Control of Coca with a Plant Pathogenic Fungus (Mycoherbicide)

Executive Summary

1. Disease-causing fungi are found on all plants, including narcotic crop plants. Certain species of fungi are candidates for biological control of weeds because they fit the requirements of target specificity, safety (non-toxicity, non-mammalian effects) and non-allergenicity), and efficacy (knockdown comparable to that seen with chemical herbicides).

2. While chemical herbicides are still the main method of controlling weeds in agricultural systems, their adverse environmental impact has led to an effort to find non-chemical controls.

3. Mycoherbicides are the answer to the above problems. A mycoherbicide is a naturally occurring plant pathogenic fungus that will attack a target plant such as a weed or narcotic plant. Mycoherbicdes are naturally occurring and have no impact on the environment or other plant species. Development of mycoherbicides to control weeds is a long-standing global field of science. The few successes in developing mycoherbicides include the two products available in the US: 'Devine' to control Strangler vine in citrus and 'Collego' to control northern jointvetch in rice.

4. Mycoherbicides do not need to be genetically engineered. They can be taken directly from nature. The collected fungi are taken through a series of tests to determine if they meet the above standard requirements. The fungi are then field-tested which requires an EPA experimental use permit. If the pathogen is effective in controlling the target weed in these tests, the pathogen will be screened for human toxicity and environmental safety. The Environmental Protection Agency (EPA) requires a "sixpack" series of tests, called Tier One Toxicity testing, that consists six tests to verify the safety of the mycoherbicide from the point of toxicity and probable environmental impact at a cost of $40,000 per each fungal strain. Mycoherbicides can only be released after the EPA has declared them safe.

5. The Department of Agriculture (USDA) studied the possibility of using microbes to control narcotic plants in a series of projects in the 80's and 90's. A *Fusarium oxysporum* f. sp. *erythroxyli* was described. This fungal pathogen is the cause of a natural epidemic of coca in the Upper Huallega Valley of Peru (See attachment A). The pathogen was also isolated from diseased plants in a research station in Kauai (See attachment B). The Hawaiian pathogen was initially characterized by researchers at Montana State University (MSU) who worked on contract with the USDA Agricultural Research Service (ARS). Researchers in the USDA further characterized both the Hawaiian pathogen and the Peruvian pathogens. This pathogen will selectively attack and kill *Erythroylum coca* and *E. novogranatense* (Fig. 1).

Fig. 1 Field evaluation of *Fusarium oxysporum* f. sp. *erythroxyli* for control of coca. The left row of plants was inoculated with the pathogen and the right row of plants was not inoculated. The picture was taken 6 months after inoculation.

6. Congress appropriated an additional 23 million dollars to validate and deploy this mycoherbicide to control coca in South America. The USDA received the money and was directed to oversee this project. The USDA was to use 13 million for USDA research on control of narcotic crops and award 10 million to a private company to implement the technology.

~~7.~~ A company (Ag/Bio Con) was formed by Professor Sands specifically to submit a proposal to implement this technology. Ag/Bio Con submitted a 300 page 3-year proposal to the USDA in January of 1998. They proposed to develop the agents, prove their safety, validate their efficacy and to produce an economic delivery system and provide enough inoculum to cover Colombia's coca growing regions. Ag/Bio Con also proposed to continue work done at the USDA and MSU on biological control of opium poppy. This proposal was not reviewed by the USDA and returned to Ag/Bio Con.

~~8.~~ Mycoherbicide technology could also be used to control illicit *Cannabis sativa*. Dr. Sands presented the technology to the State of Florida. The presentation was leaked to the Florida press and to the National Organization for the Reform of Marijuana Laws (NORML). NORML has sponsored an intensive campaign to discredit the research and prevent release of plant pathogens capable of eradicating *C. sativa*. They have not validated their interpretation of the data presented by Dr. Sands and the USDA. ~~has been less than accurate.~~

9. The USDA, as well as Montana State University, decided not to associate themselves with this proposal, possibly for reasons of personnel safety. The USDA did spend the $13,000,000 allocated in the bill over approximately 2 years, on projects involving alternate crops. The money not spent by the USDA ($10,000,000) was turned over to the State Department, who asked the United Nations Office of Drug Control and Crime Prevention (UNODCCP) to submit a proposal implementing the use of mycoherbicides on coca.

