

**U.S. Wheat and Barley Scab Initiative  
Annual Progress Report  
September 15, 1999**

**Cover Page**

<b>PI:</b>	<b>Jim Pestka</b>
<b>Institution:</b>	<b>Michigan State University</b>
<b>Address:</b>	<b>234A GM Trout FSHN Bldg East Lansing, MI 48824</b>
<b>Email:</b>	<b>pestka@pilot.msu.edu</b>
<b>Phone:</b>	<b>517-353-1709</b>
<b>Fax:</b>	<b>517-353-8963</b>
<b>Year:</b>	<b>FY1999</b>
<b>Grant Number:</b>	<b>59-0790-9-060</b>
<b>Grant Title:</b>	<b>Fusarium Head Blight Research</b>
<b>Amount Granted:</b>	<b>\$48,780.00</b>

**Project**

<b>Program Area</b>	<b>Objective</b>	<b>Requested Amount</b>
Food Safety, Toxicology, Utilization	Study Human Susceptibility To Trichothecene Mycotoxins Associated With Fusarium Head Scab.	\$50,000
	<b>Requested Total</b>	<b>\$50,000<sup>1</sup></b>

---

Principle Investigator

Date

---

<sup>1</sup> Note: The Requested Total and the Amount Granted are not equal.

**Project 1: Study Human Susceptibility To Trichothecene Mycotoxins Associated With Fusarium Head Scab.**

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

Vomitoxin (VT or deoxynivalenol) and other trichothecenes are elaborated during head blight and thus pose a potential threat to human health. Based on studies in the mouse immune system, we believe that the most critical step for VT toxicity induction is its action on leukocytes (white blood cells). We propose to determine if human leukocyte cytokine dysregulation and/or apoptosis induction are indeed targeted by the same levels of VT and related 8-ketotrichothecenes as are their mouse equivalents. If this is true, then the risk of low ppm levels of VT to humans will be extremely small when one considers the diversity of the human diet and the actual potential level of VT exposure in human tissues. Such evidence is critical because it would support the argument against establishing lower action levels than those currently set for VT.

2. Please provide a comparison of the actual accomplishments with the objectives established.

Using the funds that began in June, we have conducted preliminary experiments using cloned human T cell and macrophage cultures. First, it was observed that VT was indeed capable of inducing apoptosis in these cell lines in vitro as determined by DNA fragmentation patterns and by changes in cell morphology. Second, it was observed in T cells that VT could superinduce expression of the cytokines IL-2, IL-4 and IL-5. These results mimic those observed in the mouse model. We are now examining the effects on cytokine production the macrophage cell lines. We will then begin detailed dose response and structure function studies.

3. What were the reasons established objectives were not met? If applicable.

We are meeting established objectives according to schedule.

4. What were the most significant accomplishments this past year?

In looking at these cultures, we have observed that the VT rapidly turns on a group of stress-activated protein kinases known as MAPkinases. These are involved in signaling cascades that can turn on or off many cellular activities such as apoptosis or cytokine production. Interestingly, MAPkinases are evolutionarily conserved and thus can be found in plant and fungi. The ability of trichothecenes to alter cell function in this manner may have relevance to virulence in plants and to signaling within the fungus.

Year: 1999  
PI: Jim Pestka  
Grant: 59-0790-9-060

Progress Report

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.

No publications to date since funds were just made available in June, 1999.