

Pharmaceutical Rice in California



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Potential Risks to Consumers, the Environment and the California Rice Industry

SUBMITTED TO:

CALIFORNIA DEPARTMENT OF HEALTH SERVICES
CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY
CALIFORNIA DEPARTMENT OF FOOD AND AGRICULTURE

July 2004

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KEY ISSUES AND RECOMMENDATIONS

BACKGROUND

- Ventria Bioscience or its predecessor Applied Phytologics has been conducting outdoor field trials of genetically engineered, pharmaceutical-producing rice in California's Central Valley since 1997.
- Field trial acreage has increased from 6 acres in 1999 to 93 acres in 2003.
- Ventria's bid to begin commercial production on 120 acres in Southern California in 2004 was temporarily blocked by California and federal authorities, though the company may re-apply. Meanwhile, Ventria has received permission to grow still another test plot in the Central Valley.

WHY CALIFORNIA AUTHORITIES NEED TO TAKE ACTION

- The National Academy of Sciences, the food industry, and even the editors of a leading biotechnology journal all acknowledge that it is virtually inevitable that plant-made pharmaceuticals will contaminate the food supply when drug-bearing food crops such as Ventria's rice are grown out-of-doors.
- Federal regulators properly maintain a "zero tolerance" standard for drugs in food, yet they continue to condone outdoor cultivation of pharm crops rather than ban this hazardous practice.
- Ventria's rice-grown pharmaceutical proteins pose potential health threats to all consumers and environmental risks to the California environment (see Executive Summary).
- Discovery of pharmaceuticals in California's rice could have devastating consequences for the state's farmers. Quality-conscious export markets like Japan and South Korea would likely shun California rice, much as they shunned U.S. corn after the StarLink corn contamination debacle.
- Federal regulation of genetically engineered (GE) crops is seriously deficient. Field trials of GE pharmaceutical crops are not monitored to detect potential contamination of neighboring fields. These experimental pharm crops are not subject to mandatory health or environmental assessments, and no consideration is given to the likely economic impacts of contamination.

EXPERIMENTAL AND UNPROVEN

- Pharmaceutical crops such as Ventria's rice represent an *experimental* and *unproven* application of biotechnology. Not a single "plant-made pharmaceutical" (PMP) has been approved by the U.S. Food and Drug Administration (FDA), despite numerous clinical trials, industry promises, and field trials dating back to 1991.
- Meanwhile, over 100 biotech pharmaceutical proteins produced in contained and controlled fermentation facilities have been approved by the FDA and are already helping people in need.

RECOMMENDATIONS

We call on the California Department of Food and Agriculture (CDFA), the California Department of Health Services (CDHS), and the California Environmental Protection Agency (Cal-EPA) to conduct a thorough review of Ventria's pharmaceutical-producing rice. CDFA should examine the likely economic impacts of contamination on rice farmers. CDHS should subject Ventria's rice to a thorough health assessment, while Cal-EPA should review Ventria's rice for potential environmental impacts. However, because of the potential risks and the great scientific uncertainty surrounding this unproven application of biotechnology, we believe a prudent approach is called for to protect the interests of California consumers and farmers. Thus, we further urge California authorities to consider a moratorium on the cultivation of Ventria's pharmaceutical rice and other pharm crops.

EXECUTIVE SUMMARY

BACKGROUND

Since 1997, Ventria Bioscience or its predecessor Applied Phytologics has been conducting outdoor field trials of rice varieties genetically engineered to produce pharmaceuticals in California's rice-growing Central Valley. These pharmaceutical compounds include artificial versions of the human milk proteins lactoferrin, lysozyme and alpha-1-antitrypsin. Proposed uses for the whole rice and/or extracted pharmaceuticals include poultry feed, treatment of diarrhea, infant food and topical wound treatment. Field trial acreage has increased from 6 acres in 1999 to 93 acres in 2003. Ventria's bid to begin commercial production on 120 acres in Southern California in 2004 was temporarily blocked by California and federal authorities, though the company may re-apply next year. Meanwhile, Ventria has received permission to grow still another test plot in the Central Valley.

EXPERIMENTAL AND UNPROVEN

Pharmaceutical crops such as Ventria's rice represent an *experimental* and *unproven* application of biotechnology. Not a single "plant-made pharmaceutical" (PMP) has been approved by the U.S. Food and Drug Administration (FDA), despite numerous clinical trials, industry promises, and field trials dating back to 1991. While pharm crops have failed to provide useful drugs, over 100 biotech pharmaceutical proteins produced in contained and controlled fermentation facilities have been approved by the FDA and are already helping people in need.

