

**USDA-ARS/  
U.S. Wheat and Barley Scab Initiative  
FY05 Final Performance Report (approx. May 05 – April 06)  
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**Cover Page**

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<b>Fiscal Year:</b>	<b>2005</b>
<b>FY05 ARS Agreement ID:</b>	<b>59-0790-4-119</b>
<b>Agreement Title:</b>	<b>Human Susceptibility to Trichothecenes.</b>
<b>FY05 ARS Award Amount:</b>	<b>\$ 93,710</b>

**USWBSI Individual Project(s)**

<b>USWBSI Research Area*</b>	<b>Project Title</b>	<b>ARS Adjusted Award Amount</b>
FSTU	Human Susceptibility to Trichothecenes.	\$ 93,710
	<b>Total Award Amount</b>	<b>\$ 93,710</b>

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Principal Investigator

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Date

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\* BIO – Biotechnology  
CBC – Chemical & Biological Control  
EDM – Epidemiology & Disease Management  
FSTU – Food Safety, Toxicology, & Utilization  
GIE – Germplasm Introduction & Enhancement  
VDUN – Variety Development & Uniform Nurseries

**Project 1:** *Human Susceptibility to Trichothecenes.*

**1. What major problem or issue is being resolved and how are you resolving it?**

We are conducting research to resolve two major problems.

First, during head blight of wheat and barley, deoxynivalenol (DON or “vomitoxin”) and other trichothecene mycotoxins are elaborated that can potentially cause adverse health effects in individuals who consume the infected grain. Although DON is regulated in the U.S. at 1 ppm in finished food, the European Economic Union and Codex Alimentarius have proposed much lower limits based on a few rodent studies and assumes greater sensitivity of children to DON.

A second issue is that although agricultural workers are exposed to airborne DON during harvest, threshing and milling of infected wheat and barley, virtually nothing is known about the adverse effects of inhaling this toxin. Thus, a critical knowledge gap exists relative to the true risks presented to consumers and grain handlers by DON and other trichothecenes elicited during outbreaks head blight.

**2. List the most important accomplishment and its impact (how is it being used?).  
Complete all three sections (repeat sections for each major accomplishment):**

**Accomplishment #1:** A modified DON ELISA was developed that has improved sensitivity and efficiency of the assay, making it capable of handling more samples for research studies.

**Impact:** This assay can be applied to study kinetics of DON uptake and metabolism in tissues of experimental animals for hazard and risk assessment determination. The assay will also be useful for more efficient monitoring DON in grain samples

**Accomplishment #2:** We have determined that DON is absorbed similarly by young and adult mice. Inhalation of DON also causes marked proinflammatory cytokine induction (a marker for DON toxicity) in spleen, liver and lung in adults but a much reduced response occurs in young mice.

**Impact:** This finding suggests that children might actually be less sensitive to the effects of DON than adults. Thus it might not be necessary to set extremely low tolerances for DON in children’s food as is currently being done in Europe.

**Accomplishment #3:** We have determined that DON is absorbed similarly by inhalation and oral route. Inhalation of DON also causes marked proinflammatory cytokine induction in spleen, liver and lung.

**Impact:** These observations show for the first time a potential health effect with respiratory exposure and is persuasive in suggesting the need for adequate risk characterization and risk management for grain handlers.

**As a result of that accomplishment, what does your particular clientele, the scientific community, and agriculture as a whole have now that they didn’t have before?:**

- Grain producers, millers and the scientific community now have improved multi-sample DON detection capability that can be used to ensure safe food.
- Critical new information is now available for science –based risk assessment and for establishing/modifying DON tolerances.
- A potential hazard for agricultural workers handling Fusarium-contaminated grain has been identified. This will be an important consideration in for establishing safety measures for workers occupationally exposed to DON during grain handling.

**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. Pestka, J. J., and Smolinski, A. T. (2005). Deoxynivalenol: toxicology and potential effects on humans. *J Toxicol. Environ. Health B Crit Rev.* 8(1), 39-69.
2. Cousin, M.A., R.T. Riley, and J.J. Pestka. Foodborne mycotoxins: Chemistry, biology, ecology, and toxicology. In "Foodborne Pathogens: Microbiology and Molecular Biology", pp 164-226. P.M. Fratamico and A.K. Bhunia (ed) Horizon Scientific Press, Ltd., Norfolk, UK. 2005.
3. Zhou, H. R., Islam, Z., and Pestka, J. J. (2005). Induction of competing apoptotic and survival signaling pathways in the macrophage by the ribotoxic trichothecene deoxynivalenol. *Toxicol. Sci.* 87(1), 113-122.
4. Li, M., Cuff, C. F., and Pestka, J. (2005). Modulation of murine host response to enteric reovirus infection by the trichothecene deoxynivalenol. *Toxicol. Sci.* 87(1), 134-145.
5. Zhou, H. R., Jia, Q., and Pestka, J. J. (2005). Ribotoxic stress response to the trichothecene deoxynivalenol in the macrophage involves the SRC family kinase Hck. *Toxicol. Sci.* 85(2), 916-926.
6. Kinser, S., Li, M., Jia, Q., and Pestka, J. J. (2005). Truncated deoxynivalenol-induced splenic immediate early gene response in mice consuming (n-3) polyunsaturated fatty acids. *J Nutr. Biochem.* 16(2), 88-95.
7. Pestka, J. J., Uzarski, R. L., and Islam, Z. (2005). Induction of apoptosis and cytokine production in the Jurkat human T cells by deoxynivalenol: role of mitogen-activated protein kinases and comparison to other 8-ketotrichothecenes. *Toxicology* 206 (2), 207-219.
8. Riley, R.T. and Pestka, J. Mycotoxins: metabolism, mechanisms and biochemical markers. In "The Mycotoxin Blue Book" Duarte Diaz, Ed., pp 279-294. Nottingham University Press, Nottingham, UK.
9. Mbandi, E., and Pestka, J. J. (2006). Deoxynivalenol and satratoxin G potentiate proinflammatory cytokine and MIP-2 induction by *Listeria* and *Salmonella* in the macrophage. *J. Food Prot.* 69(6):1334-9
10. Islam, Z., Gray, J.S., and Pestka, J. J. (2006). p38 mediates IL-8 induction by the ribotoxin deoxynivalenol in human monocytes. *Toxicol. Sci.* 213(3):235-244
11. Islam, Z., and Pestka, J. J. (2006). LPS priming potentiates and prolongs proinflammatory cytokine response to the trichothecene deoxynivalenol in the mouse. *Toxicol. Appl. Pharmacol.* 211(1):53-63