PI: James Pestka **PI's E-mail: pestka@msu.edu**

Project ID: FY12-PE-010 **ARS Agreement #: 59-0206-9-058**

Research Category: **FSTU** **Duration of Award: 1 Year**

Project Title: Hormonal Biomarkers for Deoxynivalenol Risk Assessment.

PROJECT 1 ABSTRACT

(1 Page Limit)

The long term goal of this research is to improve understanding of mechanisms, biomarkers, and thresholds for trichothecene-induced health effects for application to risk assessment. During Fusarium head blight of wheat and barley, deoxynivalenol (DON or "vomitoxin") and other trichothecenes are elaborated. These mycotoxins potentially cause illness in individuals who consume the infected grain and thus are an important public health concern. DON is regulated in the U.S. at 1 ppm in finished food, but the European Food Safety Administration has enacted much lower limits (200 ppb for infant food) largely based on reduced weight gain (i.e. growth retardation) observed in mouse studies. Similar tolerances are being considered by Canada. While DON-induced growth impairment occurs in many animal species and is strongly linked to anorexia induction, there is critical need to improve understanding of the mechanisms underlying this adverse effect and to translate this knowledge to human risk assessment. In recent work, we have developed a robust murine bioassay for DON-induced anorexia that will facilitate biomarker discovery that is directly applicable to susceptibility studies and human risk assessment. We have further discovered that DON-induced food refusal in this model corresponds closely to secretion of two gut satiety hormones, cholecystokinin (CCK) and peptide YY (PYY). Both of these hormones are known to inhibit food intake at low concentrations but cause vomiting at high concentrations in animals and humans which mimics the two principal effects of DON. Here we propose to test the hypothesis that the gut satiety hormones CCK and PYY can be used as biomarkers of DON toxicity. This will be accomplished by achieving two objectives: (1) Relate DON-induced anorexia to plasma elevation in the gut satiety peptides CCK and PYY and (2) Relate gender- and age-related susceptibility differences in DON-induced anorexia to gut satiety hormone responses. Several positive outcomes are anticipated to result from this work. First, we will confirm the validity of these two new sensitive biomarkers of DON's growth effects that can also complement biomarkers of exposure in human studies. Second, we will gain further insight into whether prolonged DON exposure evokes tolerance as reflected by reduced anorectic and biomarker responses. Third, we will relate the biomarkers to potential of age and gender to affect susceptibility to DON. Collectively, this research will update the science on which DON regulation is based, resulting in quantitative data that can be applied to DON-specific safety factors. This will ensure precision to DON regulation and balance consumer protection and food supply and is consistent with the goals of the Food Safety, Toxicology and Utilization of Mycotoxin-Contaminated Grain Research Area.