CONTAMINATION IS INEVITABLE

The federal government has a "zero tolerance" standard for PMPs in food. Yet scientists and agronomists agree that it is virtually impossible to keep PMPs from entering the food and feed supply when food crops are engineered to produce these compounds. The National Academy of Sciences warned of this risk in two recent reports. The editors of a leading journal in the field, *Nature Biotechnology*, recently compared growing drugs in food crops to a pharmaceutical manufacturer "packaging its pills in candy wrappers or flour bags or storing its compounds or production batches untended outside the perimeter fence." These concerns are validated by numerous episodes in which conventional crops and *certified seed stocks* have become contaminated with transgenic traits. In two incidents in 2002, pharmaceutical corn adulterated 500,000 bushels of soybeans in Nebraska and 155 acres of corn in Iowa; the adulterated soy was seized and destroyed, the corn burned, costing millions of dollars. Continued cultivation of Ventria's rice could have a similar outcome.

DEFICIENCIES IN VENTRIA'S CULTIVATION PROTOCOL

Ventria's pharmaceuticals could contaminate food-grade rice through transport of seeds in the guts of birds, flooding, "volunteer" pharm rice sprouting from unharvested seed, pollen dispersal by bees or in high winds, or human error in transport and processing. Ventria reportedly has not adequately explained how it will prevent birds from spreading its rice, what constitutes proper disposal of rice plants, or whether nearby growers will be notified.

POTENTIAL HUMAN HEALTH IMPACTS

Aggravated Infections

While human lactoferrin has antimicrobial properties, it paradoxically poses the potential hazard of exacerbating infections by certain pathogens capable of using it as a source of needed iron. Such pathogens include bacteria that cause gonorrhea and meningitis, as well as the *H. pylori* bacteria implicated in causing ulcers and certain forms of stomach cancer. According to Dr. Eugene Weinberg, human lactoferrin “might not be a successful therapeutic agent for *H. pylori* and, indeed, could intensify the infection.” The possibility of aggravated infections is a potential risk from the contamination of food rice by lactoferrin that argues against growing this rice outdoors.

Allergenicity

Ventria’s rice-expressed lysozyme and lactoferrin have two characteristics of proteins that cause food allergies: resistance to digestion and to breakdown by heat. Its lactoferrin has a third characteristic, structural similarity to a known food allergen, lactoferrin from cows. These allergenic properties may explain why noted food allergist Steve Taylor stated that FDA regulations “will have to be rethought before rice-grown lactoferrin ... can be approved for production.”

Autoimmune Disorders

Pharmaceutical proteins generated by inserting human genes into plants, bacteria or other mammals are usually different than their natural human counterparts. These differences may cause the body to perceive them as foreign, resulting in immune system responses. These immune reactions can deactivate the pharmaceutical, and in some cases also deactivate the body’s natural version of the protein, resulting in autoimmune disorders. Careful study is required to determine whether rice-expressed lactoferrin or lysozyme could cause such potentially dangerous reactions.

Amyloidosis and Mutant Proteins

Certain mutations to human lysozyme have been associated with a condition known as hereditary amyloidosis. Although it is unknown whether consumption of these mutant proteins could cause amyloidosis, the available evidence suggests that Ventria has not adequately examined its rice-expressed lysozyme to rule out these or other mutations.

POTENTIAL ENVIRONMENTAL IMPACTS

Ventria’s rice-produced pharmaceuticals have antibacterial and antifungal properties. If these traits are passed to related weed species such as wild and annual red rice, they could lend these weeds a fitness boost, promoting their spread. These weed species, as well as contaminated food-grade rice that sprouts in subsequent years from unharvested seed, could harbor these pharmaceutical traits and thus serve as a “genetic bridge” to pass the traits back to food-grade rice in the future.

ECONOMIC IMPACTS OF ADULTERATION

Any adulteration of food rice with Ventria's pharmaceuticals would likely lead to a decline or even an end to rice exports to Japan and other quality-conscious export markets. Since the U.S. has a zero tolerance standard for PMPs in food, adulterated rice, like StarLink corn, would be excluded from the domestic market as well.

STATE ACTION NEEDED DUE TO LOOPHOLES IN FEDERAL REGULATION

Federal regulators have a fundamentally contradictory policy. While they properly ban even trace amounts of plant-made pharmaceuticals in food or feed, they allow open-air cultivation of Ventria's crops, virtually ensuring contamination of rice meant for food and feed use.

- *FDA*: The FDA does not regulate Ventria's pharm rice in the field, and does not consider the potential human health impacts of exposure to these pharmaceuticals as contaminants in food.
- *EPA*: The EPA has not assessed Ventria's pharm rice despite evidence that its pharmaceutical proteins have pesticidal properties and could disrupt soil ecology.
- *USDA*: Though USDA has authority over Ventria's pharm rice in the field, it has not done a single environmental assessment to determine whether Ventria's pharm traits are spreading to food-grade rice or related weed species, nor has it examined the potential for a noxious weed risk from the spread of Ventria's traits.