Project Description

Studies of Copper Toxicity and Nutritional Supplements

TERA is helping the International Copper Association in the coordination and oversight of two human studies to identify an acute nausea threshold for copper in drinking water. *TERA* has identified four research institutions of excellence and has written two research protocols to attempt to provide a dose response in humans that shows a threshold for bolus ingestion of copper in drinking water.

The first protocol was approved for use at the three research centers originally identified to participate in the study. This study was unique in the use of three separate populations on three different continents. In addition, the study was designed to help nutritional toxicologists understand the potential toxic effects of ingesting copper in dietary supplements. This is the first study to provide data on the acute ingestion of copper in drinking water over a very narrow and well-controlled dose range. *TERA* has inspected each research facility to insure compliance to Good Laboratory and Clinical Practices and each institution's Institutional Review Board policies for human subject studies. *TERA* is also overseeing the research, coordinating the compilation and statistical analysis of the results, and writing report summaries.

The results of Phase I are complete. TERA is coordinating the incorporation of the data from the three sites and will be submitting the manuscript to *Regulatory Toxicology & Pharamacology*. The results of Phase I have clearly delineated a NOAEL and LOAEL for the acute bolus exposure to copper in drinking water in human volunteers, which has not been reported previously. These data will be of importance to regulatory agencies that are grappling with establishing drinking water guidelines for copper and possible for other regulatory agencies with concerns of excess copper ingestion from nutritional supplementation products.

Phase II of the study will be looking at other factors, such as dose and volume effects of copper ingestion, as well as reconfirming the dose response data determined from Phase I. Addressing the effect of copper concentration in the drinking water is of particular importance, since the effect occurs at the portal of entry (the stomach). This raises the question of whether the critical determinant of toxicity is the total daily dose (as in traditional RfDs), or the concentration of copper in the drinking water. Thus Phase II of the study is designed to address this question. Other activities that may be included in future phases of the project include developing a comprehensive copper risk assessment based on the results of the human studies, formatting the assessment consistent with IRIS documentation, and providing an external peer review of the final documentation.