

# **Oregon Biopharmaceutical Committee: Policy Statement & Recommendations October 30, 2006**

## **Background**

The Oregon Department of Agriculture (ODA) and Department of Human Services (DHS), charged by the Governor and the Senate, convened a Biopharmaceutical Ad Hoc Committee, in November 2005. The Committee's goal was to develop a consensus policy recommendation to the Governor for the possibility of future biopharmaceuticals to be produced in Oregon. Biopharmaceuticals or biopharm refers to the use of plants that have been modified via recombinant DNA processes (i.e. "genetic engineering") to produce medicinal compounds such as vaccines and enzymes. The Committee, chaired by Jim Rue and vice chaired by Keith Harcourt, had ten standing members including three members from the State Board of Agriculture, three members from the Public Health Advisory Board, two scientists from Oregon public universities and two non-voting ex-officio members, the director of the Department of Agriculture and the administrator for the Office of Environmental Public Health.

The committee convened in November 2005 and met a total of 11 times through October 2006. During the first seven meetings, the committee heard detailed oral and/or written testimony from 12 academic and national institute scientists, state and federal regulatory officials, an economics consultant, and a representative of a non-governmental organization.<sup>1</sup> The speakers had diverse expertise and expressed a wide variety of views on the benefits and risks of biopharm crops. An opportunity for public comment was included on the agenda at each meeting, in addition to public notification for meeting dates and locations. Public input on a draft of this report was solicited during a 30-day public comment period.

The committee considered a number of formal recommendation options for the Governor of Oregon, ranging from a complete ban of biopharm crops to unqualified endorsement. The committee chose "endorsement, moderate scope" to indicate that it supports wisely chosen and carefully studied applications of biopharm technology in Oregon. The "endorsement" of biopharming was based on the recognition that this technology has the potential to prevent or treat disease of public health significance. The "moderate scope" choice option, however, reflected the committee's interest in substantial State of Oregon involvement in federal regulatory decisions about where and how biopharm crops may be grown in Oregon; how specific farmers, products, and markets for State products may be impacted; substantial concerns over safety and/or legal risks should biopharm versions of food or feed crops be grown outdoors; limited public information on the benefits and

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<sup>1</sup> The presenters were Joseph Cortright, Imprensa Consulting; Eric Flamm, FDA; Dr. Daniel Goldstein, MD, Monsanto; Prof. Richard Goodman, PhD, University of Nebraska; Douglas Gurian-Sherman, PhD, Center for Food Safety; Neil Hoffmann, PhD, USDA-BRS; Prof. Paul Jepson, Toxicology, Oregon State University; Dean Metcalfe, PhD, National Institute for Allergy & Infectious Disease, NIH; Prof. Carol Mallory-Smith, Crop Science, Oregon State University; Gary Marchant, Esq., Arizona State University; David Nunekamp, California Dept. Food and Ag.

safety of specific products; and because of the complexity of this technology, the importance of communication to the public about benefits and risks. “Endorsement, moderate scope” does not imply that the committee categorically endorses biopharmaceutical products in food or feed crops nor does it categorically endorse outdoor field trials.

The committee also identified as a key issue the lack of federal standards with respect to the requirement for, and scope of early food safety evaluations that address the risk of unintended spread. These are critical to help characterize the public health and legal risks during field research and commercial production.

### **Proceedings**

The committee considered in depth the contentious issue of the outdoor use of food or feed crops for biopharm products<sup>2</sup>. In some cases, food or feed crops are expected to be the best means for production because of advantages in storage, stability, consistency, purity, yield, rapid scalability to meet highly diverse and customized medical needs, and changing demand (e.g., in response to disease epidemics). The economic efficiencies from use of field-grown food and feed crops could also be substantial and enabling in cases where large scale and low cost production are critical (e.g., for an animal vaccine against avian flu). However, there are potential adverse effects for human health, the environment and the economy if biopharmaceutical products are released during outdoor field trails or commercial use.

