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## Evaluating Mycoherbicides for Illicit Drug Crop Control: Rigorous Scientific Scrutiny is Crucial

### **Overview**

The "Office of National Drug Control Policy Reauthorization Act of 2006" (P.L. 109-469) requires that ONDCP submit to Congress a plan to conduct a scientific study of mycoherbicides as means of illicit drug crop elimination, including an evaluation of the likely environmental and human health impacts if these toxin-producing fungi were to be deployed. The legislation states explicitly that the study should be undertaken "by an appropriate Government scientific research entity, including a complete and thorough scientific peer review" (full text of provision appears below).

While mycoherbicides have been discussed in Congress as early as the late 1990s, this particular provision originally came from House Republicans, including Representatives Mark Souder (R-IN) and Dan Burton (R-IN), who were concerned about the continuing high levels of coca cultivation in Colombia (notwithstanding the aggressive aerial spraying of herbicides in that country) and also concerned about rising

levels of opium poppy production in Afghanistan. Despite little evidence that mycoherbicides would actually constitute an effective means to reduce illicit drug crop cultivation, and ample cause for concern that their use could pose significant dangers to human health and the environment (see 2006 report from the Drug Policy Alliance at <u>http://www.drugpolicy.org/docUploads/Mycoherbicide06.pdf</u>), Representatives Souder et al. appear determined to move ahead as swiftly as possible to deploy mycoherbicides.

Indeed, on February 7, 2007, Republican Representatives Ileana Ros-Lehtinen (R-FL), Mike Pence (R-IN), Dana Rohrabacher (R-CA), and Elton Gallegly (R-CA) wrote to Secretary of State Rice and Secretary of Defense Gates requesting that mycoherbicide research be "fast-tracked" so that the fungi could be used in Afghanistan soon. They called for measures to be taken to provide for:

"Expediting and moving forward on the Office of National Drug Control Policy (ONDCP) research plan on possible safe, tested use of mycoherbicides to help eliminate the massive opium crop in Afghanistan, without any damage to the environment or humans, as mandated in the recently passed ONDCP authorization bill. This R&D-first effort should be fast tracked."

In light of the desire on the part of some in Congress to push ahead quickly with mycoherbicides, we consider it of the utmost importance that the study mandated by the ONDCP reauthorization be undertaken with the appropriate scientific rigor. Given that ONDCP will be submitting its plan for such a study to the Congress, we believe that Congress has a crucial role to play in ensuring that the eventual study is, in fact, planned and conducted in as scientifically rigorous a manner as possible. The many potential risks of deploying mycoherbicides (described below) require that the closest possible scrutiny and engagement of the field's best scientists be brought to bear.

The comments below are therefore offered as guidance to Congress in responding to ONDCP's forthcoming plan for the mycoherbicides study and in order to ensure that the study is conducted in the rigorous manner that the topic requires.

#### **Recommendations**

• No single agency of the United States government has the mandate to encompass all aspects of the complex research needed to determine mycoherbicide safety.

As such, preliminary non-field research should be undertaken by three separate agencies: the Agricultural Research Service of the Department of Agriculture (USDA-ARS), the Food and Drug Administration (FDA), and the National Institutes of Health (NIH). If these agencies, after conducting their research, are in accordance with the field-testing of the fungi, then the Environmental Protection Agency (EPA), under the aegis of the National Environmental Policy Act (NEPA), should perform an environmental impact study (EIS) within United States territory.

It may well be the case that the USDA-ARS, FDA, and NIH could conclude, on the basis of their research, that it would be unwise or unacceptable to proceed with field testing. Even if the above agencies deem it acceptable to undertake field testing, the legislation unequivocally states that such tests cannot be conducted in any foreign country.

- The agencies of the U.S. Foreign Service should also be tasked with conducting a study assessing the potential political repercussions of deploying mycoherbicides, especially in light of the risk that using mycoherbicides could be construed as engagement in biological warfare (see May 2000 letter to President Clinton from Nobel Laureate Joshua Lederberg, at http://www.wola.org/publications/LederbergLetterToClinton2000.pdf).
- It is further recommended that the scientific peer-review of the research include input from former National Science Foundation Director and National Medal of Science recipient, Nobel Laureate Joshua Lederberg, Ph.D., who specializes in molecular biology.

