DuPont Haskell Laboratory Visit
Meeting Minutes
June 30, 2000

In Attendance

DuPont:
John O'Connor, Reproductive and Developmental Toxicology
John Gannon, Environmental Fate
Bob Hoke, Ecotoxicology
Gary Jepson, Pharmacokinetics
Gerry Kennedy, Director of Applied Toxicology

3M:
Sue Beach
John Butenhoff
Dan Hakes (at beginning only)
Paul Lieder
Nelda Marecki
Geary Olsen
Mike Santoro

Purpose of Meeting
The stated purpose of the meeting was to "clear our mutual understanding of the pertinent data on PFOA."

Nota bene: Through several comments made during the meeting, it became evident that this DuPont team was charged with developing a recommendation to be presented to business leaders at DuPont relative to PFOA and, perhaps, telomer-based products as well.

Agenda:
Three primary areas for discussion were agreed upon:
1. Environmental data, in particular, biomagnification
2. Biopersistence and the current understanding of elimination half-life
3. Descriptive toxicology, in particular, functional reproduction

The subjects above were taken in the order indicated.

Then meeting began at approximately 9:15 am and continued through lunch with adjournment at approximately 1:30 pm.

Environmental Data

From an environmental standpoint, it was 3M that provided most of the information on PFOA, the testing results, monitoring studies planned (Decatur and the biosphere programs), and the work 3M has done to assess technology solutions for removal from wastewater. 3M explained the PFOS program in general terms, especially the biosphere monitoring program. 3M stated that much of the information has already been submitted to EPA, and therefore available. As additional information is developed by 3M, it will be submitted.

DuPont did not appear to have any substantial information to contribute and had not as yet developed the analytical methodology. A copy of the DuPont submission to EPA was provided, as promised, by Gerry Kennedy. It was obvious from the summary level information and comments made from the DuPont representatives that little environmental and ecotox work had been completed on PFOA. An exposure document in the form of an UEIP was filed with EPA on June 26th.

The DuPont representatives inquired about the availability of ^{14}C-labelled PFOA. They had obtained a sample in the past from 3M. 3M responded that a sample existed; however, it was not immediately available for use.

Biopersistence and the Current Understanding of Elimination Half-Life

Human Data:
DuPont was interested in any measurements of PFOA in general population samples. Geary provided an overview of what we currently understand and showed the recent data from deceased individuals matched liver and serum samples.

Geary then gave an overview of on-going or planned research, including the Hopkins collaboration, the Group A *Strep.* clinical-trial pediatric samples, the Pacific NW geriatric samples and the adults aged 20-59 samples from blood banks. DuPont expressed an interest in the outcome of these sampling programs with respect to PFOA determinations.

3M emphasized, once again, that the presence of telomer in samples has not been a focus of our investigations.

Elimination Half-Life:
DuPont asked for 3M's understanding of the elimination half-life for PFOA. Geary showed the recent data from our retiree monitoring program. This data suggests a much longer half-life of elimination from serum that has been

observed in other species, including cynomolgus monkeys. While it is consistent with the reported elimination half-life in 3M's previous publications, DuPont did not seem to accept that this was real, and intimated that they believed there was a problem with the data. DuPont offered no rationale concerning the contention that the half-life data may be in error other than the differences between experimental species and man. While they suspected re-exposure, Geary indicated that this factor had been taken into consideration.

Nota bene: The impression was conveyed that DuPont assumed the EPA was less concerned with PFOA due to the shorter serum elimination half-life observed in research animals. The data Geary presented, which currently suggested a slightly higher median half-life for PFOA as opposed to PFOS appeared to raise some concern.

Kinetics:
Other than the data that 3M was already aware of, DuPont had little to offer in regard to pharmacokinetics or human sampling. They will proceed with employee monitoring and are currently communicating with the Environmental Lab to develop serum analysis techniques.

Gary Jepson had a list of questions related to his "Approach for Descibing PFOA Kinetics," a document he provided to us (attached). His questions included: 1) sex differences; 2) absorption coefficients for dermal and oral exposure (they estimate the dermal absorption coefficient to be 1 x 10-5 cm/hr in 20 % aqueous solution); 3) tissue partition coefficients; 4) skin exposure data; 5) oral distribution (3M offered a copy of the radiolabel study); 6) oral absorption rate constant; and, 7) information on partitioning, diffusion, protein binding (3M offered fatty-acid carrier-protein binding studies).

DuPont asked for our participation in assisting them with a better understanding of PFOA kinetics. They did contend that there could be species differences in binding or other characteristics that might explain the longer elimination half-life in humans.

Descriptive Toxicology, in particular, Functional Reproduction

On this topic, DuPont had one question: when was the planned two-generation reproduction / developmental study going to commence? 3M stated that this study was temporarily "de-prioritized." Gerry Kennedy conveyed that the study was important to conduct. I (John Butenhoff) explained that I had been instructed to hold-off on commencing this study for the time being. I indicated that, if and when 3M conducts the study, DuPont is certainly welcome to review

the proposed study plan. Gerry indicated that this was a crucial issue that our respective senior management should address.

Nota bene: This remains a significant gap in the PFOA data package. Please recall that I was specifically asked to commit 3M to completing this study at the APME meeting in Europe in February of this year and reinforced that message at the March APME meeting in Philadelphia. The expectation of the APFO producers and users involved in APME has been and continues to be that 3M will do the study independently. The next meeting of the APME APFO Toxicology Committee is August 3-4 in St. Andrews, Scotland. A resolution of this issue before that meeting would be most helpful in that it would allow for alternative plans to be developed, if necessary.

It was confirmed that the single-dose tumorigenesis study which included APFO had still not been written up into a report format.

Summary

The information sharing at the meeting seemed weighted toward 3M providing information, since DuPont was not able to contribute substantial information. The DuPont team is apparently tasked with bringing forward a recommendation to their management on the level of risk associated with continued use of APFO. It is possible that they are being requested to bring forward similar recommendations with regard to telomers. The EPA has not yet asked for data on telomer compounds.

DuPont wishes to work with 3M in gaining a more complete understanding of APFO. The environmental fate and effects, kinetics and reproductive biology are key areas of interest.

Prepared by John Butenhoff on July 11, 2000

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