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Identification of Fluorochemicals in Human Tissue

The objcetive of this study is to determine the concentration ratios, in humans, of liver to serum, liver to bile and bile to serum for perfluorooctanesulfonate (PFOS). An application for securing liver, gallbaldder, bile and serum from donors was approved by the International Institute for the Advancement of Medicine (IIAM). IIAM is a non-profit organization whose purpose is to faciliate the placement of non-transplantable human organs and tissues for biomedical research and education. All tissues are procured with the informed consent of the donor or the donor's next of kin, in accordance with the Uniform Anatomical Gift Act. Donors may be from anywhere in the United States and Canada. It is estimated to take approximately 1 year to secure tissues from 12 donors. A final report should be available by March 1, 2001.

Corporate Occupational Medicine Section/Epidemiology Unit
Proposal to EHS&R Committee
3/1/98

Title: Identification of Fluorochemicals in Human Tissue

Purpose: Evidence that organic compounds containing the element fluorine chemically bonded to carbon can be found in human blood has been known for more than 30 years. Within the past 12 months it was estimated that serum PFOS (perfluorooctane sulfonate) levels are within the 20 to 50 ppb range in the general population. This is primarily based on pooled serum samples. Although PFOS is known to concentrate in the liver and to undergo enterohepatic circulation, we do not know what tissue concentrations may be among humans. The purpose of this study is to determine the level of several fluorochemicals from the serum, liver and bile of the same individual (human).

Significance: Determination of the tissue concentrations of selected fluorochemicals will provide for a more specific understanding of the distribution of these compounds in the human. The ratio of liver to serum, liver to bile and bile to serum will be compared to data obtained from studies in nonhuman primates. Ultimately, these data will be used in defining and confirming assumptions necessary in human health risk assessment.

Objectives: The objective of this study is to determine the ratio of liver:serum, liver:bile and bile:serum to the following fluorochemicals: PFOS, PFOSA, PFOSAA, M570, M556, PFHS and POAA among 12 human donors. Total organic fluorine will also be analyzed should analytical methods permit.

Protocol: An application for securing liver, gallbladder (bile) and serum from donors will be submitted to the International Institute for the Advancement of Medicine (IIAM). IIAM is a non-profit organization whose purpose is to facilitate the placement of non-transplantable human organs and tissues for biomedical research and education. IIAM is a division of the Pennsylvania Regional Tissue and Transplant Bank, an inspected and accredited program which meets or exceeds all of the Food & Drug Administration (FDA) and the American Association of Tissue Banks standards. All tissues are procured with the informed consent of the donor or the donor's next-of-kin, in accordance with the Uniform Anatomical Gift Act. Proof of donor consent to the applicant (i.e., 3M) is not always possible because it may involve the photocopying of privileged information. However, a donor identification number is provided to the applicant. A copy of a blank consent form is available upon request. Donors may be from anywhere in the United States and Canada. All donors are tested for HIV, hepatitis B, hepatitis C, HTLV and syphilis. IIAM procures and distributes tissues on an investigator request basis. The IIAM Application Review Committee reviews each application for ethical considerations, scientific merit and feasibility. Upon approval, the 3M request is placed in the rotation for the tissue of interest. IIAM abides by U.S. legislation governing the consent process for organ tissue donation, the protection of human subjects through confidentiality

(Health and Human Services 45 CFR PART 46) and Title III of the National Organ Transplant Act, which prohibits the buying and selling of organs and tissues excluding reasonable reimbursement of expenses associated with recovery and placement

Liver and serum analyses are planned for analytical analyses using methods developed and/or approved by 3M's Environmental Laboratory. The method for fluorochemical analysis of bile is currently being developed in a European laboratory under 3M's Environmental Laboratory guidance. A total of 12 donors will be obtained. IIAM estimates that they will send 1 to 3 sets of tissue (liver, gallbladder/bile and serum) to 3M on a monthly basis. Total quantity per donation is: liver (10 grams); gallbladder/bile (intact); and serum (5 to 10 cc).

PI/location/cost: Geary Olsen will be the PI on this project. Jean Burris and Jeff Mandel are co-investigators. Kris Hansen will serve as the contact within the 3M Environmental Laboratory. It is currently expected that the serum analyses will be conducted by Northwest Laboratory. The 3M Environmental Laboratory will conduct the liver analyses. A European laboratory currently validating a method for fluorochemical determination in the bile of primates will likely extend this validation to human bile. Approximate total cost per donor is $1665. The distribution of this cost is the following: shipping of sample $50; obtaining sample from IIAM $710 (liver, 10 grams, $120; gallbladder/bile, intact, $545; serum, 5 to 10 cc, $50); tissue fluorochemical analysis $900 (liver $300; gallbladder/bile $300; serum $300). Total cost for 12 donors: 12 x $1665 = $19,980. This cost does not include the validation of fluorochemicals in human bile by the European Laboratory.

Timeline: IIAM estimates that tissue from 1 to 3 donors per month can be provided to 3M. Thus, to obtain samples from 12 donors may take between 4 and 12 months. Due to the immediate need to understand this fluorochemical distribution within human tissues, samples will be submitted for analysis upon receipt by 3M. If the last sample is obtained by the end of a six month time frame, we estimate a final report of all 12 donors can be completed within 90 days after receipt of the last donor's tissue. The final report will include the fluorochemical tissue concentrations/levels, descriptions of the age, gender, race and geographical location (state or) of the nonidentifiable donors , and pertinent medical history information that may be supplied by IIAM (e.g., cause of death, known liver disease) of the donor.