#### **Background**

In December 2006, Congress authorized the testing in the U.S. of fungal plant diseases called mycoherbicides against illicit drug crops. Included in the ONDCP Reauthorization Act of 2006 (P.L. 109-469, signed by President Bush on December 29, 2006), the relevant provision states in full:

# SEC. 1111. REQUIREMENT FOR SCIENTIFIC STUDY OF MYCOHERBICIDE IN ILLICIT DRUG CROP ERADICATION.

(a) Requirement – Not later than 90 days after the date of enactment of this Act, the Director of the Office of National Drug Control Policy shall submit to the Congress a report that includes a plan to conduct, on an expedited basis, a scientific study of the use of mycoherbicide as a means of illicit drug crop elimination by an appropriate Government scientific research entity, including a complete and thorough scientific peer review. The study shall include an evaluation of the likely human health and environmental impacts of mycoherbicides derived from fungus naturally existing in the soil.

(b) Study – The study required by this section shall be conducted in United States territory and not in any foreign country.

There are two mycoherbicide candidates that have been proposed for use against illicit drug crops. One of these is *Fusarium oxysporum* and the other is *Pleospora papaveracea*. Both are toxic molds that attack their targets ("hosts") through the secretion of cell-dissolving chemicals called mycotoxins.

#### Fusarium oxysporum

*Fusarium oxysporum* was the candidate developed for use against marijuana, coca and Ephedra and is the most researched of the mycoherbicides. In 1999, Florida's drug czar proposed a research project under controlled laboratory conditions with the aim of later using it on Florida's outdoor marijuana crop, but the plan – even for a laboratory study and not a field study – was rejected because of environmental concerns. In 2000, *Fusarium oxysporum* was congressionally-approved for use as part of Plan Colombia in that country against coca, but this use was "waived" because the Clinton administration deemed that such use would be globally perceived as a first use by the United States of biological weapons. The Andean Community of Nations, including Colombia, specifically "rejected" or banned the use of the mycoherbicide *Fusarium oxysporum* anywhere within the member countries' territories.

*Fusarium oxysporum* is a fungus with a reputation for mutating, potentially attacking other biota, especially when applied massively as it would be in a mycoherbicide spray program, and overcoming the other microorganisms that keep it in check under normal conditions. For instance, *Fusarium oxysporum* wilt is the reason that Los Angeles is losing its palm trees, and *Fusarium* epidemics have caused significant crop losses worldwide.

There are also human health risks associated with *Fusarium oxysporum*. Some strains cause deadly infections in humans, others can damage eyes, as has been the case of a recent series eye infections associated with contact lens wearers using a commercial brand of cleaning solution.

Some of the mycotoxins produced by Fusaria species, including *Fusarium* oxysporum can infect various grains and cereals, which can then be eaten by humans and animals. One epidemic involving a *Fusarium* species (containing some of the same mycotoxins as *Fusarium oxysporum*) occurred during the last years of WWII in the Soviet Union, when hundreds of thousands of people died after eating bread baked from with flour made from infected grains. More recently, in 1991, 31 babies were born with "anencephaly" (brainless) around the Rio Grande area of Texas. Their mothers had eaten mycotoxin-laden corn tortillas during pregnancy. Because of the dangers associated with mycotoxins, the FDA is charged with setting maximum levels for all known mycotoxins for both human and animal consumption. Grain that tests too high (over 2 parts per million [2ppm] for humans) is destroyed.

Because of the stability and toxicity of the *Fusarium* mycotoxins, especially a subgroup known as the "T2" toxins, these compounds have been weaponized. Although the T2 toxins are only one tenth as potent as the nerve gas Sarin and also less potent than the Ricin or Botulinum toxins, they are not easily broken down or made inactive. High concentrations of sodium hydroxide and sodium hypochlorite are required to detoxify them. (In the Soviet experience, these mycotoxins killed hundreds of thousands after surviving the heat of being baked into bread.) *Fusarium* mycotoxins – or

"Fusariotoxins," as they are known – were found to be effective as aerosol-delivered weapons. Unlike many chemical warfare agents, they dissolve cell walls on contact, causing necrosis at any point of contact, such as skin, eyes and lungs. One of the reasons cited for the recent U.S.-led invasion of Iraq was a purported program supposedly involving the Iraqi government's manufacture of *Fusarium* mycotoxins.

