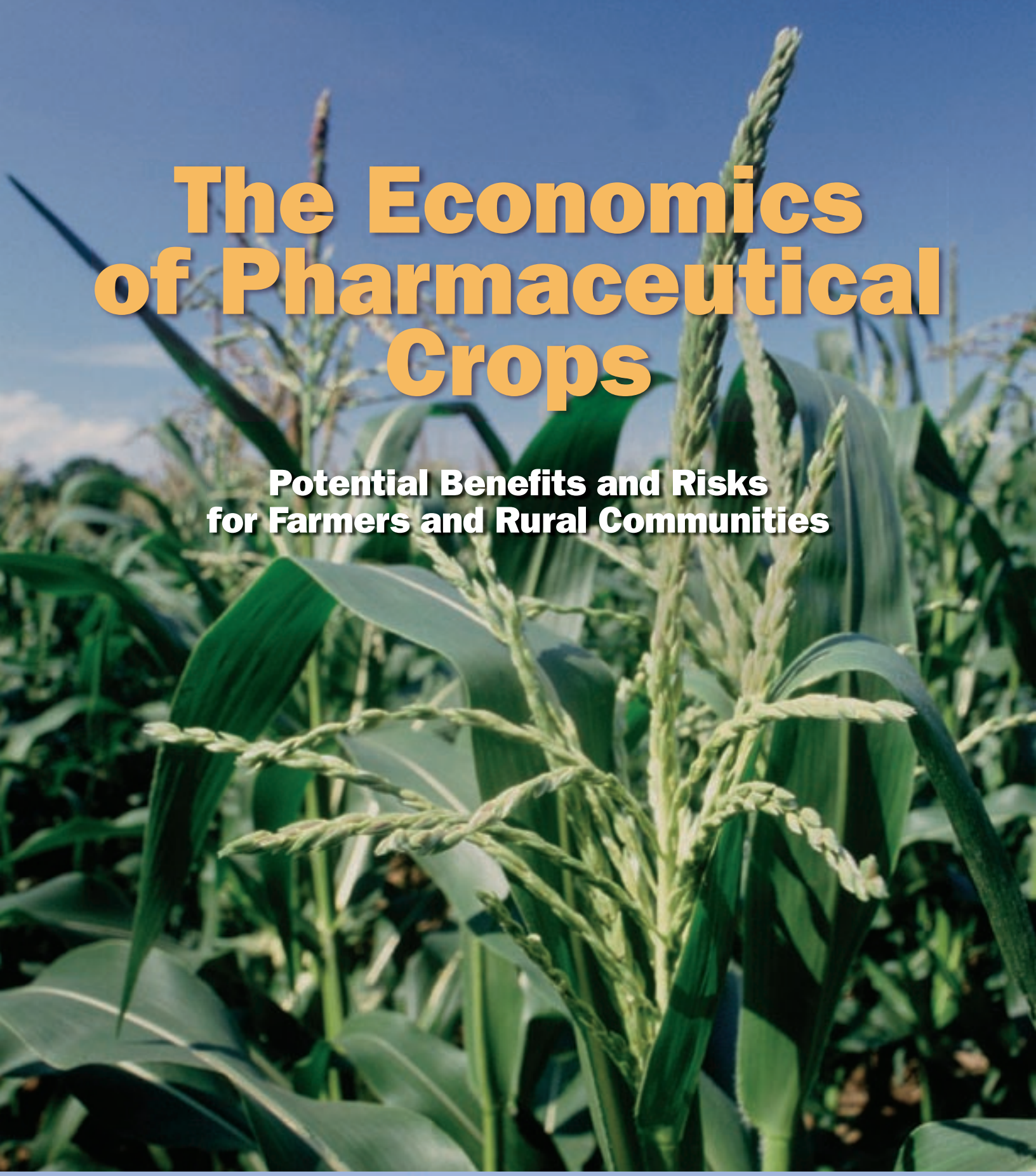

The Economics of Pharmaceutical Crops

Potential Benefits and Risks for Farmers and Rural Communities

Union of Concerned Scientists
Citizens and Scientists for Environmental Solutions

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Union of Concerned Scientists
December 2005

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The Union of Concerned Scientists is a nonprofit partnership of scientists and citizens combining rigorous scientific analysis, innovative policy development, and effective citizen advocacy to achieve practical environmental solutions.

The goal of the UCS Food and Environment Program is a food system that encourages innovative and environmentally sustainable ways to produce high-quality, safe, and affordable food, while ensuring that citizens have a voice in how their food is grown.

More information about UCS and the Food and Environment Program is available on the UCS website at *www.ucsusa.org.*

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Contents

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We are also grateful for reviews provided by Dr. Silvia Secchi and Bill Freese. We appreciate their valuable comments and advice but note that neither Dr. Wisner's report nor the UCS preface necessarily reflects their opinions.

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Preface

The current debate over genetically engineered pharmaceutical and industrial crops (or "pharma" crops) is replete with assertions by the pharma crop industry that these crops will generate enormous economic benefits for rural America—especially for farmers suffering economic hardships and eager for new opportunities. One state, Missouri, has even subsidized a new research center in pursuit of those benefits.

Though often repeated, these expansive claims remain just that, claims—assertions not backed by economic analyses. This lack of analysis represents a big gap in an important debate.

To fill that gap, the Union of Concerned Scientists (UCS) commissioned Dr. Robert Wisner, University Professor in the Department of Economics at Iowa State University, to examine the purported economic benefits of pharma crops. His report provides a thoughtful assessment of the issue—identifying the sources of potential benefits, qualitatively estimating the magnitude of these benefits (it is too early for *quantitative* analysis), and identifying those who may or may not benefit from pharma crops and under what circumstances.

While the pharma crop industry is in its early stages and its course is uncertain, ***the report leads UCS to the inescapable conclusion that pharma crop proponents' claims are inflated and, importantly, whatever benefits do materialize, most farmers will not be major beneficiaries.***

The key findings that contributed to this conclusion are summarized below.

- The potential benefits envisioned for consumers, farmers, and rural communities are highly tentative projections that fail to adequately address risks to the food supply when the same crops are used for both food and pharmaceutical production.
- Reduced drug-production costs, which are expected to be the primary source of potential benefits, will depend on the level of containment needed to protect the food system from pharma crop contamination. Containment-related costs may be high enough to at least partially outweigh potential savings in other areas of drug production.

- Pharma crops have other potential economic downsides including the liability that must be assumed by food manufacturers, farmers, and pharma crop companies for potential contamination of the food supply.
- Farmers are unlikely to be major beneficiaries because:
  - They will be unable to negotiate with pharma crop companies from a position of strength. Market forces, including foreign competition, will drive farmer compensation down to the lowest levels that pharma crop companies can achieve.
  - The acreage likely required for a successful pharma crop industry is so small compared with commodity crop acreage that only a small number of growers would be needed.
- Rural communities are unlikely to be major beneficiaries unless:
  - The local pharma crop industry brings in substantial research contracts for universities and private research firms; and
  - Pharmaceutical processing companies locate in the area.

Overall, the report suggests that the potential benefits from pharma crops may have been overstated when all costs and potential risks are included.

Of particular interest to us is the report's finding that most pharma crop benefits are far more likely to go to pharmaceutical companies than farmers. Farmers and rural communities (and those who want to help them) should therefore carefully examine the pharmaceutical industry's rosily optimistic, but unsubstantiated, portrayal of this new technology's economic rewards.

Margaret Mellon, Director
Jane Rissler, Deputy Director and Senior Scientist
UCS Food and Environment Program
December 2005

Executive Summary

State legislators, governors, university administrators and faculty, rural development councils, some farmer groups, and pharmaceutical firms all see potentially substantial economic benefits in encouraging the production of pharmaceutical crops. This report examines the sources of these benefits, issues affecting the magnitude of these benefits and who will receive them, and the economic risks associated with pharmaceutical crops. It also discusses key issues that these crops raise for farmers and rural America. Because the industry is in its infancy, this economic analysis has no firm numbers on which to rely but rather provides a framework for analyzing expected benefits in light of familiar economic principles.

Pharmaceutical crops, referred to in this report as "pharma" crops, are versions of traditional crops that have been genetically engineered to produce pharmaceuticals and industrial chemicals. The emerging pharma crop industry is believed by many to offer substantial new sources of farm income to diversify agriculture, overcome some limitations of commodity production, and provide much-needed assistance in the economic development of rural communities. It is also seen as a potential source of lower-cost medications and industrial raw materials.

