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(1 Page Limit)

During head blight of wheat and barley, deoxynivalenol (DON or “vomitoxin”) and other trichothecene mycotoxins are elaborated that can potentially cause adverse health effects in children and adults who consume the infected grain. DON is regulated in the U.S. at 1 ppm in finished food, however, the European Economic Union and Codex Alimentarius have proposed much lower limits based on a few rodent studies. Of particular concern is susceptibility of infants and young children. A further concern is that although agricultural workers are exposed to airborne DON during harvest, threshing and milling of infected wheat and barley, virtually nothing is known about the adverse effects of inhaling this toxin. Thus, a critical knowledge gap exists relative to the true risks presented to consumers and grain handlers by DON and other trichothecenes elicited during outbreaks of head blight. Our *in vitro* data suggest that the key steps for DON toxicity induction are induction of stress signaling and cytokine expression in human and mouse leukocytes (white blood cells) which ultimately mediate acute and chronic illness. To accurately measure the hazardous potential of trichothecene to humans, it is now essential to relate these *in vitro* studies to threshold dose, duration of exposure, exposure route, and magnitude of toxic effect in the mouse model. We hypothesize that the minimal tissue concentrations of DON required for stress activation and cytokine induction in murine immune tissue in vivo correlate with concentrations that elicit identical effects in vitro in human and mouse leukocytes. Two specific objectives are proposed: (1) Compare threshold doses of acute and subchronic oral DON exposure required for stress activation and cytokine upregulation in the young and adult mouse; and (2) Determine the threshold doses of acute and subchronic intranasal DON exposure required for stress activation and cytokine upregulation in the mouse and corresponding DON tissue levels. In these two objectives, we will identify the lowest observed adverse effect level (LOAEL) and the no observed adverse level (NOAEL) for DON toxicity and these will be further related to DON tissue concentrations in the exposed animals. Finally, DON tissue levels corresponding to these thresholds will be compared to previous investigations with human leukocytes. The resultant data from this study will be used to estimate the true risks of DON and related trichothecenes to humans following exposure via diet or occupational exposure. Over the long term, these data will be used (1) by the U.S. and other governments in improved accurate, safety assessments relative to consumption of grain products and (2) by wheat and barley industries for enhanced safety of their workers. This proposal is consistent with FY06 Research Priorities for Food Safety, Toxicology and Utilization Area of USWBSI.