10. At present, the UNDCP will not proceed on mycoherbicide research without Colombia's active participation. Thus, nothing has happened. The technology remains in the freezers of the USDA, and the money is being spent on other projects.

Below is a white paper written by a scientist, who spent several months researching the potential use of mycoherbicides to control illicit narcotic crops. Although this scientist has no background in the field, we verify the validity of the writer's well considered arguments. Of special interest is the section (Section 6 of Chapter 5, Ecology) on the huge negative environmental impacts of illicit drug plant cultivation, and processing.

Analyzing the Debate Over Mycoherbicides for Coca Control

Introduction: Mycoherbicides have been proposed as an effective and environmentally safe means to eliminate certain species of coca plants, the source of cocaine. Mycoherbicides are natural plant pathogenic fungi that are used to selectively attack and kill a target plant such as a weed or narcotic plant. Advocates maintain that these pathogenic fungi are environmentally safe, specific to the target crop (unlike chemical herbicides), and will not harm humans or other animals. Yet, opponents raise concerns of toxicity and severe ecological consequences. This analysis endeavors to address the key scientific issues centered on this emerging technology. It also addresses the introduction of an almost identical mycoherbicide into Africa for large-scale control of Striga, a devastating parasitic weed infesting sorghum, maize and other crops.

Balance of Nature: Plants and animals exist in a continuous state of equilibrium with microbial organisms. Culture a few cells from the surface of a plant and one would find a complex combination of bacteria and fungi - most of them benign - and some disease-causing pathogens. Under most circumstances the plant resists attack by these pathogens maintaining balance between health and disease. Monocropping frequently alters balance by increasing the density of the pathogens over time and decreasing the genetic diversity of the host plant. This is a lesson learned by farmers over eons: grow crops in the same field year after year and the likelihood of disease will increase. Ecologists have long recognized that monocropping is the antithesis of biodiversity and leads to highly unstable situations where a single disease may destroy vast areas of plant growth.

In the Beginning: A Fungus Attacks Peruvian Coca: Vascular wilt disease of coca in Peru was reported as early 1932. With the advent of large scale monocropping, intensified fertilization and shortened cultivation time in the early 1980s, the incidence of this disease increased sharply. By the end of the decade, Peruvian farmers were reporting an epidemic of wilt disease that spread over thousands of acres and forced abandonment of coca fields. Coca leaf production reduced significantly in the 1990 -1992 time period, particularly in the major growing region of the Upper Huallaga River Valley in the north central Andean foothills. Peruvian agronomists inspected the diseased crops and concluded that only a certain forma specialis of *Fusarium oxysporum*, a soil-borne fungal pathogen, had caused the epidemic. A subsequent joint US - Peruvian survey of 10 different areas of Peru showed that this fungus existed in both the northern and southern growing areas - a region over 500 miles long running along the eastern slopes of the Andes.

Claims by farmers that the coca disease was attacking other crops were investigated by Peruvian scientists and never validated. Plant pathogen identification by DNA technology was not then available. However, the joint survey indicated that about 22 percent of the *Fusarium oxysporum* isolated from coca were other forms of *Fusarium oxysporum*. These forms, while nonpathogenic to the coca, may have caused some of the wilt diseases on other crops. This is an expected result and does not imply any sort of mutative behavior. This diversity of forms does explain the farmers' complaints to some extent. Today a wide variety of cultivated and wild plants grow in the abandoned coca cultivation areas - presumably still infested with the long surviving spores of the coca-destroying fungus. No animal or human fungal diseases related to *Fusarium oxysporum* have since been identified. The evidence is clear: that this fungus has existed in equilibrium with the natural flora and ecology of Peru for many decades - only when man destabilized the environment with coca monocropping did epidemic levels of the disease occur.

