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March 22, 2005

E-MAIL AND FEDERAL EXPRESS

Dr. Sue Shallal
U.S. Environmental Protection Agency
EPA Science Advisory Board Staff (1400F)
1200 Pennsylvania Avenue, N.W.
Washington, DC 20460

Re: Science Advisory Board Perfluorooctanoic Acid Risk Assessment (PFOA)
Review Panel: Supplemental Comments

Dear Dr. Shallal:

As mentioned in our February 11, 2005, comments submitted to the referenced panel, our clients include individuals who have consumed or are consuming PFOA-contaminated drinking water in the West Virginia and Ohio communities near DuPont's Washington Works Plant in Wood County, West Virginia, where DuPont has used PFOA since the 1950s (the "DuPont Plant"). On behalf of those clients, we are providing supplemental information to the panel in response to the March 9, 2005, submission from DuPont (the "DuPont Comments"). Our supplemental comments are as follows:

Although we fully support the panel considering additional, new information from interested parties and agree that interested parties should provide as much new information as possible to assist the panel, we object to the manner in which DuPont provided its comments to the panel outside the public process, effectively avoiding any public discussion or scrutiny of the comments during the scheduled public forum on February 22-23, 2005. Pursuant to the Federal Register notice issued by the SAB on January 12, 2005, the SAB confirmed that a public meeting was scheduled for February 22-23, 2005, to address the panel's charges and that all "written comments are accepted until the date of the meeting (unless otherwise stated)", which it was not

otherwise stated, and that all such written comments "should be received in the SAB Staff Office at least five business days prior to the meeting date." (70 Fed. Reg. 2157-8 (Jan. 12, 2005)) The SAB also clarified that those wishing to provide information to the panel should "bring at least 35 copies of their comments and presentation slides for distribution to the reviewers and public at the meeting." (*Id.*) Although essentially all of the information provided by DuPont to the panel on March 9, 2005, was known to DuPont and available to DuPont prior to and during the February 22-23, 2005, public meeting, DuPont did not submit any of the information to the panel prior to the meeting or make copies of any of the information available to the public for review and discussion during the meeting. In addition, DuPont does not identify any "new" information first acquired by DuPont after February 23, 2005, that justifies the delay of its submission until after the public process had concluded.

By sidestepping the public process established for this review, DuPont deprived the panel and the public of any opportunity to explore the information provided by DuPont during the public meeting or to ask any questions in the public forum. If DuPont had followed the same public comment process followed by everyone else, the basis of DuPont's comments and analysis could have been discussed with the panel during the public meeting, including the following:

1. DuPont's statement that "[a]verage serum levels in workers are 100-3000 times greater than the average serum level in the general population" ignores the fact that, as pointed out in our February 11, 2005, comments and oral comments during the February 22-23, 2005, public meeting, levels of PFOA in serum samples from non-occupationally-exposed "general population" residents consuming PFOA-contaminated drinking water near DuPont's Washington Works Plant and nearby PFOA-contaminated landfill are as high and, in some situations, even higher than the level of PFOA in the serum of some workers at the plant.

2. DuPont's assertion that there are "no human health effects ... known to be caused by PFOA exposure" and that "[n]o known health effects have been observed in an occupational setting due to exposure to PFOA" directly contradicts the voluminous data already provided to the panel on this point, including results of the first study of adverse health effects reported among the general population exposed to PFOA in the communities near DuPont's Washington Works Plant (provided to the panel with our February 11, 2005, comments), all of which reveal strong associations between PFOA exposure and serious adverse health effects in both worker and general population exposure groups.

3. DuPont's argument that its own internal epidemiology data for PFOA-exposed workers cannot be used to support any conclusions as to associations between PFOA exposure and adverse health effects because "[o]nly about 25% of the Washington Works employees work with PFOA" ignores the fact that plant-wide health effects are directly relevant to PFOA exposure because all Washington Works employees are, in fact, getting exposed to high levels of

Dr. Sue Shallal
March 22, 2005
Page 3

PFOA, whether by virtue of residential air and/or drinking water exposures or otherwise, rendering the entire plant population a PFOA-exposed group. This point is confirmed through DuPont's own PFOA serum sampling at the Washington Works Plant (provided to the panel with our February 11, 2005, written comments) that shows an average level of PFOA in the serum of employees who allegedly have had no direct occupational exposure to PFOA to be over 100 parts per billion - approximately 25 times higher than the "average general population" PFOA serum rates referenced by DuPont.