Universities and private firms in major agricultural areas have been actively involved in research to develop these new products, and local governments have created research parks and business incubators to move products from research to actual production. If the industry is successful, it will likely fulfill at least some of its high expectations. However, the pharma crop industry is very young. There is much yet to be learned about its potential costs, benefits, and risks.

A BRIEF HISTORY OF PHARMA CROPS

Most pharma crops are modifications of traditional food and feed crops: corn, soybeans, and rice. And most are grown (or will likely be grown) in areas of the country that are major producers of food and feed versions of the same crops. Corn ranks first and soybeans second as preferred host crops for plant-produced pharmaceuticals and industrial chemicals. The preference for corn reflects its relatively low production cost, ease of genetic modification, and storability of seed until it is needed for pharmaceutical processing. Tobacco, the main non-food crop being used for these purposes, is rated third in preference; rice is fourth.

These crops have become potential hosts for pharmaceutical production because of important recent advances in the ability to genetically modify these plants. Pharma crop production involves the insertion of genes from other life forms (plant, animal, fungal, bacterial, or human) into the host plant.

The resulting products are expected to include therapeutic proteins; medical and veterinary drugs for treating diarrhea, heart disease, cancer, AIDS, and other illnesses; and vaccines that would be administered by consuming the modified grain or fruit. Other products reported to be in the research and/or development stage include an antibody to protect against herpes, a blood thinner, a blood clotting medicine, and a human contraceptive. Traditional food crops are also being modified to produce raw material for plastics, detergents, paints, and other research and industrial chemicals.

The U.S. Department of Agriculture (USDA) has approved field testing of pharma crops since the early 1990s, much of which has been conducted in the major corn-, soybean-, and rice-producing

regions of the country. And despite approximately 15 years of research, the Food and Drug Administration (FDA) has yet to approve any pharma crop medical drugs (though a few are reportedly in clinical trials). As with all other medical drugs, extensive testing of the pharma product is required before it can be approved. Six chemicals from pharma crops have reportedly been produced for research.

The use of food crops, especially corn, has raised major concerns that pharma crop production systems should be designed to ensure virtually zero chance of commingling with food and feed supplies. Corn pollen, for example, can be carried long distances by the wind, creating the risk of cross-pollination with corn intended for food or animal feed. Major food processing and retailing associations, consumer and environmental groups, and a National Research Council report have stressed the critical importance of ensuring that pharma crops be kept separate from food supplies. These concerns have been heightened by actual occurrences of pharma crops and unapproved genetically modified food or feed crops commingling with food supplies.

The most striking case involved StarLink corn, a genetically modified, insect-resistant variety initially approved only for animal feed in the United States. StarLink corn accounted for less than 0.5 percent of all U.S. acreage planted with corn, but because of cross-pollination and commingling, was found at a low level in a substantial percentage of U.S. corn supplies in 2000 and 2001. This led to the shutdown of food processing plants for cleaning, the recall of products from grocery shelves, extra testing of supplies at all points in the marketing system, the redirection of shipments to markets where they could be used, the rejection of export shipments, and related complications that involved significant costs and a loss of confidence in the U.S. regulatory system.

Several other incidents also influenced the call for virtually zero risk of commingling between pharma crops and food and feed supplies, including two cases in 2002 in which pharma crops from test plots were accidentally commingled with food crops. The USDA's Animal and Plant Health Inspection Service in 2003 modified its regulations relating to pharma crop production to reduce these risks, but food processors and environmental and consumer groups alike have called for additional changes to ensure virtually zero risk.

ESTIMATING THE POTENTIAL BENEFITS

The need for changes in production systems creates uncertainty about the actual costs of producing pharmaceuticals from crops. Some researchers and industry sources show large potential cost savings compared with conventional production processes, but confinement-related changes in production systems may reduce these savings. In at least one case, industry sources indicate costs for conventional production of a pharmaceutical will approximately match those projected for a similar product that one pharma crop firm is expected to produce.

Projected lower costs for medication are one of the major driving forces behind the pharma crop industry, but the actual costs (once the industry begins producing FDA-approved medicines) will be important in determining the potential benefits for consumers. Another potential source of cost savings is the ability to scale up pharmaceutical production rapidly if larger supplies are needed to meet consumer demand. Expansion of conventional production systems could take much more time, due to the need to obtain environmental permits and approvals to build or expand plants and then complete the construction. Expanding pharma crop production, on the other hand, is envisioned largely as planting more pharma crop acres.

POTENTIAL BENEFICIARIES

Those who may benefit from pharma crops include pharma crop companies and growers, medical patients, universities, private research firms, rural communities, and state and local governments (through increased tax revenues). Some groups looking for significant new economic development view increased farm income as a key source of these benefits. They anticipate that farmers will receive large returns for growing a crop that may be valued at several hundred thousand or perhaps millions of dollars per acre.

However, returns to farmers are likely to be based on comparable returns for performing similar services in other crop production enterprises, plus extra compensation for any significant risks not covered by the firm contracting to have the crop produced. In the end, only a small part of the pharma crop's value would be expected to go to the farmer.

Returns to farmers will also be determined in an international setting. The technology is easily transferable across national borders, and excessive production costs in the United States could encourage production to move abroad.

If the pharma crop industry becomes a substantial contributor to rural economic development, a major part of its contribution is likely to come in the form of research contracts for universities and private research firms. The extent of benefits for this group and the resulting impact on state and local economies and tax receipts will depend on the number and size of such contracts. The processing of pharma crops into medical drugs may also contribute to economic development if it is done in the area where the crops are produced.

There is strong competition among rural states to become the pharma crop "capital of the world," with states and local communities offering tax concessions, assistance in infrastructure development, and other incentives. Some have questioned whether these and other concessions are needed for an industry projected to enjoy a bright future and high economic returns, and whether multi-state efforts risk excessive duplication of facilities and research. Others counter that such efforts set the stage for specialization, where some states would focus on pharma crops suitable to their region and other states would focus on different crops.

Answers to the question of whether subsidies are needed for pharmaceutical firms will be determined by individual states and communities. The extent of subsidies, tax rebates, and other incentives may influence the degree of economic development that results.

> **Only a small part of the pharma crop's value would be expected to go to the farmer.**

RISKS TOO SERIOUS TO IGNORE

While the pharma crop industry is projecting significant potential benefits for consumers, pharma crop producers, rural communities, and companies that sell the pharmaceutical products, risks created by the industry should also be recognized. The following groups could be placed at substantial risk in the event of accidental commingling of pharma crops with food or feed crops:

- other crop farmers
- livestock and poultry producers
- domestic grain- and feed-handling firms
- grain exporters
- food and feed processors
- food retailers
- consumers
- foreign grain- and feed-handling firms
- foreign food processors
- seed companies

Commingling risks raise questions about who is responsible, who pays the cost of retrieving and disposing of commingled supplies, and who compensates for human or animal health problems, rejected supplies in domestic and export markets, and the possibly lower value of organic and conventional crop and livestock production.

The impact on economic development will also be influenced by the total number of acres required for pharma crop production. Most industry observers believe pharma crops would require only a small percentage of the nation's cropland, but the exact amount is uncertain. In the years ahead, provided pharma crop production can be successfully isolated, dozens or perhaps even hundreds of different types of these crops may be developed. Even so, these crops are expected to require only a small part of the approximately 231 million acres currently used in this country to produce corn, other feed grains, wheat, rice, and soybeans. A group working to establish a pharma crop industry in 15 northwest Missouri counties anticipates that 0.57 percent of the area's cropland will be used for pharma crops.

Because the pharma crop industry is in its infancy, the potential benefits being envisioned should be viewed as tentative projections and balanced with the inherent risks to food supplies when the same crops are used for both food and pharmaceutical or industrial purposes. The industry's future may ultimately depend on whether a pharma crop production system can be established that will provide virtually zero risk of commingling the industry's products with food and feed supplies.

Because the pharma crop industry is in its infancy, the potential benefits being envisioned should be viewed as tentative projections and balanced with the inherent risks to food supplies when the same crops are used for both food and pharmaceutical or industrial purposes.

Part 1

Introduction

> ***"Drug-growing plants…cross the divide between medicine and agriculture not just in the public mind, but on the ground. Can they deliver on their promise of miracle vaccines and cheap drugs? Much will depend on whether the industry can meet the exceedingly difficult challenge of imposing the exacting standards of drug production on the inherently uncontrollable conditions of nature."*** —BILL FREESE, 2002[1]

State legislators, governors, university administrators and faculty, rural development councils, some farmer groups, and pharmaceutical firms all see potentially substantial economic benefits in raising crops genetically engineered to produce pharmaceutical and industrial compounds (referred to in this report as "pharma" crops). However, key U.S. food industry associations, environmental and consumer groups, and the National Research Council have recommended against the use of traditional food and feed crops for this purpose.

