Meeting with Office Of Environmental Health Hazard Assessment regarding PERFLUOROOCTANOIC ACID (PFOA)

Sacramento, California
June 27, 2006

DUPONT®
The miracles of science™

Meeting Regarding PFOA

PARTICIPANTS

- **OEHHA**
  - Joan M. Denton, Ph.D,
    Director
  - Val F. Siebal
    Chief Deputy Directory
  - George Alexeeff, Ph.D.
    Deputy Director, Scientific Affairs
  - Lauren Zeise, Ph.D.
    Branch Chief, Reproductive & Cancer Hazard Branch
  - Martha Sandy, Ph.D.
    Chief, Cancer Toxicology & Epidemiology Section
  - Carol Monahan-Cummings
    Chief Counsel

- **DUPONT**
  - Susan M. Stalnecker
    Vice President, Risk Management
  - Robert W. Rickard, Ph.D.
    Science Director, Haskell Laboratory
  - David W. Boothe
    Global Business Manager, Fluoroproducts
  - William P. Raiford, Ph.D.
    Global Technology Manager, Fluoroproducts
  - Thomas R. Jacob
    Government Affairs Manager, Western Region
  - Arthur Lawyer, Ph.D.
    Technology Sciences Group Inc.
  - Jay Murray, Ph.D.
    Murray and Associates
  - Stanley W. Landfair
    McKenna Long & Aldridge LLP

Meeting Regarding PFOA

AGENDA

- Background on PFOA
- Studies Assessing Health Effects of Exposure to PFOA
- Expedited Consideration of PFOA for Listing Under Proposition 65 Is Unnecessary and Inappropriate

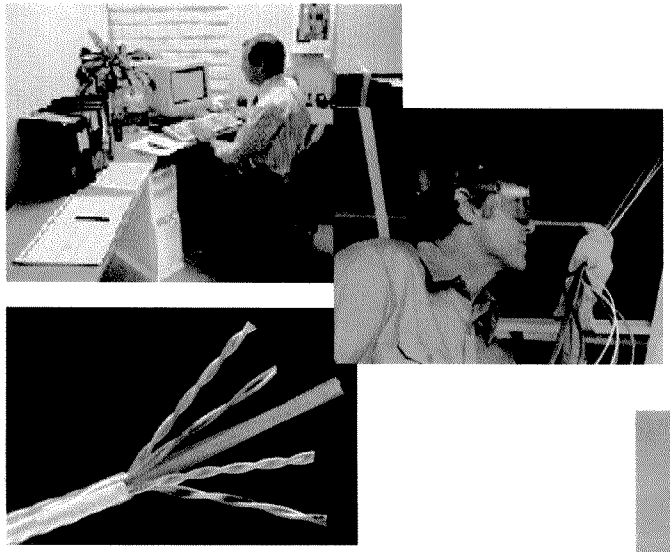
Background

What is PFOA?

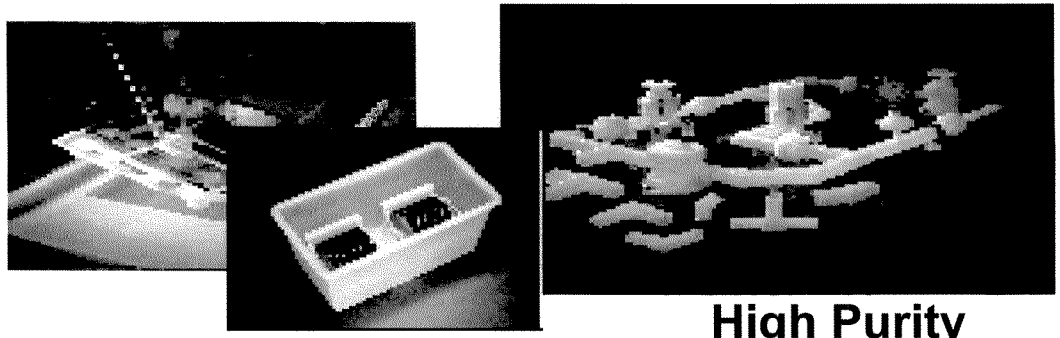
- PFOA is a surfactant used as an essential processing aid to produce fluoropolymer high-performance materials.
- PFOA is not used to make fluorotelomers, but is found at trace levels in some fluorotelomer products as a byproduct of their synthesis.
- PFOA also is an unintended byproduct of the manufacture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

