**Cover Page**

<table>
<thead>
<tr>
<th>PI:</th>
<th>James Pestka</th>
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<tbody>
<tr>
<td>Institution:</td>
<td>Michigan State University</td>
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</table>
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| Fiscal Year: | FY12 |
| USDA-ARS Agreement ID: | 59-0206-9-058 |
| USDA-ARS Agreement Title: | Mechanisms and Biomarkers for Deoxynivalenol-induced Growth Retardation. |
| FY12 USDA-ARS Award Amount: | $56,906* |

**USWBSI Individual Project(s)**

<table>
<thead>
<tr>
<th>USWBSI Research Category**</th>
<th>Project Title</th>
<th>ARS Award Amount</th>
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<tbody>
<tr>
<td>FSTU-R</td>
<td>Hormonal Biomarkers for Deoxynivalenol Risk Assessment.</td>
<td>$56,906</td>
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<td><strong>Total ARS Award Amount</strong></td>
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*7/15/2013*  
Principal Investigator: James Pestka  
Date: 7/15/2013

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* Partial funding for this research is under ARS agreement # 59-0206-9-057  
** MGMT – FHB Management  
FSTU – Food Safety, Toxicology, & Utilization of Mycotoxin-contaminated Grain  
GDER – Gene Discovery & Engineering Resistance  
PBG – Pathogen Biology & Genetics  
BAR-CP – Barley Coordinated Project  
DUR-CP – Durum Coordinated Project  
HWW-CP – Hard Winter Wheat Coordinated Project  
VDHR – Variety Development & Uniform Nurseries – Sub categories are below:  
SPR – Spring Wheat Region  
NWW – Northern Soft Winter Wheat Region  
SWW – Southern Soft Red Winter Wheat Region
Project 1: Hormonal Biomarkers for Deoxynivalenol Risk Assessment.

1. What major problem or issue is being resolved relevant to Fusarium head blight (scab) and how are you resolving it?

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 (ie. growth retardation) observed in mouse studies. Similar tolerances are being considered by Canada.

This project addresses Goal #2 of the FSTU Action plan “Provide requisite information on DON/trichothecene safety issues to producers, millers, researchers, risk assessors and regulators.” Although DON-induced growth impairment has long been observed in many animal species, a critical research gap exists relative to understanding the mechanisms for this effect, thus creating a source of uncertainty in human risk assessment.

Here we proposed to test the hypothesis that the gut satiety hormones CCK and PYY can be used as biomarkers of DON toxicity. We see to accomplish this by: (1) Relating DON-induced anorexia to plasma elevation in the gut satiety peptides CCK and PYY and (2) Relating gender- and age-related susceptibility differences in DON-induced anorexia to gut satiety hormone responses.

2. List the most important accomplishment and its impact (i.e. how is it being used) to minimize the threat of Fusarium head blight or to reduce mycotoxins. Complete both sections (repeat sections for each major accomplishment):

   **Accomplishment:**
   
   We have successfully demonstrated that both CCK and PYY mediate DON-induced anorexia in the mouse model. This confirms the validity of two new sensitive biomarkers of DON’s growth effects that can also complement biomarkers of exposure in human studies. We have now used these markers to compare toxicity of other 8-ketotrichothecenes. We have further determined that young mice do not differ from adult mice in terms of sensitivity to DON-induced anorexia. However, elderly mice are extremely sensitive.

   **Impact:**
   
   This improved knowledge of mechanisms and thresholds for DON-induced food refusal and growth retardation will reduce the present uncertainties in risk assessment and ensure better quantification of human susceptibility. Over the long term, knowledge from our studies will bring precision to tolerable daily intake values of DON. The resulting data can be directly
applied safety assessments and enable determination of the accuracy of existing hazard data being used for establishing and harmonizing practical and achievable international guidelines. We have presented our findings in the U.S. and 5 other countries last year. In February 2013, CODEX ALIMENTARIUS Commission published “Proposed Draft Maximum Levels For Deoxynivalenol In Cereals And Cereal-Based Products And Associated Sampling Plans”. Our new data are being provided to CODEX for use in ongoing discussions.
Include below a list of the publications, presentations, peer-reviewed articles, and non-peer reviewed articles written about your work that resulted from all of the projects included in the grant. Please reference each item using an accepted journal format. If you need more space, continue the list on the next page.

Flannery, B.M., Clark, E.S., Pestka, J.J., 2012. Anorexia induction by the trichothecene deoxynivalenol (vomitoxin) is mediated by the release of the gut satiety hormone peptide YY. Toxicol.Sci. 130, 289-297. PMID: 22903826