These groups are concerned about food safety risks where food and feed crops engineered to produce pharmaceuticals and chemicals are grown in major U.S. food and feed crop production areas. Some farm groups have been especially concerned about the production of drugs in corn and flax, two crops whose pollen can drift long distances and put commodity or organic versions of the crops at risk if adequate safeguards are not present.

Products expected to result from this new industry include therapeutic proteins; medical and veterinary drugs for treating diarrhea, heart disease, cancer, AIDS, and other illnesses; and vaccines that would be administered by consuming the modified grain or fruit.[2] Other products reported to be in the research and/or development stage include an antibody for protection against herpes, a blood thinner, a blood clotting medicine, and a human contraceptive.[3] Traditional food crops are also being

1 Freese, B. 2002. *Manufacturing Drugs and Chemicals in Crops: Biopharming Poses New Threats to Consumers, Farmers, Food Companies and the Environment.* Friends of the Earth (FOE) and Genetically Engineered Food Alert, 15. On the FOE website at *http://www.foe.org/camps/comm/safefood/biopharm/BIOPHARM_REPORT.doc*.

2 Giddings, G., G. Allison, D. Brooks, and A. Carter. 2000. Transgenic plants as factories for biopharmaceuticals. *Nature Biotechnology* 18:1151–1155.

Pew Initiative on Food and Biotechnology (PIFB). 2001. *Harvest on the Horizon: Future Uses of Agricultural Biotechnology*, 53–62. On the PIFB website at *http://pewagbiotech.org/research/harvest*.

3 Elias, P. 2002. Isle corn may help company make drug for herpes. Associated Press, July 11. On the *Honolulu Star-Bulletin* website at *http://starbulletin.com/2002/07/11/news/story1.html.*

Elias, P. 2001. "Pharming" to find cures takes root. Associated Press, October 28. On the AgBioWorld website at *http://www.agbioworld.org/biotech-info/articles/interviews/cure.html.*

Freese. *Manufacturing Drugs and Chemicals in Crops*.

Giddings et al. Transgenic plants as factories for biopharmaceuticals.

McKie, R. 2001. GM corn set to stop man spreading his seed. *The Observer*, September 9. On *The Observer* website at *http://observer.guardian.co.uk/international/story/0,,548964,00.html.*

modified to produce raw material for plastics, detergents, paints, and other research and industrial chemicals.[4]

Products derived from pharma crops offer the potential to develop less expensive and possibly new medications, as well as industrial products based on renewable raw materials rather than petroleum. But there are substantial risks and costs to be considered when these products are being produced from food or feed crops.[5]

4 Pew Initiative on Food and Biotechnology. *Harvest on the Horizon.*

5 Andow, D., H. Daniell, P. Gepts, K. Lamkey, E. Nafziger, and D. Strayer. 2005. *A Growing Concern: Protecting the Food Supply in an Era of Pharmaceutical and Industrial Crops*. Union of Concerned Scientists (UCS). On the UCS website at *http://www.ucsusa.org/food_and_environment/genetic_engineering/pharmaceutical-and-industrial-crops-a-growing-concern.html*.

Freese. *Manufacturing Drugs and Chemicals in Crops*.

Part 2
Purposes and Outline

This report looks at the potential sources of benefits from pharma crops and the economic mechanisms that will influence how the value of the pharma crop industry's output will be shared by various market participants. It also discusses key issues that pharma crops raise for farmers and rural America.

Because the industry in its infancy, this economic analysis has no hard numbers on which to rely but rather provides a framework for analyzing expected benefits in light of familiar economic principles. The primary focus will be pharmaceutical-producing crops, although similar incentives and challenges exist for industrial crops.

One major challenge is that food or feed crops modified to produce pharmaceuticals could prove harmful to consumers and animals if accidentally commingled with commodity or organic versions of the same crop. Because of such food safety concerns, significant private and public costs may be associated with this new industry in order to maintain its complete separation from the food system.[6] At this writing, the full extent of these costs is unknown. Several groups indicate that major changes in pharma crop production and regulatory systems are needed to maintain virtually zero risk of contaminating the food supply.[7]

The first part of this report describes current and anticipated types of pharma crops and products made from them, reviews the status of U.S. pharma crop production, and looks at reasons for the strong interest in pharma crops in major agricultural states. The report then goes on to describe expected sources of benefits, identify those who may benefit or suffer from development of the industry, detail conditions that will influence the distribution of benefits, and examine the implications of pharma crops for rural economic development. Two case studies—in the rice and flax industries—illustrate several of the important issues raised in the report.

6 Andow et al. *A Growing Concern.*

Bailey, A. 2005. Pharming hurdles: plant-based pharmaceuticals have challenges to overcome before products will hit the market. *Agweek*, May 9.

7 Andow et al. *A Growing Concern.*

Fabi, R. 2003. US food groups urge halt to "bio-pharm" crops. Reuters Securities News, February 7.

Food Products Association (FPA). 2003. Comments to USDA Animal and Plant Health Inspection Service, RE: Docket No. 03-031-1. Field testing of plants engineered to produce pharmaceuticals and industrial compounds. *Federal Register* 68(11337), March 10. On the FPA website at *http://www.fpa-food.org/content/regulatory/comments_view.asp?id=43.*

Grocery Manufacturers of America (GMA). 2003. GMA says stringent FDA and USDA bio-pharma regs needed to maintain food supply purity. Press release. February 6. On the GMA website at *http://www.gmabrands.org/news/docs/newsrelease.cfm?docid=1063.*

Grocery Manufacturers of America (GMA). 2002. GMA urges the use of non-food crops for biotech drugs. Press release. November 14. On the GMA website at *http://www.gmabrands.org/news/docs/newsrelease.cfm?docid=1029.*

Part 3

Current Status of Pharma Crops

Pharma crops are varieties of commercial crops that have been genetically modified by the insertion of genes from other life forms (plant, animal, bacterial, fungal, or human) to produce specific types of human and veterinary medical drugs.[8] In most cases, the seed or leaf portion of the crop requires extensive processing and purification to produce the desired drug, vaccine, or chemical. And as with all U.S. government-approved medicines, extensive testing and Food and Drug Administration (FDA) approval are required before pharma crop drugs can be marketed. These steps, as well as assessments of the environmental impact of outdoor drug production, add to the cost of producing pharmaceuticals.

PHARMA CROPS MAY LOWER MEDICATION COSTS

Economists and others have tended to separate new technological developments into "processes for producing the product" and "new products," but with pharma crops, one author notes that this distinction becomes blurred. Aziz Elbehri of the U.S. Department of Agriculture (USDA) Economic Research Service indicates it may only be through pharma crop production that many anticipated new medical products will be developed.[9] He explains that pharma crops are likely to provide a greater range of available drugs than those produced from conventional processes and may offer improved success in treating cancer, cardiovascular diseases, and various infectious diseases.[10] Most researchers and industry promoters believe, if current and future efforts are successful, the major benefit of pharma crops will be reduced production costs for medical drugs.[11]

For individuals and groups outside of pharma crop companies and medical fields, interest in pursuing pharma crops stems from the prospects for a high per-acre value and anticipation that a significant part of this value will be passed on to farmers. States and communities are also interested in being seen as a future hub for the emerging pharma crop research and processing industry. Each hopes to share not only in the returns generated by pharma crop research and production, but also a subsequent increase in spending by farmers.

States and communities hope to share not only in the returns generated by pharma crop research and production, but also a subsequent increase in spending by farmers.

8 Kostandini, G., B. Mills, and G. Norton. 2004. Potential impacts of pharmaceutical uses of transgenic tobacco: the case of human serum albumin (HSA). Selected Paper #118832 prepared for presentation at the annual meeting of the American Agricultural Economics Association, August 1–4. On the AgEcon Search website at *http://agecon.lib.umn.edu/cgi-bin/pdf_view.pl?paperid=14293&ftype=.pdf*.

9 Elbehri, A. 2005. Biopharming and the food system: examining the potential benefits and risks. *AgBioForum* 8(1). On the AgBioForum website at *http://www.agbioforum.org/v8n1/v8n1a03-elbehri.htm*.

10 Ibid.

11 Biotechnology Industry Organization (BIO). No date. Plant-made pharmaceuticals. On the BIO website at *http://www.bio.org/healthcare/pmp*.