Beyond the aforementioned problems, *Fusarium oxysporum* is no longer considered to be a good candidate for controlling drug crops because it rarely kills all of the plants it comes into contact with, and those that survive infection gain an immunity, which may last generations. This has been the case with coca in the Huallaga Valley of Peru, which survived a *Fusarium oxysporum* epidemic during the 1980s and 1990s and has now made a big comeback. Offspring of many of the *Fusarium oxysporum* – resistant strains were smuggled into Colombia where they are now cultivated and probably retain their resistance to the fungus. In the case of the *Fusarium* epidemic in Peru during the 1980s and 1990s, many other crops succumbed to the same disease, according to numerous reports and State Department cables.

Experience and science suggest that - in addition to the probability that mycoherbicides will not kill all of the plants they are targeted against - *Fusarium* mycotoxins will probably infect other plants and life forms, especially if applied in the large amounts that would be used in eradication programs.

#### Pleospora papaveracea

*Pleospora papaveracea* is the mycoherbicide candidate proposed for use against Afghanistan's opium poppy crop. Although *Pleospora papaveracea* has been studied since the 1940s, it has not received the same scientific scrutiny as *Fusarium oxysporum*. *Pleospora papaveracea* is a mold that will attack all known species of poppy, from the Opium poppy (*Papaver somniferum*), the common ornamental called "Oriental poppy" (*Papaver orientale*) and *Papaver bracteatum*, the poppy used to produce thebaine, a compound that is a precursor to many legal narcotics.

Little is known about *Pleospora* mycotoxins. They have not been isolated, named and tested for toxicity and biodegradation. Scientists who have worked around the fungus report that exposure of small amounts cause irritation at the site of contact – most often respiratory problems – and therefore must be propagated using sterile procedure and protection. Dr. Howard Stead of the United Nations Office on Drugs and Crime (UNODC) has stated that the yet-unnamed *Pleospora* mycotoxins function in a way similar to that of the *Fusarium* species.

Thus far, most of the research on *Pleospora papaveracea* has been carried out in a Soviet-era biowarfare facility in Tashkent, Uzbekistan. After decades of research the active mycotoxins have yet to be isolated, elucidated or named, yet alone tested for toxicity. If the *Pleospora* mycotoxins are, as Dr. Stead says, anything like those produced by *Fusarium*, there will be not one, but several distinct toxins and these will be produced in different amounts and concentrations depending upon the media upon which

they are grown. The indicated agency to carry out this initial work of isolating, elucidating and naming the mycotoxins is the USDA's Agricultural Research Service. ARS-USDA should isolate all of the *Pleospora* mycotoxins by cultivating the fungus on a variety of media, including various poppy species in quarantined greenhouses.

ARS-USDA can also determine mutagenicity and determine which other plants *Pleospora* might attack with massive applications. It should be noted here that *Pleospora* is a disease that has co-evolved with poppy. As in the case of the *Fusarium* fungus, *Pleospora* should never be expected to destroy all of the poppy to which it is applied.

Once the mycotoxins have been isolated, chemically elucidated, and named, they should be tested for toxicity and degradability by both the FDA and the NIH. Toxicity tests should be carried out in a variety of biota, including mammals. FDA should also set maximum acceptable levels for the mycotoxins in human food and poppy products, such as poppy seed and poppy seed oil.

ARS-USDA, FDA, or NIH should also determine if any of the mycotoxins could contaminate the licit opiate market through co-extraction in the case that the legal opium crops in Turkey and India or other countries were inadvertently contaminated.

After the preliminary research described above is completed, and in the case that field testing is considered acceptable, those tests should be carried out on a remote U.S. island to eliminate the possibility of the disease spreading onto the mainland where it could attack legal crops.

The Foreign Service, which in this case should include the U.S. Department of State, the Central Intelligence Agency, United States Agency for International Development (USAID) and various entities of the Department of Defense should also determine whether the use of a mycoherbicide by the United States in Afghanistan would be a violation of the Biochemical Weapons Convention (BWC), and what, if any, political repercussions of its use could have.

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