase from controls statistically significant

# Animal Toxicology Data

- Carcinogenicity Studies in Rats
  - Benign tumors produced in male rats
    - Hepatocellular adenoma of liver
    - Acinar cell adenoma of the pancreas
    - Leydig cell (interstitial cell) adenoma of the testis
  - All three benign tumors have been observed as class effects of peroxisome proliferators in rats
  - No increase in malignant tumors produced in males or females at any dose
  - No increase in tumors produced in female rats at any dose

# SAB Panel Recommendations

- Mammary Gland Tumors in Rats
  - Mammary tumor incidences were an important consideration in the SAB Panel recommendation on Descriptor for Carcinogenic Potential as “Likely”
  - However, SAB Panel recommended
    - that EPA “consider new information that has been verified and peer-reviewed prior to use in their revision of the Draft Risk Assessment.”
    - that “an independent, appropriately-designed histopathology review of ... female mammary glands from the Sibinski study be conducted to re-analyze the resulting tumor incidence data”
  - Full Pathology Working Group (PWG) review was conducted for mammary tumors in a 2-year study
    - Results not available in time for incorporation into Draft Risk Assessment

# Animal Toxicology Data

- Pathology Working Group Review of Mammary Glands – Methods
  - Conducted in general accordance with requirements for a PWG as stated in US EPA PR 94-5
  - All mammary glands re-examined microscopically by a reviewing pathologist
  - All primary neoplasms of the mammary gland as diagnosed by the original or review pathologists were evaluated by the PWG pathologists
    - Slides examined by PWG without knowledge of treatment group
    - Used diagnostic criteria and nomenclature recommended by the Society of Toxicologic Pathologists

# Animal Toxicology Data

- Pathology Working Group Review – Mammary Glands
- (50 rats/group)

| CONCENTRATION (PPM)           | 0              |     | 30             |     | 300            |     |
|-------------------------------|----------------|-----|----------------|-----|----------------|-----|
|                               | ORIGINAL STUDY | PWG | ORIGINAL STUDY | PWG | ORIGINAL STUDY | PWG |
| ADENOCARCINOMA (%)            | 16             | 18  | 28             | 32  | 10             | 10  |
| FIBROADENOMA (%)              | 16             | 32  | 26             | 32  | 38             | 40  |
| FIBROADENOMA,<br>MULTIPLE (%) | 4              | 4   | 12             | 12  | 4              | 6   |

# Animal Toxicology Data

- PWG Results and Conclusions: Mammary Tumor Effect
  - No statistically-significant (Fisher's Exact Test, NTP Program Poly-3 procedure) increases in incidence of mammary tumor type, of total benign neoplasms, or total malignant neoplasms
  - No increase in tumor multiplicity
  - Morphologic appearance of the neoplasms in treated groups was similar to that of controls
  - Incidence of mammary gland neoplasms observed in this study was similar to historical control incidences

# Epidemiological Data

## 3M Studies

- Over 50 years of experience
- Thousands of workers across three plant sites
- PFOA exposures: average serum levels 1-7 ppm, some studies confounded by PFOS exposure
- Multiple studies
- Multiple publications: 1980-present
- Parameters evaluated include:
  - Mortality incidences (includes cancer)
  - Liver function
  - Lipid profiles (cholesterol and triglycerides)
  - Reproductive hormones
  - Incidences of care

# Epidemiological Data

- Mortality Study of 3M Cottage Grove Facility Workers (Alexander, 2001)
  - Studied approximately 4000 workers (~108,000 person years) exposed to PFOA:
    - All cancer mortality SMR = 0.9 (0.7-1.1)
    - Cancer of the breast SMR = 1.0 (0.6-1.4)
    - Cancer of the liver SMR = 0.6 (0.3-3.3)
    - Cancer of the pancreas SMR = 1.4 (0.5-3.1)
    - Cancer of the prostate SMR = 1.2 (0.4-2.5)
  - There is no evidence of carcinogenicity of PFOA in humans

# Epidemiological Data

- Washington Works Study (2006)
  - DuPont Washington Works, West Virginia facility
  - 6000 employees, 50 years
  - No increased mortality risk