However, food processors, millers, retailers, exporters, and others in the food industry, as well as a National Research Council report, have expressed concern about the potential for pharma crop contamination of the food supply.[12] These concerns stem from recent problems involving the accidental commingling of pharma crops and unapproved genetically modified food or feed crops with commodity versions of the same crops. In some cases, such problems led to the shutdown and cleaning of processing plants, recalls of products from grocery shelves, added testing to ensure that unapproved products were not present, additional costs for redirecting supplies to sites where they would be accepted, and rejections of U.S. grain by foreign buyers.[13]

MOST PHARMA CROPS ARE FOOD CROPS

Thus far, the pharma crop industry has focused largely on producing drugs in food crops such as corn, soybeans, and rice rather than non-food crops. Corn is favored as a pharma crop because of its low production cost, ease of genetic modification, and storability of the raw material over an extended time until it is needed for processing. The industry's second preference is soybeans, and tobacco is third.[14]

Pharmaceutical versions of all three crops have been grown on a small-scale experimental basis in several states for more than a decade.[15] Tobacco is the only significant non-food plant the industry has found useful for drug production; other food or feed crops that can be used include rice, wheat, barley, potatoes, tomatoes, flax, sugarcane, rapeseed, sunflower, safflower, and alfalfa.

NO DRUGS FROM PHARMA CROPS HAVE BEEN APPROVED

Through late 2005, despite approximately 15 years of field trials, the FDA had yet to approve the medical use of any drugs from pharma crops. A few are reportedly in clinical trials.[16]

At this writing, six products from pharma crops have been produced for research and/or manufacturing purposes: four from engineered corn and two from engineered rice.[17] One of the corn-derived

12 Brasher, P. 2004. Scientific panel issues warning about biotech crops. *Des Moines Register*, January 21. On the Mindfully website at *http://www.mindfully.org/GE/2004/Warning-Biotech-Crops21jan04.htm*.

Fabi. US food groups urge halt to "bio-pharm" crops.

Food Products Association. Comments to USDA Animal and Plant Health Inspection Service.

Grocery Manufacturers of America. GMA says stringent FDA and USDA bio-pharma regs needed.

Grocery Manufacturers of America. GMA urges the use of non-food crops for biotech drugs.

National Research Council. 2002. *Environmental Effects of Transgenic Plants: The Scope and Adequacy of Regulation* (Washington, DC: National Academy Press).

13 Harl, N., R. Ginder, C. Hurburgh, and S. Moline. 2003. The Starlink situation. Iowa State University Extension, November 18. On the Iowa State University website at *http://www.extension.iastate.edu/grain/resources/publications/buspub/0010star.PDF.*

14 Rissler, J. 2005. A growing concern. *Catalyst* 4(1). On the UCS website at *http://www.ucsusa.org/publications/catalyst/page.jsp?itemID=27225597*.

15 Union of Concerned Scientists (UCS). No date. Pharma Crop Database, Food and Environment Analysis. On the UCS website at *http://go.ucsusa.org/food_and_environment/pharm/index.php?s_keyword=XX*.

16 Biotechnology Industry Organization (BIO). No date. Plant-made pharmaceuticals: frequently asked questions. On the BIO website at *http://www.bio.org/healthcare/pmp/factsheet2.asp*.

17 Large Scale Biology (LSB). No date. Recombinant aprotinin for pharmaceutical and other biomedical uses. On the LSB website at *http://www.lsbc.com/thera.html#followon*.

ProdiGene. 2004. TrypZean™. On the ProdiGene website at *http://www.prodigene.com/pdf/TrypZean(tm)%20Backgrounder.pdf*.

ProdiGene. 2004. AproliZean™. On the ProdiGene website at *http://www.prodigene.com/pdf/AproliZean(tm)%20Backgrounder.pdf*.

Sigma-Aldrich. 2005. A8706 avidin from egg white, recombinant, expressed in corn. On the Sigma-Aldrich website at *http://www.sigmaaldrich.com/catalog/search/ProductDetail/SIGMA/A8706*.

Sigma-Aldrich. 2005. L4040 lactoferrin from human milk, expressed in rice. On the Sigma-Aldrich website at *http://www.sigmaaldrich.com/catalog/search/ProductDetail/SIGMA/L4040*.

Sigma-Aldrich. 2005. L1667 lysozyme from human milk, recombinant, expressed in rice. On the Sigma-Aldrich website at *http://www.sigmaaldrich.com/catalog/search/ProductDetail/SIGMA/L1667*.

products is also produced in tobacco. The genes used to develop these products originated in humans, cattle, chickens, and bacteria. The two rice products are reportedly derived from human genes.

PHARMA CROPS ARE PRODUCED IN MAJOR FOOD CROP REGIONS

For economic reasons, pharma crops are grown in regions where the food and feed versions of these crops are produced commercially. For example, pharma corn—the most common pharma crop—has been produced mainly in the Corn Belt.

Pharma crops have been field-tested in the United States since the early 1990s. In fact, publicly available data from the USDA's Animal and Plant Health Inspection Service show that field trials of pharma crops were permitted on approximately 300 sites spread across the majority of states from 1991 through 2004. However, these data do not indicate the location of sites within states or whether all approved sites have been used for production.[18]

In the continental United States, the top four states in number of permits issued through 2004 were Nebraska, Iowa, Wisconsin, and Illinois, in that order. Three of these states are the nation's top corn producers, and Corn Belt states as a whole account for more than half of all U.S. permits for pharma crops. California and Texas are important rice producers and are tied for fifth place among states with pharma crop permits.[19]

SUCCESS WOULD LEAD TO MORE PHARMA CROPS

Because the pharma crop industry is in its infancy, there is much to be learned about the implications of using food crops and tobacco for drug production. The experiences and research of the next few years, as well as the risks and costs, may significantly influence the net value of the industry's output and its potential returns to participants in research, production, and marketing.

If the visions of pharma crop researchers materialize, hundreds and perhaps thousands of products may ultimately be developed. That, in turn, will increase the importance of completely isolating pharma crops from their commodity and organic counterparts. It will also make the challenges and costs of doing so more obvious to the industry and to government regulators, as well as others in the agricultural and food marketing sectors.

18 Andow et al. *A Growing Concern.*

Union of Concerned Scientists. Pharma Crop Database, Food and Environment Analysis.

19 Union of Concerned Scientists. Pharma Crop Database, Food and Environment Analysis.

Part 4
Sources of Potential Benefits

A recent study from Virginia Polytechnic Institute and State University suggests that benefits from pharma crops could be derived from: (1) the speed with which new products can be brought to market; (2) an increased variety of pharmaceutical products; and (3) substantial savings resulting from not having to invest in new buildings and other components of a physical production system.[20] Certain pharma crop drugs may also treat serious illnesses in more effective ways than conventionally produced drugs.[21] Most pharma crop industry personnel and researchers see dramatically reduced production costs as the main potential advantage of this technology.[22]

Under current assumptions about cost savings, annual growth in pharma crop production is projected by some to exceed 15 percent over the next decade.[23] This projection is based on the recent market growth of similar types of pharmaceuticals.[24] The total annual value of existing U.S. biopharmaceutical industry output, excluding pharma crop processes, is reported to be about $41 billion, with a recent annual growth rate of 20 percent.[25] If the industry were to grow at a similar rate, the potential value of pharma crops would be significant.

Such optimistic growth projections should be examined carefully, however, given the fact that actual costs and benefits are still uncertain. In addition, the potential size of the pharma crop industry will be influenced by its impact on the agricultural industry, which pharma crops could place at risk. The total value of U.S. agricultural production in 2004 was $279 billion.[26] Furthermore, U.S. consumers in 2000 spent an estimated $661 billion for food, excluding imports and seafood.[27]

LOWER STARTUP AND EXPANSION COSTS

With current production technologies, many pharmaceuticals are produced in large quantities under controlled, enclosed conditions by fermentation of genetically engineered animal cells, bacteria, yeast, or fungi.[28] These processes require large investments in buildings and equipment. Rapid growth in demand for new products is reportedly straining the existing processing capacity and could create serious supply limitations in the

20 Kostandini et al. Potential impacts of pharmaceutical uses.

21 Elbehri. Biopharming and the food system.

22 Biotechnology Industry Organization. Plant-made pharmaceuticals.

23 Elbehri. Biopharming and the food system.

24 For examples of growth rates for various pharmaceutical products, see: IMS. 2003. IMS world markets. On the IMS website at *http://www.imshealth.com/web/content/0,3148,64576068_63872702_70260998_70960214,00.html*.

25 AS Insights. 2003. Biopharmaceuticals: current market dynamic & future outlook. On the MarketResearch.com website at *http://www.marketresearch.com/product/display.asp?productid=935534&xs=r*.

26 U.S. Department of Agriculture Economic Research Service (USDA ERS). 2004. Farm financial indicators. On the USDA ERS website at *http://www.ers.usda.gov/StateFacts/US.HTM#FFI*.