PFOA is not Teflon®

Background: Fluoropolymers Applications - Resins



Telecomm
Wire & Cabling

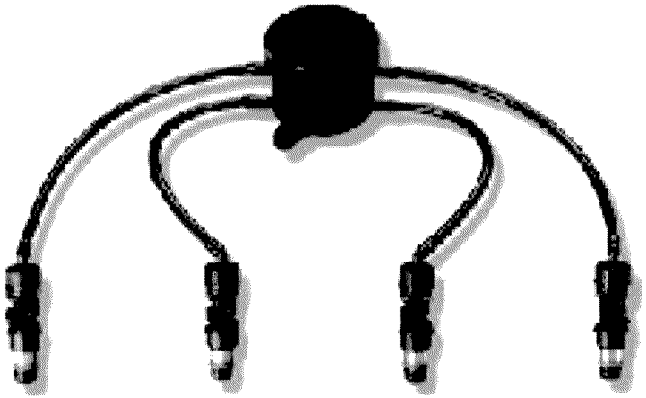


Semiconductor Manufacture

High Purity
Liquid Handling

Chemical Processing
Valves, Lined Piping, Tanks

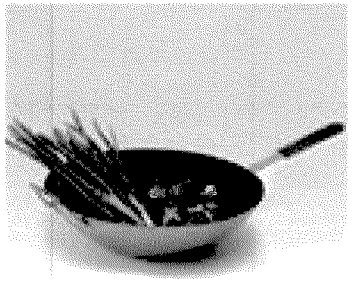
Aerospace Materials
Hydraulic Tubing
Wire & Cabling Flares

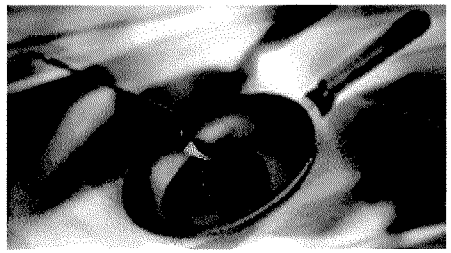


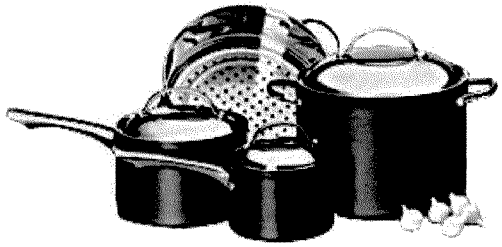
Low Permeable
Automotive Fuel Hose

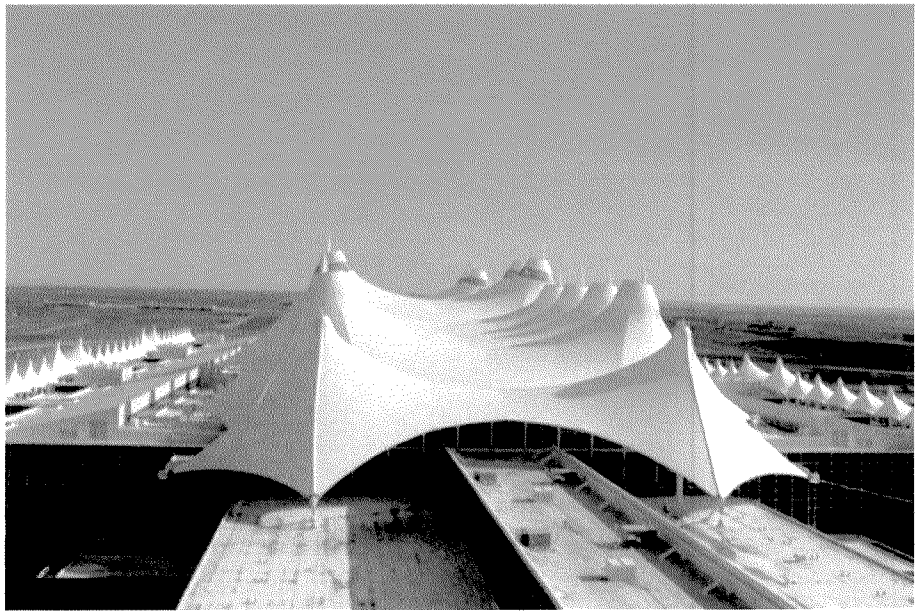
Background: Fluoropolymer Applications - Dispersions