Chapter 2 - Hawaii Encounters the Fungus: A similar situation occurred on the Hawaiian island of Kauai in the mid 1970s where coca was being cultivated for extraction of alkaloids used in soft drink manufacture. Thousands of seeds from Trujillo and Cuzco, Peru were found to be infected with a 'damping off disease" and only about 20 percent germinated. In 1975, in an attempt to overcome the seed disease problem, healthy seedlings were planted in three separate field nurseries. Quite rapidly, a soil borne wilt disease caused by *Fusarium oxysporum* began killing these plants. Systematic pathogenicity and host-range evaluations of the pathogen conducted in 1988 confirmed that the wilt was caused by the specific form of *Fusarium oxysporum* (forma specialis *erythroxyli*). The standard microbiological 'Koch's Postulate' was employed to verify these findings (wherein the pathogen is isolated, tested against the plant, and re-isolated). Although the fungus was easily transported from one field to another, presumably on the surface of shoes and tools, there was no evidence of it affecting other species of nearby plants.

Chapter 3 - USDA Laboratory, Greenhouse and Field Research: *Fusarium oxysporum* is a fungal species that is distributed throughout the world. This complex group of fungi is divided into 'forma specialis' based on the specific plant species (or range of related species) that the fungal isolate attacks. For example, *Fusarium oxysporum* forma specialis *lycopersici* attacks only plants in the tomato family. It does not attack plants outside of the tomato family such as pea. Notably, *Fusarium oxysporum* forma specialis *erythroxyli* attacks the coca species *Erythroxylum coca* and *Erythroxylum novogranatense* and has been observed in Peru, Colombia and Hawaii. It does not attack other plants, consistent with the taxonomy of the pathogen. This host-specific nature was a major factor in assessing its potential as a mycoherbicide for control of coca. Thus in 1987, USDA scientists began a systematic program of research into the properties of the organism. During the ensuing years, over 100 plant species have been tested for susceptibility to this pathogen. None have been adversely affected, thus further confirming the host-specific behavior observed in the natural environment of Peru and in Hawaii. Additional testing (USDA Tifton, Georgia) has already been conducted to verify the absence of mycotoxin production by this forma specialis. Specialized field tests were conducted over an extended period in Kauai to systematically measure the efficacy and distribution of the fungal spores. This naturally occurring plant pathogen was found to be a highly effective means to destroy these plants when applied with sufficient density to change the natural balance.

Chapter 4 - Colombia Also Has The Fungus: In order to determine if the disease existed in Colombia, a series of isolates were acquired from accessible areas. Cultures and DNA tests confirmed the presence of *F. oxysporum* forma specialis *erythroxyli* and give credence to the supposition that the disease exists throughout the coca-growing region of South America. The ecological and environmental conditions of the Andean foothills in Peru, Colombia and Ecuador are essentially identical from a plant pathology perspective so it should come as no surprise that over time the disease has migrated across the region.

Chapter 5 - The Current Debate: In the opinion of plant pathologists familiar with the details of this particular mycoherbicide, the accumulated body of scientific data is sufficiently compelling to proceed with a systematic program of field trials and mycoherbicide registration consistent with international standards. However, in the opinion of opponents, there are many issues. Unfortunately these concerns have been relayed to the media with many alarmist words and little scientific validation. The following discussions focus on the more popular themes and misconceptions at the lay reader level. (In addition, for those seeking more technical information, detailed scientific responses with appropriate references are included in the technical addendum).

1. *Toxicity*: "Fusaria are dangerous to public health; they produce fusariogenin, a known toxin".