27 U.S. Department of Agriculture Economic Research Service (USDA ERS). 2000. Food marketing and price spreads: current trends. On the USDA ERS website at *http://www.ers.usda.gov/Briefing/FoodPriceSpreads/trends*.

28 Ibid.

Elbehri. Biopharming and the food system.

Mison, D., and J. Curling. 2000. The industrial production costs of recombinant therapeutic proteins expressed in transgenic corn. *BioPharm* 13:48–54.

next several years because of time lags required to build new facilities.[29]

Elbehri gives an example of laboratory production requiring five to seven years for plant approval and construction, with a cost of approximately $450 million. He estimates that the same amount of production would be possible on 500 acres of corn for an approximate investment of just $80 million.[30] When expanded capacity is needed for pharma crops, assuming no additional regulatory approvals are required, the only additional investment will be for more seed and acres and perhaps more building space and facilities to process the pharma crop.[31]

As a result of these lower costs, Elbehri reports that pharma crop production could be four to five times less expensive than conventional systems. Other estimates suggest pharma crop production could be 10 to 100 times less expensive for some products.[32]

UNCERTAINTY ABOUT COSTS

Projected costs vary from one drug to another and should be viewed as highly tentative. Some industry observers question whether current projections are realistic. For example, according to Texas-based Agennix, which uses conventional microbial fermentation processes to manufacture a drug known as human lactoferrin, its production costs are equal to those projected by a competing firm, Ventria Bioscience, that plans to produce the same or an equivalent product from pharma rice.[33] In addition, the food industry and other groups insist the current pharma crops production system needs major changes to prevent risks to food supplies—changes that would increase production costs.

At this stage of the industry's development, it should be stressed that lower production costs and faster expansion of production capacity—the primary sources of value for pharma crops—are only projections.

Lower production costs and faster expansion of production capacity—the primary sources of value for pharma crops—are only projections.

COMPANIES TURNING ELSEWHERE?

Two large biotech companies appear to have recently shifted their emphasis away from pharma crops. Trade sources indicate Monsanto has closed its pharma crops subsidiary, and Novartis Pharma, the leading biopharmaceutical manufacturer, recently allocated six billion dollars to develop traditional fermentation systems for medical drug production.[34]

In addition, three smaller companies have reportedly exited from pharma crops or shifted to conventional production methods.[35] These changes hint that some players in the industry may see smaller returns and/or greater obstacles to pharma crop development than previously anticipated.

29 Elbehri. Biopharming and the food system.

30 Ibid.

31 Ibid.

32 Ibid.

33 Cole, N. 2005. Competition grows in the biopharming market. *Arkansas Democrat-Gazette*, May 5. On the ellinghuysen.com website at *http://www.ellinghuysen.com/news/articles/16224.shtml*.

34 Freese, B., and R. Caplan. 2004. *Plant-Made Pharmaceuticals: Financial Risk Profile.* Friends of the Earth and U.S. Public Interest Research Group. On the National Campaign for Sustainable Agriculture website at *http://www.agmatters.net/GE/GE_BFreese_PMPs_Risky_Business.doc*.

35 Ibid.

Part 5

Who Gains and Who Loses with Pharma Crops?

Rational decisions about policies to encourage pharma crop production need to be based on the gains and losses that could result. If the visions of researchers and the pharma crop industry materialize, individuals and groups in agriculture, the general public, the private sector, and universities will benefit. However, until a system is developed to prevent pharma crop contamination of the food supply, the technology also poses risks for important groups in the agricultural and food sectors.

GROUPS THAT COULD BENEFIT

Groups and institutions that have the potential to benefit economically from pharma crops include:

- pharma crop growers
- pharma crop companies
- medical patients
- universities
- private research firms
- rural communities
- state and local governments (through increased tax revenues)

GROUPS THAT COULD SUFFER

On the other hand, in certain situations, several groups could experience substantial economic losses resulting from pharma crop production. Such losses would most likely occur if pharma crops were commingled with commodity seed, feed, or food supplies. Groups potentially at risk include:

- other crop farmers
- livestock and poultry producers
- domestic grain- and feed-handling firms
- grain exporters
- food and feed processors
- food retailers
- consumers
- foreign grain- and feed-handling firms
- foreign food processors
- seed companies

Economic risks to these groups could result from: (1) lowered product value and (2) higher costs associated with additional testing, clearing out supplies of commingled/contaminated products, canceled sales contracts, and loss of markets to foreign competitors.

Because of the availability of patents, economic theory dictates that the largest gains from pharma crops will go to pharma crop, pharmaceutical, and biochemical companies that own the technology.

MAJOR POTENTIAL BENEFICIARIES

Because of the availability of patents, economic theory dictates that the largest gains from pharma crops will go to **pharma crop, pharmaceutical, and biochemical companies** that own the technology.[36] These firms, by owning the exclusive

36 Moschinni, G. 2001. Biotech—who wins? Economic benefits of biotechnology innovations in agriculture. *Este Centre Journal of International Law and Trade Policy* 2:93–117.

production rights for the life of the patent (and benefiting from the potentially lower production costs of pharma crops), are in a position to reap substantial returns for their efforts.

Medical patients could benefit from a more adequate supply of drugs and possible lower costs. The amount of the savings that would be passed through to consumers, however, is still open to question. For example, avidin, a research chemical made from pharma corn, reportedly costs far less to produce than if made by conventional methods, but has been sold at a higher price than the conventional product.[37]

The pharma crop industry also offers potential benefits to **universities and private research firms** in the form of research contracts. The impact of these benefits is difficult to determine and will vary with the circumstances (such as the details of individual contracts and the number of research commitments).

RISK REDUCTION COULD ADD TO PRODUCTION COSTS

To reduce the risks of pharma crops accidentally commingling with the food supply, pharma crop companies and policy makers may consider producing such crops in isolated areas (such as the southwestern United States) rather than in regions where commercial crop production is common.[38]

Growing pharma food and feed crops in the Southwest would require added investments in irrigation but might reduce problems with diseases and pests compared with the Corn Belt. Fewer regulatory costs would be expected, due to the Southwest's isolation from major food and feed grain production areas, but land costs could be either higher or lower than the Midwest depending on the proximity to major urban areas. And, depending on the crop, environmental risks could still be present in regions isolated from the Corn Belt. Another more expensive alternative would be to produce pharma crops in greenhouses.[39]

The net benefits of pharma crop production will be affected by costs necessary to provide virtually total isolation of pharma crops from the food production and marketing system.

RISK REDUCTION COULD AFFECT POTENTIAL BENEFITS

The net benefits of pharma crop production will be affected by costs necessary to provide virtually total isolation of pharma crops from the food production and marketing system. Food retailing, processing, and manufacturing associations as well as the Union of Concerned Scientists and others have concluded that the current regulatory system is inadequate to provide complete isolation, and therefore argue that the safety and integrity of the food system must be given top priority.[40] Their

37 Freese. *Manufacturing Drugs and Chemicals in Crops,* 15.

38 Andow et al. (*A Growing Concern*) raise the question of whether pharma crops should be produced in geographically isolated areas. The southwestern United States would be one potentially suitable region, since commodity corn production there (except for the Texas panhandle) is minimal.

39 As an example of possible greenhouse technology, see: Brashier, M. 2005. Pharming 101: confined corn. *Feedstuffs* 77(27):16.

40 Andow et al. *A Growing Concern*.

Food Products Association. Comments to USDA Animal and Plant Health Inspection Service.

Grocery Manufacturers of America. GMA urges the use of non-food crops.

Grocery Manufacturers of America. GMA says stringent FDA and USDA bio-pharma regs needed.

conclusions are based partly on recent instances of unapproved genetically modified crops commingling with food and feed grains.

The costs associated with providing virtually total isolation of pharma crops from the food, seed, and feed marketing systems may be substantially higher than those projected under existing regulations. Public policy will determine how much of the additional regulatory cost is passed back to pharmaceutical firms and how much must be absorbed by the public. If the outcome makes pharma drugs more expensive to produce than currently projected, the potential benefits will be reduced.

As evidence that commingling is a realistic concern, ProdiGene, Inc. paid $250,000 in fines for allowing a small amount of pharma corn to contaminate soybeans in a grain elevator after the 2002 harvest. The company was also required to pay for disposal of the contaminated crops and post a one-million-dollar bond to cover possible future occurrences of similar problems.[41] The contaminated crop was removed from the marketing system before contamination of the larger food and feed supplies could occur, but if the contaminants had been detected at a later stage, the costs would have been much higher.