As mentioned above, there is essentially no "new" information provided by DuPont in its comments that was not known to or available to DuPont prior to or during the February 22-23, 2005, public meeting that justified DuPont's delaying submission of the information to the panel until weeks after the public meeting. For example, the data DuPont provides from its own research indicating that PFOA *is* a full agonist for human PPAR alpha surely was available to DuPont during the February 22-23, 2005, public meeting but was not presented to the panel. Given the importance of this data to the issues debated by the panel during the public discussions, such data should have been presented and discussed with the panel during the public process.

Interestingly, some of the key PFOA health data that did, in fact, first become available after the February 22-23, 2005, public meeting is not mentioned anywhere in DuPont's Comments. In particular, although DuPont urges the panel to consider additional data to support its view that there is no association between PFOA exposure and breast cancer, DuPont does not disclose to the panel the results of the new USEPA research presented during this month's Society of Toxicology (SOT) meeting that actually strengthens and further supports a connection between PFOA exposure and breast cancer. (*See Exhibit A*) Also, DuPont provides no new rationale for rejecting the concurrent controls or the dose response for the Riker (1987) study. In addition, new research was reported during the SOT meeting further supporting an association between PFOA exposure and respiratory effects, supporting what was found in the study of community residents exposed to PFOA in their drinking water in West Virginia and Ohio, which we provided to the panel in our February 11, 2004, comments. (*See Exhibit B*) New USEPA research also was presented during the SOT meeting suggesting that PFOA exposure caused defects in embryonic mice of a nature warranting reevaluation of the unusual facial defects found in two of the five children born to PFOA-exposed women at DuPont's Washington Works Plant in 1981 (1981 data was provided with our February 11, 2005, written comments). (*See Exhibit C*)

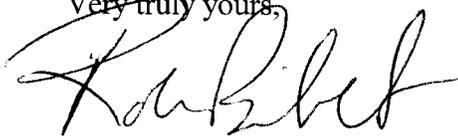
The reasons given by DuPont as part of its continuing efforts to persuade the panel to dismiss pituitary weight changes relate to the alleged lack of a dose response, magnitude of the changes, the fact that they were not seen in males or the parental generation, or were not associated with histological findings. It is our understanding that none of the issues, other than

Dr. Sue Shallal
March 22, 2005
Page 4

that relating to the dose response, can legitimately be used to reject statistically significant organ weight changes, according to USEPA guidance. We further understand that pituitary weight changes are clearly dose-related and simply reflect saturation of the effect at 3 mg/kg/day and higher.

Although we agree with DuPont that even more work is currently underway or will be started soon to help further assess the nature and extent of adverse human health effects associated with PFOA exposure, we strongly disagree with DuPont's request that the panel delay its PFOA review until some indefinite, undefined future date when the results of more work might or might not be available. We respectfully urge the panel to move forward as expeditiously as possible with the information available now so that adequate protection of human health and the environment is not delayed.

Very truly yours,



Robert A. Bilott

RAB/mdm
Enclosures

cc: Dr. Charles M. Auer (w/ encls.)
Dr. Jennifer Seed (w/ encls., by e-mail)
Mark J. Garvey, Esq. (w/ encls.)
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EPA FINDS BREAST CANCER LINK FROM THREE HIGH-PROFILE POLLUTANTS

NEW ORLEANS — EPA research on three high-profile pollutants — dioxin, atrazine and perfluorooctanoic acid (PFOA) — suggests a link to the trend of early puberty among U.S. girls, and one agency scientist involved in the studies says the findings may also shed light on breast cancer risk factors.

The findings could result in the compounds being given a high priority in the agency's Endocrine Disruptor Screening Program (EDSP), for which the agency is still developing a research strategy. In the studies, carried out by the Office of Research and Development (ORD), female mice subjected to prenatal exposure to each of the substances demonstrated an effect on mammary gland development, said ORD researcher Suzanne Fenton in a presentation of the findings at the Society of Toxicology's annual meeting March 7.

