PI: Pestka, James **PI's E-mail: pestka@msu.edu**
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PROJECT 1 ABSTRACT
(1 Page Limit)

Deoxynivalenol (DON or "vomitoxin") and other trichothecenes are elaborated during head blight and thus pose a potential threat to human health. Potential regulations that would lower the tolerance level for DON in wheat and wheat products either in the U.S. or other countries could threaten the ability of U.S wheat, barley and resultant products to compete in the national and global economies. Should such regulations be proposed, it is absolutely essential that basic information be available relative to human sensitivity. Based on studies in the mouse immune system, we believe that the most critical step for DON toxicity induction is its action on cell signaling in leukocytes (white blood cells) and cytokine induction which then mediate illness. During the previous grant period, we have found that blood leukocytes from some human donors were much more sensitive to cytokine induction than other donors in terms of minimum effective DON concentration and magnitude of response. This might imply that a human population exists that is particularly susceptible to trichothecenes. To accurately measure the hazard of these toxins to humans, it is thus essential that the existence of such susceptible populations be verified and their sensitivity compared to responses previously observed in animal models. *We hypothesize that the levels of DON and closely related 8-ketotrichothecenes required for stress activation and cytokine induction in sensitive human leukocyte is identical to observed in the mouse*. To test this hypothesis, two critical leukocyte types, the macrophage and T cell, that are found in human blood and immune organs will be used. Specifically we will: (1) Compare the sensitivity of blood macrophages from different human donors to DON-induced stress activation and cytokine upregulation; (2) Compare the sensitivity of T cells from different donors to DON-induced stress activation and cytokine upregulation; and (3) Determine effects of related 8-ketotrichothecenes on human macrophage and T cell function. The resultant data from this study will be used to assess the potential hazard of DON and related trichothecenes to humans and, ultimately, incorporated into future safety assessments employed by the U.S. and other governments. If we prove our hypothesis, ie. that the most sensitive human cells have the same susceptibility as mouse cells, then the risk of low ppm levels of DON to humans will be extremely small when one considers the diversity of the human diet and the actual potential level of DON exposure in human tissues. Such evidence is critical because it would support the argument against establishing lower action levels than those currently set for DON.