   This misleading statement comes from confusing the genus Fusarium, with the species Fusarium oxysporum. There are approximately 60 species of Fusarium. This mistake is the same as stating that the mushroom genus Amanita is poisonous because some species produce amanitine, a known toxin, whereas the species Amanita calyptrate is an edible and excellent food. The species *Fusarium oxysporum* is further divided into over 100 *forma specialis*. A few of these *forma specialis* of *Fusarium oxysporum* do produce phytotoxins (and most of these already exist in South American agriculture). Thus, each *forma specialis* must be individually tested for mycotoxin production. The specific form that attacks coca does not produce any known mycotoxins, as measured by USDA testing in Tifton, Georgia, USA. Humans and other animals that might ingest the fungus would not be harmed.

2. *Human Health*: "The death rate caused by Fusarium infections in humans is 76%".

   This statement is entirely misleading and suffers from the same faulty logic as the toxicity claims. Generalized statements about the Fusarium genus attacking humans are not applicable to *Fusarium oxysporum* forma specialis *erythroxyli*. In any event, the particular cases referenced pertained to immune-suppressed cancer patients whose defense levels were very low making them vulnerable to almost any microbe. Individuals having these severe conditions are hospitalized and quarantined and not exposed to coca spraying. Furthermore, the normal EPA mycoherbicide registration procedure requires extensive testing related to human and animal health and toxicity, thus ensuring that no dangerous products would be released.

3. *Host Range*: "Some strains have a broad host range, infecting even distantly related plant species".

   This is an incorrect statement, perhaps due to a misinterpretation of the literature. As indicated previously, a forma specialis of Fusarium oxysporum is defined by its host plant or closely related range of plants. There are approximately 100 different forms of Fusarium oxysporum. Each form has a narrowly defined host range. They do not attack other plants and do not mutate to attack other plants. Anecdotal reports of non-host plants being infected by wilt disease are often true - and the organism causing the disease may well be a species of the genus Fusarium - but it is not *Fusarium oxysporum* forma specialis *erythroxyli*. For the layman or farmer, it is important to note that simple observation of the disease is not sufficient; a correct determination can only be ascertained by host range and DNA testing.

Beyond the *forma specialis*, the plant pathogen is even further divided into races that are specific to one or a few cultivars (varieties) of the same plant species.

The fungus *Fusarium oxysporum* forma specialis *erythroxyli* strain EN4 was selected for its overall efficacy and specificity against both of the most common illicit coca forms, *Erythroxylum novogranatense* and *Erythroxylum coca*.

4. *Mutagenesis*: "*Fusarium oxysporum* forma specialis *erythroxyli* can change from one form to another".

   This is an incorrect statement. As indicated previously, the *forma specialis* is actually defined by its host plant or closely related range of plants. The taxonomy has been studied by scientists since 1910 and found to be highly stable. Due to the economic importance of *Fusarium oxysporum* wilt diseases; each of the principal agricultural strains has received extensive attention by plant pathologists over decades. There are no documented cases of mutations expanding the host range of this pathogen. The detailed genetic reasons for this specificity are compelling, but complex, and are discussed in the technical addendum. The most profound *in situ* test of the mycoherbicide is its stable behavior even at the epidemic levels found in Peru.

5. *Genetic Engineering*:

   Allegations of genetic engineering and the need for exercising extreme caution because a "GMO pathogen" is being proposed are simply incorrect. This natural pathogen works extremely well when applied at increased density levels.

6. *Ecology*:

   Statements regarding the "ecological harm" of mycoherbicides are particularly egregious because they lack balance, perspective and scientific validation. As previously noted *Fusarium oxysporum* forma specialis *erythroxyli* currently exists in South American countries and has reached epidemic levels in Peru without creating ecological issues. On the other hand coca cultivation has devastated the ecology of the Upper Huallaga River Valley and is currently doing the same in many areas of Colombia. Consider the following documented ecological impacts of coca growth and related cocaine base production in these areas:

- Extensive monocropping - the most unstable form of agricultural ecology
- Use of thousands of tons of insecticides, herbicides, fungicides and fertilizers
- Use of thousands of liters of highly toxic chemicals for the conversion of each farmer's leaf yield to cocaine base in local maceration pits
- Pollution of major watersheds, rivers and aquifers
- Kill off of fish and wildlife exposed to polluted water
- Destruction of native plants due to herbicide drift
- Extensive erosion and top soil runoff
- Massive 'slash and burn' - as much as 30,000 hectares per year in Colombia alone of prime forest habitat
- Loss of indigenous food crop production
- Loss of sustainable agriculture for the region affected

A mycoherbicide could eliminate the 'slash and burn' approach because it could also be applied to the adjacent forested areas without concern (host specificity) and can exist for decades. An initial attempt to cultivate coca in treated forests adjacent to growing areas would result in rapid kill of new seedlings and discourage further expansion.

7. *The African Contribution - A Model for the Future:*

It is a curious fact that while a contentious debate ensues over the use of one *Fusarium oxysporum* form to eradicate approximately 200,000 hectares of coca in South America, there is no debate in sub Saharan Africa about another strain of *Fusarium oxysporum* that is being promoted as a means to increase corn and sorghum production and save thousands of lives. This strain of *Fusarium oxysporum* could be used to eradicate the plant parasitic weed, Striga, on up to 50,000,000 hectares of cropland. Better known as 'witchweed', Striga invades fields of cereal crops such as sorghum, depleting the nutrients and decimating the crop. Farmers are forced to give up and move to the cities, increasing the problems of urbanization while also having to turn to imported grains for sustenance. Researchers at McGill University in Montreal have recently achieved major successes in the control of Striga with a specific form of *Fusarium oxysporum* and have received international recognition for their contributions.

From a scientific standpoint there is no significant technical difference in the two initiatives. Certainly the overall 'risk' associated with coca is far less, both because of the relatively small area to be treated and the significantly greater body of data that has been acquired. The Striga work is proceeding along an established methodological approach for testing and qualification of a new mycoherbicide. It has political and policy support and should contribute significantly to the global challenges of sustainable food in the new millennium. Is the coca research any less valuable? Will it receive comparable political and policy support to help eliminate the expanding global scourge of cocaine addiction?

8. *Final Assessment*:

This assessment has validated the science supporting the proposal to use mycoherbicides as an effective and environmentally safe means to eliminate coca plants.

It determined that none of the issues cited in various sources proved to be valid under detailed scrutiny. In addition an example was provided that established there are no substantive scientific differences between the emerging application of one forma specialis of *Fusarium oxysporum* to control the noxious weed *Striga* in Africa and another to control the coca of South America.

The proposal should be viewed as low risk, assuming the product is properly registered with the EPA. Several other mycoherbicide weed control formulations are registered and in use in both the U.S. and international markets. Adequate procedures exist to evaluate and register mycoherbicides, including human health testing (toxicology, personnel exposure, and dietary, food and occupational risk), environmental testing (terrestrial and aquatic animals, plant host range, environmental fate and transport, ecological exposure and risk characteristics) and other risk assessment factors.

The science of mycoherbicide control of plants has reached a significant level of maturity. A portfolio of microbial identification methods and pathogen testing procedures has been developed that effectively eliminates ambiguity and misinterpretation of diseases. The field is one of sophisticated expertise requiring extensive knowledge of plant pathogenicity, microbial organisms, genetics and environmental factors. A limited, but growing number of experts can be found in a few research institutes, but unfortunately the various issues and concerns were not directed to these experts.

A suggested way to improve the dialogue between mycoherbicide specialists, non-governmental organizations, policy makers and the general public would be to complete all requisite EPA testing (six-pack) so that the safety of this solution can be properly and prudently evaluated.

We at Ag/Bio Con would be more than willing to submit a comprehensive plan with phases necessary to achieve a very significant reduction in coca production by the use of mycoherbicides.

Respectfully submitted,

David C. Sands