Non-stick Coatings for Cookware and Small Electrical Appliances



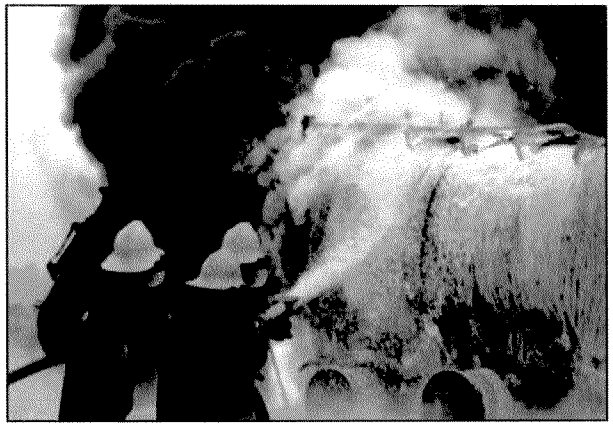




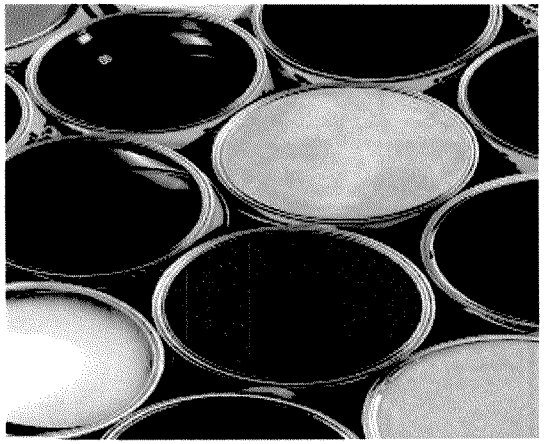


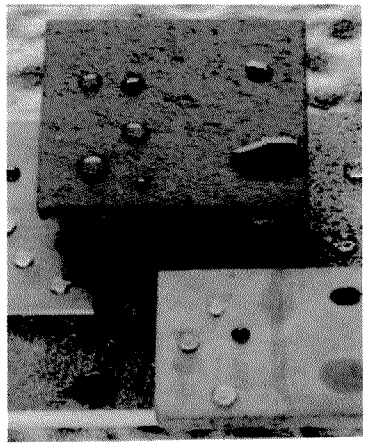
Construction Architectural Fabric

Background: Fluorotelomer Applications



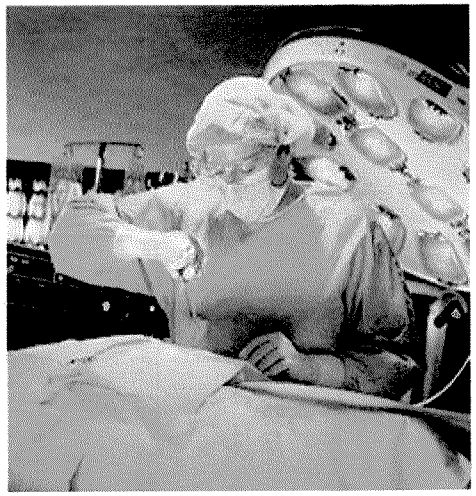
Industrial Fire Fighting



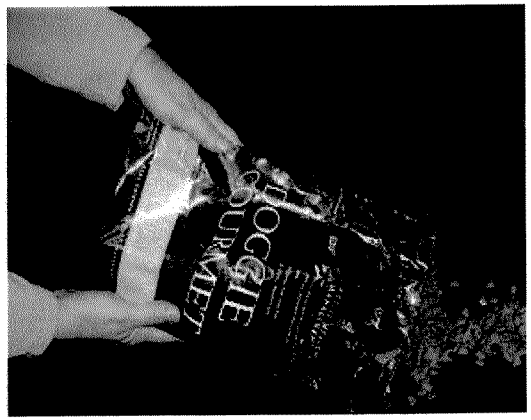


Architectural Coatings and Sealers

Carpet & Textiles



Health Care



Grease Resistant Packaging

Background

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, Executive Director of Harvard Center for Risk Analysis
- *Environmental Science & Technology* 2005, 39(11), pp.3904-3910

