SPP

PROPOSAL FOR FEASIBILITY ASSESSMENT

Estimating Exposure, Biopersistence, and Potential Liver Effects from Workplace Exposures to Organofluorines: A determination of the feasibility of appropriate analyses of historical surveillance data

Introduction

Concern regarding organofluorine exposure (C-8, [redacted] etc.) is based on the results of rodent testing. In animals, these organofluorine compounds induce a biological response known as peroxisome proliferation. Research with chemicals known to produce this response suggests that long-term administration to rodents results in the development of benign tumors of the liver, pancreas, and testis. However, other data indicate that man may be at little risk for occurrence of tumors since man is a low responder to this class of chemicals, i.e., peroxisome proliferators. However, other liver toxicity may occur in man that is independent of peroxisome induction. Based on experimental data, changes in liver function may be a means of detecting human biological response to these chemicals.

Additional concern with these compounds has been that these materials have been detected in the blood of exposed employees. Exposure potential is by inhalation or skin contact. It is known that these compounds are eliminated from the body very slowly. It is estimated that the half-life of C-8 may be as long as 3-5 years. At present, there are no available human data that demonstrate increased levels of blood organofluorines with discernible adverse health effects. However, there remains concern about the possibility of such effects, particularly with regard to liver function.

Background

In 1978, the 3M Company notified DuPont that they had observed elevated organic fluorine levels in the blood of their workers exposed to ammonium perfluoro-octanoate. Although the specific 3M product was not used at Chambers Works, Chambers Works conducted a special blood monitoring program in 1978-79 for our fluorosurfactant employees. Organic fluorine levels in the blood were found to be no different than the Wilmington control group levels. As a result, the blood monitoring program was terminated in 1979.

In 1999, Chambers Works conducted another special blood monitoring program for a subset of our fluorochemicals employees. Organic fluorine levels in the blood were found to be no different than the 1978-1979 Chambers Works levels and the 1978-1979 Wilmington control group levels.

Purpose

The objective of medical and exposure surveillance in a workplace population is to detect people with exposure-associated dysfunction who are at risk for developing clinical disease. When the exposure markers and effect markers are well-quantitated, such surveillance programs can provide valuable information as to safe occupational exposure levels. In addition, risk evaluations can be based on human data.

This proposal describes a biomonitoring project with the following objectives:

1. Establish pre-placement baseline levels of fluoride ion in blood and blood perfluorooctonoate level,
2. Monitor workplace exposure to C-8 by repeating the blood sampling every month,
3. Correlate biomonitoring results with Industrial Hygiene workplace air and personal monitoring results,
4. Establish rate of bioaccumulation of C-8 in workers,
5. Establish level of biopersistence in workers by continued surveillance following cessation of exposure.
6. Correlate data on biomarkers of effect (serum liver enzyme levels) with the biomarkers of exposure (fluoride ion in blood and blood perfluorooctonoate level).
7. Examine other health effect measures (medical history questionnaire, including smoking history; complete blood count, SMA-12) for potential confounders or modifiers.

Approach

A C-8 surveillance program at Chambers Works will take advantage of the proposed C-8 recycling program soon to be initiated. If the project is approved before work begins, the ability to collect pre-exposure baselines on both the biomarkers of exposure and of effect will not be compromised. The data matrix should contain the following variables:

1. Name
2. SSN
3. Date of Hire
4. Date of C-8 task initiation
5. Date of Birth
6. Current Task Assignment (job title, task name)

7. Time spent in task
8. Standard IH measures of exposure (preferably personal monitoring, but area data could be used), with an assessment of the potential for dermal exposure
9. Use of personal protective equipment
10. Laboratory results of C-8, fluoride ion, and liver enzyme measurements retained as serial data variables.

The protocol will prescribe data collection at monthly intervals for liver enzyme measurements, and area or personal monitoring at either weekly, or bi-weekly intervals, for a period of one year. The range and variance of these measurements, along with the total number of individuals in the potentially exposed population, will provide a good indication of whether there is clinical and/or epidemiological value in continuing the data collection.

It should be recognized that while liver enzymes are generally highly sensitive, they are nonspecific and of poor positive predictive value in identifying true occupational liver disease. (In low-risk workplaces, where measured exposure is low, the prevalence of occupation-associated liver disease may be so low that the positive predictive value of the screening test may also be very low. In these circumstances, other causes of liver dysfunction are the more likely reason for abnormal screening results.) However, the widely available batteries of enyzme tests are inexpensive and have the advantage of large bodies of general population data and associated "normal" values that are useful for comparison. In addtion, the availability of pre-exposure levels will enable each C-8 exposed worker to serve as his own control as the primary purpose of the study is to measure change in these biomarkers over time.

Responsibilities

The Occupational Health personnel at Chambers Works will be responsible for the collection and submission for analysis of the blood samples and the industrial hygiene monitoring data. The Corporate Epidemiology Program will assume responsibility for constructing the analytic data file and doing the assessment of the descriptive statistics on the population results at the end of the first year of data collection.

Employees will be asked to participate in a descriptive epidemiology project that will be directed to understanding whether or not C-8 exposures result in measurable blood changes. This communication will be done in person by site personnel with the corporate epidemiologist present to answer questions. Upon completion of the project, the employees will be notified, in person and in writing, of the results. Questions concerning medical surveillance will be handled by site Occupational Health staff.

Several of our fluoroprotectant and fluorosurfactant [redacted] products and intermediates were tested in an oral dose animal screening study at Haskell Lab to compare the biopersistence of total fluorine in the blood with the specific

fluorochemical that 3M had identified. The preliminary screening information from the blood analysis after repeated oral doses so far indicates that our products do not absorb into the blood to the same high level nor persist in the blood compared with the 3M specific fluorochemical.