

**USDA-ARS/  
U.S. Wheat and Barley Scab Initiative  
FY09 Final Performance Report  
July 15, 2010**

**Cover Page**

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<b>Fiscal Year:</b>	2009
<b>USDA-ARS Agreement ID:</b>	59-0206-9-058
<b>USDA-ARS Agreement Title:</b>	Mechanisms and Biomarkers for Deoxynivalenol-induced Growth Retardation.
<b>FY09- USDA-ARS Award Amount:</b>	\$ 87,805

**USWBSI Individual Project(s)**

<b>USWBSI Research Category*</b>	<b>Project Title</b>	<b>ARS Adjusted Award Amount</b>
FSTU	Mechanisms and Biomarkers for Deoxynivalenol-Induced Growth Retardation.	\$ 87,805
	<b>Total Award Amount</b>	<b>\$ 87,805</b>

*James V Pestka*

7/15/2010

Principal Investigator

Date

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\* 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 Winter Wheat Region  
 SWW – Southern Sinter Wheat Region

**Project 1:** *Mechanisms and Biomarkers for Deoxynivalenol-Induced Growth Retardation.*

**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.” To achieve this goal , we are testing the hypothesis that DON-induced growth retardation is a consequence of cytokine-induced-SOCS mediated hepatic growth hormone signaling impairment, resulting in reduction of Insulin-like Growth Factor Acid Liable Subunit (IGF-ALS) and circulating IGF-1 . 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 1:** We have demonstrated that that oral DON exposure perturbs the growth hormone axis by suppressing two clinically relevant growth-related proteins, IGFALS and IGF1. Both have potential to serve as biomarkers of effect in populations exposed to this common foodborne mycotoxin.

**Impact:** Validation of IGF system biomarkers of effect enables mechanistic integration of animal and cell culture data as well as complements the existing biomarkers of 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.

**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.**

Amuzie, C. J., and Pestka, J. J. Suppression of insulin-like growth factor acid-labile subunit expression--a novel mechanism for deoxynivalenol-induced growth retardation. *Toxicol Sci* **113**, 412-421.

Amuzie, C. J., Shinozuka, J., and Pestka, J. J. (2009). Induction of suppressors of cytokine signaling by the trichothecene deoxynivalenol in the mouse. *Toxicol Sci* **111**, 277-287.

Bae, H., Gray, J. S., Li, M., Vines, L., Kim, J., and Pestka, J. J. Hematopoietic cell kinase associates with the 40S ribosomal subunit and mediates the ribotoxic stress response to deoxynivalenol in mononuclear phagocytes. *Toxicol Sci* **115**, 444-452

Pestka, J.J. 2010, Deoxynivalenol-Induced proinflammatory gene expression: Mechanisms and pathological sequelae. *Toxins* 2, 1300-1317. (<http://www.mdpi.com/2072-6651/2/6/1300>)

Shi, Y., Porter, K., Parameswaran, N., Bae, H. K., and Pestka, J. J. (2009). Role of GRP78/BiP degradation and ER stress in deoxynivalenol-induced interleukin-6 upregulation in the macrophage. *Toxicol Sci* **109**, 247-255.