Background

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
- Textiles (upholstery, home, technical)

Qualitative Evaluation:

- Cable, wire, hose & tubing
- Architectural membranes

Background

Risk Characterization – *Margins of Exposure*

- Ratios of estimated human exposure levels to relevant health benchmarks
- Calculated separately for each article, each endpoint, and each receptor
- Aggregate MOE calculated to consider multiple-article exposure

Background

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

Background

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^2; ~ 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

Background

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

Background

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."

Background

U.S. FDA Position:

- 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."

Health Effects Studies

Toxicology Database

- Extensive database – approximately 200 animal studies
  - Rodents – uniquely sensitive animal model
  - Acute toxicity in animals – moderate
  - Chronic toxicity in animals – liver primary target organ
  - Birth defects in animals – negative in multiple studies
  - Reproduction and developmental – rodent studies
    - No effects on reproduction
    - Pup weight, survival and markers of sexual maturation altered

Health Effects Studies

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

Health Effects Studies

Genotoxicity

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

Health Effects Studies

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

Health Effects Studies

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
- No increase in malignant tumors produced in males or females at any dose
- No increase in tumors produced in female rats at any dose
- Thresholds established for all three tumors, as no tumor increases were observed at the low dose of 30 ppm

PFOA Health Effects Data

Carcinogenicity Studies in Rats

- All three benign tumors have been observed as class effects of peroxisome proliferators in rats
- Other chemicals in this class include:
  - Pharmaceuticals used for many years in humans without evidence of carcinogenicity
    (*e.g.*, clofibrate, gemfibrozil, methylclofenapate)
  - The classic peroxisome proliferator "Wyeth 14,632"
  - Industrial chemicals (*e.g.*, phthalates — DEHP)
- This mechanism is believed to be specific to rodents

Health Effects Studies

Mammary Gland Tumors in Rats

- Study report and EPA draft risk assessment conclusion: no mammary tumor effect
- OPPT Scientific Advisory Panel of Scientific Advisory Board (SAB Panel)
  - Three-quarters of members concluded that incidences of mammary gland tumors were increased in PFOA-treated groups (one-quarter disagreed)
  - SAB Panel considered reliance on historical control data by study authors to be inappropriate

Health Effects Studies

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

Health Effects Studies

Pathology Working Group Review of Mammary Glands – Methods

- Conducted in general accordance with requirements for a PWG as stated in USEPA 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

Health Effects Studies

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, Multiple (%)	4	4	12	12	4	6

Health Effects Studies

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

Health Effects Studies

Epidemiology: Employee Health Studies

- Over 50 years of experience
- Thousands of workers across three plant sites
- PFOA exposures: average 1-10 ppm, 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

Health Effects Studies

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

Health Effects Studies

New Health Effects Studies on PFOA

- Retrospective mortality study in DuPont workers (DuPont - 2006)
- Existing worker studies of 3M updated (3M - 2006)
- Publication – Activation of PPAR Receptors by PFOA and Naturally Occurring Fatty Acids (in press – 2006)
- Mechanistic studies of rodents with modified PPAR alpha nuclear receptors (Penn State/DuPont/3M - 2006)
- Cell proliferation/apoptosis studies in rats (Plastics Europe - 2006)
- Studies on mechanistic aspects of pancreatic acinar cell tumors (Plastics Europe - ongoing)
- Pharmacokinetics and mechanistic studies (ORD, NTP)

Proposed Two-year Bioassay (NTP)

Health Effects Studies

EPA's Scientific Advisory Panel of SAB: PFOA Final Report

- Issued May 31, 2006
- In general, the SAB Panel endorsed EPA's risk assessment approach, particularly:
  - The SAB Panel strongly urged EPA to consider peer-reviewed new information to strengthen the risk assessment.
- 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."