

by the implementation team to satisfy the regulatory requirements and internal acceptance criteria for vendor supplied data collection PC software (LABCAT® data collection and reporting modules) in a networked environment. The implementation team, comprised of individuals from each discipline which would use LABCAT® modules as well as individuals from Corporate Quality Assurance and Information Technology, successfully implemented LABCAT® modules for Histopathology, Clinical Pathology, Anatomic Pathology, and *in vivo* GLP study data collection. Focus will be on the identification of key elements (such as user defined requirements, software documentaion life cycle, vendor supplied test plans, user developed function specific protocols, software acceptance summaries, error reporting and resolution strategies, development of standard operating procedures, and training) and the supporting documentation for regulatory compliance.

293 AN ANALYSIS OF THE RISK IMPACT ASSOCIATED WITH CHANGES IN SURFACE WATER STANDARDS IN FLORIDA.

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Surface water standards are developed by the USEPA based, in part, on protection of human health from the consumption of contaminated fish. Several assumptions must be made in deriving standards for surface water quality, including the average amount of fish ingested per day. While the USEPA has assumed an average fish ingestion rate of 6.5 g/day, a recent survey of approximately 8,000 Florida households has indicated that a substantial segment of the state's population has a significantly greater fish consumption rate. Based on the findings of this study, the Florida Department of Environmental Protection was petitioned to lower surface water standards that are specifically based on human health protection. In order to evaluate potential risk impacts from changes in surface water standards, an analysis was performed in which data from the Florida fish ingestion survey were used to develop population risk estimates. Monte Carlo simulations were conducted using distributions for fish ingestion for the population at large, as well as subpopulations of particular interest. Distributions for other input variables were also utilized (e.g., adult body weight) when available. Risk distributions were developed for each population group of interest for 36 different chemicals, based both on current surface water standards and potential alternative values. Comparisons among these distributions illustrate differences in risks borne by different populations within the state, and the effect on population risks that can be anticipated to result from changes in standards. These analyses will provide useful tools for regulatory decision-making as well as in setting and evaluating standards for contaminants in the environment.

294 VALUE-OF-INFORMATION ANALYSES FOR BIOMARKERS: SUSCEPTIBILITY TO CHRONIC BERYLLIUM DISEASE AT US D.O.E. SITES.

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Few analyses have been conducted to determine if the development and use of biologically-based markers (biomarkers) is cost effective. We describe a generalized framework for assessing the value of biomarkers in risk management, and apply it to the example of chronic beryllium (Be) disease (CBD), an immune-mediated pulmonary granulomatous disease. Because of their role in immune response, human leukocyte antigen (HLA)-DP genes have been investigated for their relationship to development of CBD. One of the described HLA-DP variants, HLA-DPβ1*0201, contains a substitution of glutamate for lysine at position 69 (Glu-69) that appears to have high sensitivity (86–97%) but low specificity (52–70%) in assessing CBD risk. Value-of-information analysis is used to examine the reduction in opportunity loss, as calculated from the net value of risk reduction, expected for proposed biomarker-based monitoring and intervention programs for occupational CBD. One proposed program is the use of Glu-69 as a screening device for more frequent use of the Be lymphocyte proliferation test (LPT). The LPT is used by US DOE to screen for individual sensitization to Be based on stimulation of lymphocyte proliferation by Be *in vitro*. Assuming the value of avoiding an advanced case of CBD is 1000 times the cost per person of increasing LPT frequency, the reduction in CBD risk resulting from increased LPT frequency in individuals with Glu-69 only needs to exceed 0.6% to make LPT-based screening cost-effective; in the absence of Glu-69 information, risk reduction would have to exceed 44% to support uniformly increased LPT

monitoring as the most cost-effective risk management strategy. Such information can aid the design of appropriate and effective risk management strategies, and guide the development of new cellular and molecular biomarkers. *This was work supported by Department of Energy Cooperative Agreement #DE-FCO1-95EW55084.*

295 THE VALUE OF BIOMARKER INFORMATION IN RISK BASED DECISIONS REGARDING AFLATOXIN CONTROL.

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Aflatoxins are a family of mycotoxins that have been linked to hepatocellular carcinoma (HCC) in humans. The present retrospective analysis compares the state-of-knowledge that existed in 1984, 1990, and 1995 regarding the causal role of aflatoxin B₁ (AFB₁) in HCC. Reductions in uncertainty and the impact on possible regulatory tolerance levels are demonstrated using a Monte Carlo decision analysis model. The comparative value of exposure biomarker information (measurement of AFB₁-8,9-epoxide [AFBO]-N7-guanine adducts vs. food survey information), knowledge regarding interspecies metabolic differences (the ratio of activation to inactivation defined by AFBO formation:total metabolite formation to AFBO-GSH conjugation:AFBO formation), and knowledge regarding the interaction of hepatitis B and AFB₁ in HCC risk (from recent epidemiology studies) are explicitly shown using a Bayesian Monte Carlo model. For example, use of rat data vs. human data in risk assessment may underestimate the activation/inactivation ratio of AFB₁ by a factor of 3, and use of the AFBO adduct biomarker vs. survey information may result in an approximate 40% reduction in uncertainty due to exposure misclassification. Calculations of the differences in total social costs (including control costs and health impacts) associated with control decisions without and with the benefit of improved information are demonstrated. The methods presented here are applicable to any toxicant or exposure scenario. *This project supported in part by Department of Energy Cooperative Agreement #DE-FCO1-95EW55084.*

296 UPDATE ON METHODS TO DERIVE AMBIENT AIR LIMITS.

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Increasing concern exists within the public and regulatory arena regarding the potential for adverse health effects from chemicals emitted into the air. Presently, National Ambient Air Quality Standards have been set for only seven chemicals. State agencies have made an effort to develop regulatory programs to address health concerns of many of the more than 600 chemicals used in industry. Ambient air limits (AALs), the ambient air concentrations of chemicals to which exposure is considered "safe," are used by regulatory agencies to control chemical emissions. AALs have historically been derived from occupational exposure limits (OELs). A major disadvantage is that rationale for setting an OEL is based on one or more of nine toxicological effects. Dependent upon the type of chemical effects (e.g., chronic, sub-chronic, or irritant), a single approach using OELs may be inappropriate to estimate AALs. We have developed ten different formulas or approaches to estimate AALs. These are based on (1) OELs with adjustments to account for type of toxic effect and pharmacokinetics, (2) laboratory animal no observable effect levels plus uncertainty factors or body weight scaling factors, (3) existing Environmental Protection Agency (EPA)-derived reference doses with conversion factors to arrive at airborne concentrations, (4) physiologically-based pharmacokinetic models to address continuous exposure to chemicals in the ambient air, (5) existing EPA-derived Unit Risk Values for carcinogens, or (6) Monte Carlo techniques of either several different approaches or different expert opinions. Use of these methods should yield results that are health protective when incorporated with adequate professional judgment.

297 ELEVATED BLADDER CANCER RISK IN PAINTERS: EPIDEMIOLOGICAL AND TOXICOGENETIC DATA.

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Occupational exposure to aromatic amines is a known bladder cancer risk