The committee concluded that biopharm production in food and feed crops should be reserved for products that have been through at least an initial federal safety assessment, such as the Early Food Safety Evaluation, currently recommended by Food and Drug Administration<sup>3</sup> and by the Grocery Manufacturers Association<sup>4</sup>, prior to field trials and commercial use. This safety assessment should include consideration of risks to vulnerable populations.

The committee also sees a critical need for development of federal policies to clarify the process and scope of Early Food Safety Evaluations, and the associated legal risks to businesses and research institutions from unintentional presence that might occur during research and commercial use. The committee therefore urges the FDA, in coordination with USDA, to develop clear standards for designation of safety categories, and thus of tolerances for unintentional presence. Without such clarifications, the legal risks to

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<sup>2</sup> For the purposes of this report “food and feed crops” of concern include any crops grown for human food or animal feed including sexually compatible species or varieties that are being considered for biopharming in Oregon.

<sup>3</sup> Food and Drug Administration Guidance for Industry: Drugs, Biologics and Medical Devices Derived from Bioengineered Plants for Use in Animals and Humans; accessed at <http://www.fda.gov/OHRMS/DOCKETS/98fr/02d-0324-gdl0001.pdf> on July 26, 2006.

<sup>4</sup> Statement submitted as public testimony in response to committee draft recommendations [http://www.oregon.gov/ODA/PLANT/bp\\_public\\_comment.shtml#September 22,2006](http://www.oregon.gov/ODA/PLANT/bp_public_comment.shtml#September 22,2006), viewed October 24, 2006.

industry might effectively preclude most forms of biopharm product development—including for products that might provide both high benefits and safety.

Oregon agencies should closely follow the development of federal policies that impact biopharm applications and projects that might occur in Oregon.

Because of the potential risks to human health and the possibility of serious economic harm, the committee recommends that production in food or feed crops should occur only in cases where similar results and efficiencies could not be obtained in alternative non-food, non-feed crops. Unless biopharm products have been categorized by the FDA to be highly safe in the case of accidental consumption, production in food and feed crops should require that very strict containment procedures are in place (examples include cultivation in secured greenhouses; use of highly sterile host varieties; large isolation distances from interfertile species; growth out of phenological synchrony with interfertile relatives; use of separate farm equipment; and strict monitoring, quality assurance and reporting, including full reporting of the distribution and disposition of biopharm materials). These and other safeguards are reflected in the evolving requirements for a permit for field trials of biopharm crops from United States Department of Agriculture's Animal and Plant Health Inspection Service (APHIS).

The committee recognizes that absolute containment of biopharm crops, whether grown in a secured greenhouse or in the field, is impossible to attain. This is a consequence of human error, theft, and movement of seeds and pollen via wind, water, or biological agents. This type of release would be of most concern for products with direct oral activity, resistance to digestion in the gut, potential for allergenicity, and potential to interbreed with related crops. The committee also recognizes that zero risk for any endeavor cannot be assured; rather, a practical and significant goal is the mitigation of risk to levels at which adverse or unintended effects are negligible. We think the recommendations proposed below will achieve this goal.

Finally, the committee recognizes the importance of on-going technological development and advancement that will allow Oregon agriculture, including both production and processing, to continue to be competitive in a global economy. While it is important to provide safeguards in any technology development, it is also important that laws and rules are not so restrictive that they discourage companies from investing in Oregon. In particular, the committee discourages regulations that would directly inhibit laboratory or contained greenhouse research with biopharm crops or that would repel scientists or companies from doing such research in Oregon. The State of Oregon has a policy that encourages investment in new technology and has already created and invested in one signature research center, Oregon Nanoscience and Microtechnologies Institute, and is in the process of identifying and funding two new signature research centers. The advancement of new technology also requires investment in research and development activities, which is fostered by the environment of a state that welcomes these activities.

Biopharming is certainly a new and potentially valuable technology, but the committee recognizes the importance of incorporating public health, business, and environmental safeguards during its development.

