USDA-ARS/
U.S. Wheat and Barley Scab Initiative
FY11 Final Performance Report
July 13, 2012

Cover Page

PI:	James Pestka
Institution:	Michigan State University
Address:	Department of Food Science & Human Nutrition 234A GM Trout FSHN Bldg. East Lansing, MI 48824-1224
E-mail:	pestka@msu.edu
Phone:	517-353-1709
Fax:	517-353-8963
Fiscal Year:	FY11
USDA-ARS Agreement ID:	59-0206-9-058
USDA-ARS Agreement Title:	Mechanisms and Biomarkers for Deoxynivalenol-induced Growth Retardation.
FY11 USDA-ARS Award Amount:	$ 39,024

USWBSI Individual Project(s)

USWBSI Research Category*	Project Title	ARS Award Amount
FSTU	Hormonal Biomarkers for Deoxynivalenol Risk Assessment.	$ 39,024
	Total ARS Award Amount	**$ 39,024**

James V Pestka 7/18/12

Principal Investigator Date

* 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?

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. Previous studies have suggested that DON impairs food intake by interfering with intestinal motility and the desire to eat possibly via serotonin (5-hydroxytryptamine [5-HT]) release in the gut and subsequent signaling within enteric nervous systems. We have observed in mice that acute intraperitoneal exposure to DON causes feed refusal which corresponds to increased serum 5-HT. We tested the hypothesis that that the hormone 5-HT mediates induction of feed refusal by DON and therefore can be used a biomarker of effect. This hypothesis is being tested in the mouse model because the proposed and existing DON limits are based on studies in this species.

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 confirmed that 5-HT release precedes anorexia in the mouse and can be used to predict the magnitude of food. These findings were extended to the mink in an emesis model.

Impact: These studies will facilitate full mechanistic integration of animal and cell culture DON toxicity data--all of which can complement existing biomarkers of DON exposure in human epidemiological studies. This improved knowledge of mechanisms and thresholds for DON-induced 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. .

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.

1. Riley, R.T., Voss, K.A., Coulombe, R.A., Pestka, J.J. and Williams, D.E. 2011. Developing mechanism-based and exposure biomarkers for mycotoxins in animals, In: Determining Myctotoxins and Mycotoxigenic Fungi in Food and Feed, S. DeSaeger (ed.), Woodhead, Publ., Cambridge, U.K.
2. Baldwin, T.T., Riley, R.T., Zitomer, N.C., Voss, K.A., Coulombe, R.A., Pestka, J.J., Williams, D.E., Glenn, A.E. 2011. The current state of mycotoxin biomarker development in humans and animals and the potential for application to plant systems. World Mycotoxin Journal 4:257-270.
3. Flannery, B.M., Wu, W., Pestka, J.J. 2011. Characterization of deoxynivalenol-induced anorexia using mouse bioassay. Food Chem. Toxicol. 49:1863-1869, PMID 21575669.
4. Kobayashi-Hattori, K., Amuzie, C.J., Flannery, B.M., and Pestka, J.J. 2011. Body composition and hormonal effects following exposure to mycotoxin deoxynivalenol in the high-fat diet-induced obese mouse. Mol. Nutr. Food Res. 55:1070-1078, PMID 21538849.
5. Amuzie, C.J., Flannery, B.M., Ulrich, A.M., Pestka, J.J. 2011. Effects of deoxynivalenol consumption on body weight and adiposity in the diet-induced obese mouse. J. Toxicol. Environ. Health Part A 74:658-667, PMID 21432715.
6. Pestka, J.J. A new understanding of deoxynivalenol's mechanisms of action. Proceedings of the 2011 National Fusarium Head Blight Forum, Page 109, St. Louis, MO, December 2011.
7. Flannery, B., and Pestka, J.J. Novel feeding bioassay for characterization of deoxynivalenol-induced feed refusal in the mouse. Proceedings of the 2011 National Fusarium Head Blight Forum, Page 106, St. Louis, MO, December 2011
8. Wu, W., Flannery, B., Maiko, W.Yoshiko, S-K., and Pestka, J.J. Relation of 8-ketotrichothecene structure to anorexigenic response in the mouse. Proceedings of the 2011 National Fusarium Head Blight Forum, Page 111, St. Louis, MO, December 2011.
9. Pestka, J.J. Immunomodulatory effects of the trichothecene mycotoxin Deoxynivalenol: Molecular Mechanisms, Invited Lecture. University of Hong Kong, October, 2011
10. Pestka, J.J. Mechanisms for anorexia and growth suppression by deoxynivalenol and other 8-ketotrichothecenes: new considerations for risk assessment. Mycotoxin Workshop, Norwegian Toxicology Society, Oslo, Norway August 2011
11. Pestka, J.J. Immune System and Cancer. Food and Cancer: Molecular mechanisms, biomarkers and prevention. Food and Nutritional Toxicology Lecture Series.Kuppio, Finland, August 2011
12. Flannery, B. and Pestka, J.J. Characterization of deoxynivalenol in feed refusal using mouse bioassay. Gordon Research Conference, Waterville, ME, June 2011.
13. Pan, X. and Pestka, J.J.Optimization of phosphoproteomic analysis of the dynamic

signaling network involved in deoxynivalenol-induced ribotoxic stress response. Gordon Research Conference, Waterville, ME, June 2011.

14. Wu, W., Flannery, B., Maiko, W.Yoshiko, S-K., and Pestka, J.J.. Relation of 8-keto-trichothecene structure to anorexigenic response in the mouse. Gordon Research Conference, Waterville, ME, June 2011.
15. He, K., Zhou, H.R, and Pestka, J.J. Induction of apoptosis-associated ribosomal rna (rrna) cleavage by the trichothecene deoxynivalenol. Gordon Research Conference, Waterville, ME, June 2011.