PFOA is used to manufacture various non-stick consumer products, such as Teflon cookware and Gore-Tex clothing, and has been detected in the blood levels of the general population. Dioxin is a byproduct of combustion and industrial process, such as paper manufacturing. Atrazine is a widely used agricultural pesticide. All three substances are suspected endocrine disruptors that pose developmental and other health risks.

One of the scientific questions driving the studies involved the growing trend of what is known as "precocious puberty," or the onset of puberty before the age of 8, in U.S. girls, Fenton said. While just 2.5 percent of U.S. girls reported the condition in 1969, the figure had risen to 10 percent in the 1990s.

Though they start puberty earlier, "precocious" girls actually take longer to progress through the developmental stage. The suspicion is that the delay shown in the test animals' mammary development may reflect this delayed development in U.S. girls, Fenton said.

The real danger in delayed mammary development lies in the fact that it creates a greater opportunity for cancer to develop, according to Fenton. "These delays mean a longer window for cancer susceptibility," she said.

Another concern is that the relevant exposures come very early after conception — 12 to 14 days into gestation for the test subjects, which would translate into the first trimester for women, "when many women aren't even aware they're pregnant," Fenton said.

The potential tie to breast cancer "raises the stakes for [the three chemicals] as endocrine disruptors," one environmentalist says. "These are already pretty controversial" substances, according to an agency source. But if they weren't on the list before, EDSP "may find the evidence of mammary gland impairment, not to mention relevance to breast cancer, hard to ignore," the source says.

Among EDSP's tasks is selecting a group of 50 to 100 chemicals for its initial round of screening, with testing on those flagged as significant endocrine disruptors. EPA also is conducting studies to validate its screening and testing methods. A new EPA panel charged with advising the agency on validation, the Endocrine Disruptor Methods Validation Advisory Committee, meets next month for the first time.

While the ORD research on dioxin has been completed, the findings from the other two are only preliminary at this point. The study on PFOA, which is also the subject of a class-action lawsuit against its manufacturer, should be finished within a year, and the findings on atrazine, which is a herbicide applied mainly to corn and soybean crops, should be out very soon, Fenton said. "We always make our studies available" to EDSP organizers, she said.

Toxics

JUDGE REJECTS ACTIVISTS' BID TO BLOCK EXPORT OF TOXIC NAVAL VESSELS

A federal judge has cleared the way for the Bush administration to export contaminated naval vessels for dismantling abroad, after dismissing environmentalists' lawsuit that charged the scheme violated U.S. environmental laws.

But environmentalists are still declaring a victory, saying the suit forced the Department of Transportation's Maritime Administration (MARAD) to conduct additional environmental analyses of its plans and apply to EPA for a rulemaking to determine whether the plan violated a long-standing ban on exports of polychlorinated biphenyls (PCBs).

Environmentalists in 2003 filed suit against EPA and MARAD to block the Bush administration's plans to transport 13 former U.S. military ships stored in Virginia's James River to the United Kingdom for dismantling, charging the scheme violated the National Environmental Policy Act (NEPA), the Toxic Substances Control Act (TSCA) and the Resource Conservation & Recovery Act (RCRA). The ships are contaminated with PCBs, asbestos, fuel, and other contaminants.

Environmentalists say the plan sets a negative precedent by allowing the export of contaminated vessels abroad for dismantling, including to third-world nations that lack adequate worker and environmental safeguards.