In another example, ***economists estimate that removal of unapproved StarLink corn from U.S. and international food and feed marketing systems cost hundreds of millions of dollars.*** StarLink corn was a biotech variety approved only for animal feed and non-food industrial uses, and accounted for less than 0.5 percent of the total U.S. acreage planted with corn. It was only considered a potential health concern for a small number of persons with a certain type of allergy. Even so, its discovery in the food system in 2000 led to product recalls, rejected export shipments, shutdowns of processing plants for cleaning, extra testing of shipments, and other expenses.[42]

Yet another situation involved the accidental release of an unapproved variety of genetically engineered insect-resistant corn, Bt10. Shipments containing low levels of this unapproved corn were reportedly rejected in 2005 by several foreign buyers.[43]

With the government regulatory system subject to change, the costs of providing virtually total isolation of pharma crop supplies and preventing cross-pollination with commercial supplies may be higher than currently projected. Strengthening the system would increase production costs and reduce the possible cost advantage of drugs, vaccines, and industrial chemicals produced from pharma crops compared with those produced by other methods. And these increases, in turn, may affect the amount of benefits passed through to consumers and contributions to economic development in rural areas.

CONSIDERATIONS FOR FARMERS

The economic benefits for pharma crop producers will depend on:

- returns per acre paid by the pharma crop firm for use of the farmer's land and for any expenses needed to maintain crop separation and multi-year land isolation;
- returns paid for labor and management;
- the total number of acres needed;
- any costs required to meet contractual obligations; and
- any risk of liabilities that must be assumed by the farmer in producing a crop that could

41 Gersema, E. 2002. Biotech company fined over mishaps. Associated Press, December 7. On the checkbiotech.org website at *http://www.checkbiotech.org/blocks/dsp_document.cfm?doc_id=4326*.

42 Harl et al. The Starlink situation.

43 Reuters News Service. 2005. Japan finds US biotech corn, now to test all imports. June 2. On the Planet Ark website at *http://www.planetark.com/dailynewsstory.cfm/newsid/31062/story.htm*.

seriously jeopardize food and feed supplies if commingling with commodity production occurs.

Contractual production. Pharma crop firms will almost certainly own a crop during its entire production and harvesting cycle and will contract with farmers to produce the crop according to precise specifications. These firms can be expected to compensate farmers according to the normal payment rates for tillage, planting, spraying, harvesting, and other field operations, plus an additional amount for expenses required to maintain total, multi-year separation of the pharma crop from conventional crops both in the field and in commercial marketing channels.

Equipment for planting and harvesting may be owned by the pharma crop company, but if farmers own the equipment it will need to be dedicated solely to pharma crop production. Thus, the high investment costs for such equipment can only be spread over a small number of acres, resulting in a high cost per acre. Dedicated harvesting equipment is necessary because it is difficult to clean to the tolerance levels required for virtually total separation of pharma crops from the food supply. If machinery is moved to another location and not thoroughly cleaned, there would be some risk of accidental contamination of commodity crops from kernels or seeds remaining in the machine.

Disposal of crop residues. Another potential cost, depending on the pharma crop, is disposal of the residue remaining after the pharma portion of the crop has been harvested and processed. If stalks, seed pods, and husks contain drug residues, this could represent a significant expense. Disposal of portions of the kernel remaining after drug processing could also present costs and challenges.

Some have considered using these by-products in the livestock feeding industry, but doing so would increase the risk of commingling with the food supply. Several tons of these by-products are produced per acre of pharma crop, and depending on the type of crop being grown, residue left in fields could also pose environmental hazards to wildlife.

Limited farmer initiative. Under conventional production systems, farmers earn income by providing land, labor, capital, and management. With pharma crops on the other hand, the pharma crop firm will provide detailed management specifications that must be met by the producer. The pharma crop firm will also almost certainly provide quality control personnel to ensure these requirements are met. Thus, the individual farmer's ability to use personal initiative and creativity in managing the crop will likely be minimal.

Even though pharma crops could be worth several hundred thousand dollars or more per acre, farmers should not expect to see substantially greater profits than with conventional crops unless the risks are greater as well.

Production risks. The pharma crop company or pharmaceutical firm owning the crop through its entire production process would be expected to absorb the production risks normally faced by farmers (e.g., disease, insects, hail, drought, flooding). However, it is not certain that pharma crop firms will in fact bear all of these risks. If some or all are passed back to the contracting farmer, he or she could face substantially higher costs than anticipated.

Overall farmer compensation. Even though pharma crops could be worth several hundred

thousand dollars or more per acre, farmers should not expect to see substantially greater profits than with conventional crops unless the risks are greater as well. Economic principles dictate that the farmer will be compensated based on normal charges for the work required to produce the crop and keep it isolated. Additional compensation would be expected if the farmer faces an unusual risk of liabilities stemming from possible contamination of crops planted on the same land at a later date or possible contamination of neighbors' land and/or commercial food or feed supplies. If the risk is great, the compensation should be great as well.

A recent study of production costs for a corn-based pharmaceutical by Iowa State University's Plant Science Center appears to support these conclusions. The study found that the costs associated with producing pharma corn amounted to about six percent of total annual operating costs for producing the pharmaceutical.[44] This represents a 45 percent increase above the costs for commodity corn. The higher cost was due to the extra work and expenditures needed to maintain complete isolation of the corn from neighboring fields and prevent commingling in commercial channels. After allowing for these extra costs, only a small part of the corn's value would be expected to go to the farmer.

International competition. Returns to pharmaceutical producers will be determined in a global setting. The technology is easily transferable across national boundaries, and if Argentina, Brazil, or Canada can produce pharma crops at a lower cost than the United States, one would expect production to move there. Thus, if U.S. farmers are compensated at rates above the international average for services performed and land provided, that will likely encourage production elsewhere.

44 Evangelista, R., A. Kusnadi, J. Howard, and Z. Nikolov. 1998. Process and economic evaluation of the extraction and purification of recombinant β-glucuronidase from transgenic corn. *Biotechnology Progress* 14:607–614.

Part 6

Who Is Liable for Contamination?

A key question for farmers growing pharma crops, and even those growing non-pharma versions of the same crops, is, "Who is liable if the pharma crop becomes commingled with commercial supplies?" Who is responsible for the economic damages, for example, if pollen drifts from a field of pharma corn to a neighbor's commercial corn even though all regulations and company management procedures were followed exactly? Who is responsible if a pharma crop variety is found in commercial food crops because wildlife or flooding carried its seeds to a different location, or because pharma plants grew among commercial crops, or because of some other uncontrolled factor?

Some of these situations have already occurred, despite the fact that pharma crop production has been minimal to date.[45] Fortunately, the problems were discovered before retail food and feed supplies could be contaminated—and serious economic damage incurred. The costs associated with contamination of the retail food/feed supply could include compensation for the following direct and indirect expenses:

- lost export earnings
- retrieval of contaminated grain
- reduced value of non-pharma grain or oilseeds
- recall of products from grocery shelves
- cleaning of grain elevators and processing plants
- testing expenses
- added transportation and handling costs
- lost storage and merchandising income
- long-term market loss resulting from increased foreign competition
- rejected supplies of meat, dairy products, and eggs
- animal or human illnesses

Additional costs could result from the cross-pollination of seed fields and the subsequent contamination of non-pharma crop seed supplies. Such contamination would deal a severe blow to domestic and foreign consumer confidence in the safety of the U.S. food system and food regulatory processes.[46]

One might expect these risks to be borne by the pharma crop or pharmaceutical companies that own the crop genetics, but this may not always be the case. Given the currently murky legal landscape, pharma crop or pharmaceutical firms may attempt to shift some of the liability to farmers through contracts. To the extent farmers are exposed to these risks, they ought to be compensated adequately for the risks as well as for their efforts in producing the crop and the use of their land.

Given the currently murky legal landscape, pharma crop or pharmaceutical firms may attempt to shift some of the liability to farmers through contracts.

45 Fox, J. 2003. Puzzling industry response to Prodigene fiasco. *Nature Biotechnology* 21(1):3–4.

46 For further discussion of these risks, see: Andow et al. (*A Growing Concern*) and Freese (*Manufacturing Drugs and Chemicals in Crops*).

Part 7

Risk Reduction Strategies

Various new approaches are being researched as possible ways of reducing the risk of food, seed, and feed commingling with pharma crops. Purdue University is working with a pharma crop firm on the experimental production of corn and other pharma crops in an underground limestone quarry, where the risk of cross-pollination would be eliminated.[47]

Biological approaches to limiting pharma gene transfer include producing pharma corn with male-sterile pollen, covering the corn's tassels with bags, or removing the tassels altogether. If successful, these approaches may substantially reduce the risk of commingling and the costs of maintaining complete separation from the food production and marketing system. However, these techniques are known to provide less than perfect control of pollen production and drift.