**SMRs for selected causes of death in Washington Works males, compared to DuPont Region 1: WV (less WW), OH, VA, KY, IN, PA, TN, NC; USA general population and WV state population**

|                                    | <b>MALES</b><br><b>N=4872</b><br><b>Total Mortality: 773</b><br><b>Person Years: 127,513.2</b> |                           |                           |                                  |
|------------------------------------|--|---------------------------|---------------------------|----------------------------------|
| Cause of Death                     | N  | DuPont<br>Region 1<br>SMR | U.S.A.<br>National<br>SMR | West<br>Virginia<br>State<br>SMR |
| All Causes of Death                | (773)  | 93.6                      | 66.2**                    | 58.1**                           |
| All Malignant Neoplasms            | (222)  | 100.4                     | 73.7**                    | 68.3**                           |
| Cancer of Biliary Passages & Liver |  | 133.1                     | 89.7                      | 104.2                            |
| Cancer of Pancreas                 | (11)   | 100.5                     | 74.0                      | 82.9                             |
| Cancer of Bronchus, Trachea, Lung  | (7)<br>(64)  | 81.3                      | 60.6**                    | 49.0**                           |
| Cancer of Prostate (Males only)    | (12)   | 65.3                      | 51.8**                    | 57.5                             |
| Cancer of Breast                   | (0)  | 0                         | 0                         | 0                                |
| Cancer of Kidney                   | (12)   | 184.7                     | 155.7                     | 155.2                            |
| Diabetes                           | (20)   | 183.1*                    | 81.2                      | 67.0                             |
| Cerebrovascular Disease            | (34)   | 86.1                      | 60.9**                    | 60.1**                           |
| All Heart Disease                  | (309)  | 109.9                     | 80.0**                    | 66.3**                           |
| Ischemic Heart Disease             | (236)  | 109.3                     | 81.4**                    | 69.0                             |

The number of deaths among women is too small to draw any conclusions.

\* Statistically significant (p < 0.05)

\*\* Statistically significant (p < 0.01)

# Summary

- Carcinogenicity – Summary
  - Non-genotoxic in a battery of *in vitro* and *in vivo* studies
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# DuPont Comments

Reasons Why OEHHA Should  
Not Expedite Consideration of  
PFOA Under Proposition 65

F. Jay Murray, Ph.D.  
November 16, 2006

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## Not “clearly shown” to cause cancer

- One sex, one species (male rats)
- Benign tumors only (no increase in malignant tumors)
- Not genotoxic
- Peroxisome proliferator
- Not demonstrated to cause cancer in occupational epidemiological studies

# PFOA does not meet listing criteria

## CIC Listing Criteria:

“if the weight of the evidence ***clearly shows*** that a certain chemical causes ***invasive*** cancer in humans, or that it causes ***invasive*** cancer in animals (unless the mechanism of action has been shown not to be relevant to humans), the committee will normally identify that chemical for listing.” [emphasis added]

## **PFOA has not been classified as a carcinogen by US EPA**

- PFOA has not been classified as a carcinogen by US EPA or others
- SAB Panel recommended a “likely to be carcinogenic” descriptor
- US EPA has not accepted this recommendation

# PFOA has not been classified as a carcinogen by US EPA

- EPA's conclusion:

“The SAB Panel's input will be extremely valuable as EPA continues to develop a full and comprehensive assessment of the risks associated with PFOA. In the year and a half since the draft assessment was submitted to the SAB Panel, a considerable amount of additional research has been initiated, and some has been completed. Some of this new research may impact the Panel's assessment of PFOA. For this reason, **it is premature to draw any conclusions on the potential risks, including cancer, from PFOA until all of this new testing is complete and the data are integrated into the risk assessment.**”

- PFOA is under review by US EPA, and a second review by the SAB is planned
- US EPA is actively addressing PFOA

## **PFOA would not merit expedited consideration under the 2004 Prioritization Procedure**

- Data on PFOA are not consistent with the provisions for an expedited review
  - no “new information” or “emerging public health issue”
- PFOA would not be a “high priority” under the normal Prioritization Procedure since it would not pass through the initial epidemiologic screen, which requires:
  - “chemicals with epidemiological evidence suggesting they cause cancer” or
  - “very strong evidence from animals studies” in the absence of positive epidemiological data



## **PFOA would not merit expedited consideration under the 2004 Prioritization Procedure**

**“It is unlikely that chemicals will be proposed for CIC ... review that have been recently reviewed by an authoritative body and found to have insufficient evidence of carcinogenicity ...”**

# Conclusions

- PFOA does not meet the “clearly shown” standard
- PFOA is under active review by US EPA and has not been classified as a carcinogen
- PFOA does not merit an expedited review under the 2004 Prioritization Procedure
- An expedited review is inappropriate