Judge Rosemary M. Collyer of the U.S. District Court for the District of Columbia issued a temporary restrain-

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AUGMENTATION OF OVALBUMIN - INDUCED IGE AND AIRWAY HYPERREACTIVITY RESPONSE BY PERFLUOROOCTANOIC ACID (PFOA)

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Studies were conducted to investigate the role of dermal exposure to Perfluorooctanoic acid (PFOA), an immunosuppressant with widespread use as a carpet and fabric protectant, on the hypersensitivity response to ovalbumin in a murine model. BALB/c mice were exposed dermally to concentrations of PFOA ranging from 0.01-2.0% (0.25-50mg/kg) for 4 days. In hypersensitivity studies, mice were also intraperitoneally injected with 7.5µg ovalbumin and 2mg alum on days 1 and 10 and in some studies, intratracheally challenged with 250µg ovalbumin on days 17 and 26. Endpoints for studies included body and organ weights and cellularities, IgE, airway hyperreactivity, and lung histopathology. Following exposure to PFOA, an increase in liver weights and a decrease in thymus and spleen weights and cellularities were observed. Similar immunomodulatory trends were demonstrated in mice co-administered PFOA and ovalbumin. Greater than a 2-fold increase in total IgE was demonstrated when mice were co-exposed with concentrations of PFOA ranging from 0.75-1.5%, while the ovalbumin-specific IgE response peaked after a 3-fold increase ($p < 0.01$) in 0.75% PFOA co-exposed animals as compared to the ovalbumin alone exposed animals. Antigen-specific airway hyperreactivity was increased ($p < 0.05$) in the 1.0% PFOA co-exposed group, with a dose-responsive pleiotropic cell response characterized by eosinophilia and mucin production, in animals co-exposed to concentrations of PFOA up to 1.0%, as compared to the ovalbumin alone exposed animals. PFOA was demonstrated to be immunotoxic in a murine model following dermal exposure, with an enhancement of the hypersensitivity response to ovalbumin, suggesting that PFOA exposure may augment the IgE response to environmental allergens.

Citation: K.J.Fairley, S.Kearns, L.P.Myers, R.Purdy, B.J.Meade. AUGMENTATION OF OVALBUMIN - INDUCED IGE AND AIRWAY HYPERREACTIVITY RESPONSE BY PERFLUOROOCTANOIC ACID (PFOA). Abstract No. 1210. *2005 Itinerary Planner*. New Orleans, LA: Society of Toxicology

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Abstract

Abstract: PFOA Induces Dymorphogenesis In Mouse Whole Embryo Culture.

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Perfluorooctanoate (PFOA) is a perfluoroalkyl acid (PFAA) found in numerous industrial and consumer products. Many PFAAs persist in the environment and are found in humans and animal tissues throughout the world. PFOA is a developmental toxicant in vivo producing embryonic, fetal and postnatal lethality, and altered fetal and neonatal growth. In order to determine if direct exposure of conceptuses to PFOA disrupts development, CD-1 mouse conceptuses (3-6 somite stage, GD8) were exposed to PFOA in whole embryo culture. At the end of a 24H culture period embryonic morphology was assessed and scored using a scoring system developed by our laboratory. Scores ranged from 0, for morphologically normal, to a maximum of 58 for severely affected embryos. In control medium, 82% of embryos (18/22) grew normally and the mean score was 0.4±0.2. Exposure to 0.1 or 0.2mg/ml PFOA did not alter development (4/4 and 11/17, normal embryos respectively). However, dysmorphogenesis was induced by PFOA at 0.4 (82%), 0.6 (92%), 0.75(100%) and 1.0 (100%) mg/ml. Exposure to 1.25mg/ml produced 100% embryo lethality. Prosencephalic and pharyngeal arch hypoplasia and abnormal heart outflow tract development were induced by >0.4mg/ml PFOA. Embryonic scores were increased at PFOA concentrations >0.4mg/ml and were 0.0±0.0(0.1), 1.7±0.7(0.2), 11.3±2.2(0.4), 11.3±2.0(0.6), 23.5±1.5(0.75) and 31.1±3.9(1.0). The benchmark concentration for a 5% increase in dysmorphic embryos by PFOA was 0.04±0.01mg/ml. These studies demonstrate that a direct exposure to PFOA for 24H disrupts development and induces embryo lethality. This abstract does not represent EPA policy.

Citation UFA (1)

Citation: Blanton, M. R., J. M. Padowski, E. S. Hunter Iii, J. M. Rogers, and C. S. Lau. PFOA INDUCES DYSMORPHOGENESIS IN MOUSE WHOLE EMBRYO CULTURE. Presented at Society of Toxicology, New Orleans, LA, March 6-10, 2005.

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