Researchers and pharma crop firms may also consider producing pharmaceuticals in non-food crops such as tobacco. Producing pharma tobacco in the Corn Belt could be one way of eliminating risk to the food sector while preserving economic development benefits for the Midwest.

47 Cutraro, J. 2005. Underground crops could be future of "pharming". Purdue University Extension Information Service, April 20. On the Purdue University website at *http://news.uns.purdue.edu/html4ever/2005/050420.Ausenbaugh.mine.html*.

Part 8

Implications for Rural Economic Development

Many rural states and communities anticipate that pharma crops will generate economic benefits in the form of high-paying jobs in biopharmaceutical research and processing. A Pew Initiative on Food and Biotechnology survey in 2004 and early 2005 found 58 pieces of proposed legislation at the state level designed to encourage biotechnology research and education (often by providing tax incentives to biotech companies).[48] Some of these measures were directed specifically toward the pharma crop industry.

Along with tax incentives, states and communities are offering pharma crop companies assistance with infrastructure improvements, start-up loans, research parks, joint university/private-sector research projects, and technology incubators. Interest in pharma crops as a vehicle for rural economic development is especially strong in the Midwest due to its abundant cropland but lagging local economies and job markets.

A good example of this interest is a current effort to develop pharma crop production in a 15-county region of northwest Missouri.[49] About 9,800 acres of pharma rice and barley may eventually be grown in the area, amounting to 0.57 percent of the 1,734,000 acres currently devoted to corn, soybeans, and other grains.

This project is being developed in part by Northwest Missouri State University and Ventria Bioscience, a California pharma crop firm relocating to Missouri.[50] [*Author's note: In late November 2005, as this report was nearing publication, it appeared that the northwest Missouri project was in jeopardy as a result of funding problems and Ventria Bioscience's announcement that it is reconsidering moving its headquarters to Missouri.*[51]] The university, with assistance from the governor and state legislature, has broken ground for a $23 million pharma crops research center that may house several biopharmaceutical firms.[52] And Ventria Bioscience anticipates that 25,000 acres of cropland may eventually be needed for its pharma crops business—about 1.4 percent of the area's total cropland.

48 Pew Initiative on Food and Biotechnology (PIFB). 2005. Pew Initiative finds state legislators focused on "next generation" products. On the PIFB website at *http://pewagbiotech.org/newsroom/releases/052605.php3*.

49 Drabenstott, M. 2005. Presentation at the Iowa State University Agricultural Policy Summit. July 7–9.

Drabenstott, M. 2005. New partners for a new Iowa economy. Speech at Spring Conference of Professional Developers of Iowa. May 26.

50 Drabenstott. Presentation at Iowa State University Agricultural Policy Summit.

Drabenstott. New partners for a new Iowa economy.

Maryville Daily Forum. 2005. Governor promotes biosciences during Center of Excellence groundbreaking. September 25. On the *Maryville Daily Forum* website at *http://www.marysvilledailyforum.com/articles/2005/09/25/news/news1.txt*.

51 Kelsey, M. 2005. Biosciences funding in jeopardy; Ventria looking at other options. *Maryville Daily Forum*, November 16. On the *Maryville Daily Forum* website at *http://www.marysvilledailyforum.com/articles/2005/11/15/news/news1.txt.*

52 Kelsey, M. 2004. "Down to the wire" deal brings biotech company to northwest. *Maryville Daily Forum*, November 19. On the GM Watch website at *http://www.gmwatch.org/print-archive2.asp?arcid=4643*.

Maryville Daily Forum. Governor promotes biosciences.

Young, V. 2005. Missouri funds for agricultural pharmaceutical center draw fire. *St. Louis Post-Dispatch*, May 4. On the GM Watch website at *http://www.gmwatch.org/archive2.asp?arcid=5203.*

The company and the university anticipate that their research will generate substantial economic development benefits, including payments to the local farmers who raise the pharma crops. Most of the returns, in fact, are expected to flow into the local economy, generating additional income through increased demand in related industries and increased personal consumption.

A number of agricultural leaders believe the pharma crop industry has similar long-term economic potential to that of California's Silicon Valley.[53] Whether this vision proves true will depend heavily on the number of firms and research contracts that emerge in the next few years and where this work will be performed. It is doubtful that economic development based solely on returns to farmers raising pharma crops would be great enough to generate a level of activity even close to that of Silicon Valley. For that to happen, new research institutions and pharmaceutical processing firms would need to locate their operations near the sites of pharma crop production.

ARE STATE INCENTIVES NEEDED?

While most long-term projections for the pharma crop industry's economic performance are extremely positive, a case can be made for start-up assistance in situations where new, under-capitalized pharmaceutical firms have a promising product. One New Jersey program allows early-stage firms to sell operating losses to profitable firms for cash, and the state also offers relocation assistance and job-creation grants.[54]

Unless such incentives are carefully applied, however, public costs can be high and returns uncertain. Individual states should decide whether assistance of this type is warranted for pharma crops on a case-by-case basis, after a careful assessment of the potential benefits and costs.

Unless such incentives are carefully applied, public costs can be high and returns uncertain.

ARE STATE INCENTIVES EXCESSIVE?

In the last few years, a number of states have taken steps that they hope will not only attract individual firms, but also make their state the pharma crop "capital of the world." Many have created research parks adjacent to state universities, for example.[55] Other state incentives have included business incubators for emerging technology, income tax credits, below-market renting or sale of land and research buildings, and even outright donations, property tax abatements, and subsidizing of needed infrastructure.[56]

As an example of the potential cost of such incentives, the state of Florida and Palm Beach County are reportedly investing more than $500 million in a research center meant to attract a major San Diego-based biotech firm to the state.[57] The Biotechnology Industry Organization indicated in the spring of 2004 that at least 29 states have formal plans to attract biotechnology firms.[58] Though these initiatives

53 Iowa Congressional Delegation. 2005. Discussion of Iowa congressional delegation on their agricultural policy priorities during the Iowa State University Agricultural Policy Summit. July 6.

54 Hart, D. 2005. Final word: New Jersey: biotech's ideal lab location. *BioPharm International*, July 1. On the *BioPharm International* website at *http://www.biopharminternational.com/biopharm/article/articleDetail.jsp?id=170508*.

55 For the number of states with university research parks, see: Link, A. 2003. Real numbers: university-related research parks. *Issues in Science and Technology Online*, Fall. On the *Issues in Science and Technology Online* website at *http://www.issues.org/issues/20.1/realnumbers.html*.

56 Elias, P. 2004. States, cities court biotech, but is it worth it? Associated Press, June 9. On the GM Watch website at *http://www.gmwatch.org/archive2.asp?arcid=3772*.

57 Ibid.

58 Ibid.

do not target pharma crops specifically, pharma crops are seen as a significant part of the biotechnology industry.

While the rush by individual states to attract this industry is understandable, their intense competition has the potential to result in overlapping incentives and unnecessary duplication of investment. It is therefore important to ask whether this level of government assistance is justified in the case of pharma crops.

In a few cases, the companies being courted are large, highly capitalized firms that can play one state against another to their own economic advantage. Extensive subsidies for such firms may well be unjustified. In many cases, however, pharma crop firms are relatively small.[59] The fact that pharma crop firms also retain the patents from joint public-private research could be considered an additional subsidy, raising concerns about the integrity and independence of basic research.[60] Some take the more positive view that competition among states will likely lead to desirable regional specialization.[61]

HOW MANY ACRES WILL BE NEEDED?

This is an important question in determining the impact of pharma crop production on rural economic development, especially in relation to payments to farmers. While the answer is unknown, pharma crops will (for the foreseeable future) likely account for only a small portion of the total U.S. acreage planted with a given crop.

For example, one study indicates that approximately 10,000 acres of transgenic tobacco would supply the *world's* needs for biopharmaceutically produced human serum albumin.[62] This is a minuscule amount of cropland when compared with the approximately 231 million acres U.S. farmers devote to wheat, rice, corn, other feed grains, and soybeans. With a wide variety of pharma crops expected to be developed in the next 10 to 15 years, a more substantial amount of land might ultimately be needed—perhaps a few million acres. Assuming successful emergence and growth of the industry, this would still represent a small percentage of the total U.S. acreage used for food and feed production.

Pharma crops will (for the foreseeable future) likely account for only a small portion of the total U.S. acreage planted with a given crop.

59 Freese and Caplan. *Plant-Made Pharmaceuticals.*

60 Bok, D. 2003. *Universities in the Marketplace: The Commercialization of Higher Education* (Princeton University Press).

Harl, N. 2003. Relevance of the land grant mission in the twenty-first century. Presented at Kansas State University, November 18. On the Iowa State University website at *http://www.econ.iastate.edu/faculty/harl/RelevanceoftheLandGrantMission.pdf*.

Shelley, M., W. Woodman, B. Reichel, and P. Lasley. 1990. Economic development and public policy: what is the role for biotechnology? In *Biotechnology: Assessing Social Impacts and Policy Implications*, edited by D.J. Webber (New York: Greenwood Press).

61 Denny, B. 1982. The high-technology fix. *Science* 217.

62 Kostandini et al. Potential impacts of pharmaceutical uses.

Concerns in the Rice and Flax Industries

Protecting the safety and integrity of food supplies from pharma crops is an important issue for the rice and flax industries.

Rice Industry

Ventria Bioscience, a pharma crop firm relocating to northwest Missouri, has developed pharma rice containing human genes that trigger production of human lactoferrin and lysozyme. According to Ventria, these substances (normally found in human milk, saliva, and tears) could be used in a wide variety of potential products, including those that help prevent diarrhea-related infant deaths in developing nations.[63]

Ventria's applications to produce these products in California and Missouri have generated heated debate.[64] Both states are significant producers of rice for domestic food and export markets. Local rice growers are concerned about possible accidental commingling of pharma rice with conventional seed and/or commercial production, as well as possible cross-pollination with wild varieties that are weeds, and other potentially negative environmental impacts. Commingling could result in lost markets, both domestically and abroad.

Consumers in several important foreign rice markets have much stronger negative attitudes toward genetically modified food than U.S. consumers, and many foreign food labeling programs that identify genetically modified foods represent an existing barrier to sales of U.S. pharma rice.[65] If pharma rice were commingled with commercial rice seed, sales could suffer even more.

After being rejected by California, Ventria proposed planting its pharma rice in southeast Missouri, but the nation's largest brewer, Anheuser-Busch, reportedly indicated it would not buy rice from this part of the state if pharma rice were grown there.[66] Ventria then applied for and received approval to produce pharma rice on 75 acres in North Carolina, a state with essentially no commercial rice production. The approved location, however, was less than a mile from a state- and federally operated rice seedling and quarantine nursery, raising concerns that the pharma rice might be accidentally commingled with seed at the nursery and distributed to rice-growing areas in other states.[67] Now, Ventria reportedly plans to plant pharma rice in northwest Missouri next year.

Further complicating the pharma rice issue are reports that Agennix, a Texas firm, has patents for producing the same or a nearly identical product by conventional fermentation methods. Agennix claims that its production costs are about the same as those estimated for pharma rice.[68]

Flax Industry

Flax is another pharma crop generating strong negative reactions among farmers, processors, and some consumer groups. A company named Agragen has leased space in a University of North Dakota research park and reportedly has plans for a variety of pharma flax that will produce medicines for trauma patients who need a blood transfusion.[69] Conventional and organic flax farmers are concerned that accidental commingling of pharma flax with the food crop—a distinct possibility because flax pollen is difficult to control—may jeopardize a newly emerging growth market for their product.[70] Agragen reportedly plans to delay development of its product until farmers and regulators agree that all necessary safeguards for preventing accidental commingling have been met.[71]

The examples of these two nascent pharma crop industries illustrate the challenges of producing a medical drug in an open, outdoor production system. Participants in the crop production, seed, and food industries are all likely to express concerns about the risk to their businesses and the food supply, as well as their liability for damages that could result from accidental commingling.

63 Ventria Bioscience. No date. Products: lactoferrin and lysozyme. On the Ventria Bioscience website at *http://www.ventria.com/products*.

64 Rice, D. 2005. Controversy in North Carolina: genetically modified rice in eastern North Carolina is setting off a whirlwind of criticism and concern. *Winston Salem Journal,* July 10. On the *Winston Salem Journal* website at *http://www.journalnow.com/servlet/Satellite?pagename=WSJ%2FMGArticle%2FWSJ_BasicArticle&c=MGArticle&cid=1031783753130&path=&s*.

65 For foreign market reactions and other issues involved, see: Wisner, R. 2004. Round-Up® Ready spring wheat: its potential short-term impacts on U.S. wheat export markets and prices. *ECON Staff Report,* July 1. On the Iowa State University website at *http://www.econ.iastate.edu/faculty/wisner/gmowheatreportMarch200311.pdf*.

66 Bennett, D. 2005. Anheuser Busch may refuse Bootheel rice. *Delta Farm Press*, April 11. On the *Delta Farm Press* website at *http://deltafarmpress.com/news/050411-busch-refusal.*

67 Rice. Controversy in North Carolina.

68 Cole. Competition grows in the biopharming market.

69 Comments by Cummins, J. 2005. Farmers & oilseed industry oppose flax crops laced with pharmaceutical drugs. June 15. On the Organic Consumers Association website at *http://www.organicconsumers.org/ge/flax061605.cfm*.

70 Associated Press. 2005. Growers oppose drugs made of flax. *Billings Gazette*, June 15. On the *Billings Gazette* website at *http://www.billingsgazette.com/index.php?id=1&display=rednews/2005/06/15/bui ld/state/50-flax-drugs.inc*.

71 Ibid.

Part 9
Conclusions

Many researchers and industry observers view pharma crops as a way of opening the door to a much brighter economic future for the American Midwest, where most of the nation's feed and food grains are produced. If the optimistic projections of these proponents materialize, rice-growing regions and pharmaceutical consumers also stand to benefit as a result of the much lower costs of producing pharmaceuticals from crops compared with conventional manufacturing processes, the increased ease in expanding production capacity when needed, and a potentially wider range of pharmaceuticals that are better equipped to treat specific illnesses.

However, it should be recognized that current cost savings are only projections, since pharma crop medical drugs have yet to be commercialized. There are several important factors that could push costs significantly above current projections.

Projected cost savings and hopes for new, more effective drugs are expected to be the driving forces behind pharma crop industry growth, but no pharma crop drugs have been approved by the FDA after approximately 15 years of research. With the food industry and other groups calling for a new and potentially expensive production and marketing system to prevent pharma crops from commingling with food supplies, projected cost savings and potential consumer benefits should be viewed as highly tentative.

As for the farmers who may grow pharma crops, their returns will likely be determined in a setting of global competition (since the production technology is transferable across national boundaries). So, despite the expected high value of pharma crops, farmers will likely be compensated based on the prevailing rates for producing non-pharma crops, plus a premium to cover any added costs and risks assumed by the farmer. These risks could be significant if safeguards are not built into contractual arrangements with pharma crop firms. Finally, the total land area required for pharma crops will, in all likelihood, represent only a small percentage of U.S. cropland for the foreseeable future—suggesting that the number of farmers involved will also be small.

For consumers, farmers, and rural communities, the net benefits of producing pharma crops will depend heavily on the costs of ensuring virtually zero risk of commingling with food and feed supplies.

For consumers, farmers, and rural communities, the net benefits of producing pharma crops will depend heavily on the costs of ensuring virtually zero risk of commingling with food and feed supplies. Food retailers, processors, manufacturers, the National Research Council, and others have declared that pharmaceuticals should not be produced from food crops unless virtually total isolation from food supplies can be achieved. The costs of doing so are unknown, but scientists who have carefully examined the current production and marketing system and

potential avenues of commingling conclude that a major system redesign will be needed to ensure virtually zero risk of contaminating food supplies with pharma crops.[72]

Without such a redesign, the food and animal feed industries, pharmaceutical firms, and farmers —regardless of whether they raise pharma crops, non-pharma crops, or livestock—could all be at risk of economic losses if pharma crops become commingled with another farmer's crop or with feed, food, or seed supplies. A damaging episode of commingling could also have a long-term impact on U.S. and foreign consumer confidence in the integrity and safety of U.S. food production and regulatory systems.

Pat Byrne of Colorado State University indicates that four hurdles will need to be overcome before pharma crops can succeed commercially.[73] First, drug safety and efficacy must be demonstrated. Second, appropriate confinement conditions for the crop must be determined. Third, production costs (especially purification costs) must be reduced. Finally, consumers must accept this new source of pharmaceuticals.

Pharma crops will likely provide opportunities for a small number of growers. Whether these crops prove to be a bonanza for a few rural areas will depend primarily on the number of research and pharmaceutical processing firms willing to locate in the crop-producing area and whether the four conditions identified by Byrne are met.

72 Andow et al. *A Growing Concern.*

73 Byrne, P. 2003. Bio-pharming from the ground up. *Agronomy News* 23(3).

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