## **Conclusions**

The committee concluded that a case-by-case regulatory approach, rather than a wholesale prescriptive or prohibitory approach, is warranted because of the diversity in safety and benefits from different biopharm products. The committee therefore neither endorses nor rejects all forms of biopharm technology including production in food and feed crops. Rather, required and meaningful collaboration and oversight by the State of Oregon, with respect to state-specific issues, is critical to the sustained health of the people, economy and environment of Oregon. Therefore, the Oregon biopharmaceutical committee recommends the following as appropriate state policy:

- Encourage development of new agriculture and related technology in Oregon, including biopharmaceutical production, while protecting and maintaining public health, economic vitality, the environment, and Oregon agriculture. Oregon has several attributes that may be conducive for biopharmaceutical research and production including a long and mild growing season, large greenhouse complexes, highly diverse landscapes that can be segregated over large distances, modern medical and technological infrastructure, as well as extensive expertise in agricultural and horticultural sciences. As the State of Oregon continues to invest in signature research centers and encourage technological development, biopharmaceutical production and the related area of bioindustrial/bioenergy production with genetically engineered crops, should be considered as an area of investigation. The following additional recommendations are designed to ensure that technology of this kind is developed in a manner safe for humans, the environment, and agricultural industries.
- Collaborate with the United States Department of Agriculture's Biotechnology Regulatory Services (BRS) to review all applications to grow biopharmaceuticals in Oregon. The intent of collaboration is not to duplicate the efforts of BRS, rather to allow the State to provide input on Oregon-specific issues and requirements.
- Formalize this collaboration between BRS and the State of Oregon through a memorandum of understanding (MOU) or contractual agreement. Specifically, any collaboration should contain at least the following provisions:
- As part of a state-federal cooperative review, information pertaining to the location, crop used, anticipated planting date, intended plant made pharmaceutical, applicant's analysis of risks to human health and the environment, and FDA's preliminary opinion on product safety for biopharm food and feed crops be disclosed to designated State officials (including officials at the

Oregon Board of Pharmacy<sup>5</sup>) before a trial permit is granted. To be effective, appropriate authority should be granted to the designated state officials to maintain the level of confidentiality required to protect the confidential business information<sup>6</sup> submitted as part of the application, review, monitoring and reporting process.

- All required protocols and tests conducted for bio-containment (such as sterilization techniques) and public health (such as allergenicity tests) shall be disclosed to designated state officials before a permit is granted. All monitoring, reporting and enforcement responsibilities, activities and timelines shall be disclosed to designated officials as well. State officials shall conduct a formal review of each application and this review shall include relevant expert opinion on the environmental and human risks and benefits.
- Authorize the Directors of Agriculture and Public Health to modify, restrict or veto a requested permit for biopharm field trials in the State if deemed appropriate. Both Directors of Agriculture and Public Health must approve a permit, whether or not restricted or modified, before field trials are allowed to proceed.
- The committee recommends the use of non-food, non-feed crops for biopharmaceutical applications intended for outdoor environments over food and feed crops. If food crops are proposed, the committee recommends that secure greenhouse production shall be utilized if possible. Any application for the outdoor growth of biopharmaceuticals using food or feed crops must include a detailed justification of why outdoor planting is considered desirable and safe.
- The committee strongly recommends that the state require demonstration of adequate insurance to cover potential damages. Applicants shall submit a monitoring plan that details surveillance protocols, testing methodologies, and quality assurance plans to assess if inadvertent release or unintentional presence above authorized levels has occurred. In addition, require an emergency response plan detailing mitigation procedures in the event of accidental release of biopharm material.
- Ensure the Directors of Agriculture and Public Health have all necessary statutory authority to implement a state permit review and oversight system funded by the permit applicants. A state application fee should be charged to cover the cost of staff time, consultation with experts, and other resource needs.

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<sup>5</sup> Oregon Revised Statute 689.155 authorizes the Board of Pharmacy to register and inspect any organization that is established in Oregon for the purpose of manufacturing pharmaceuticals, which includes preparation and propagation either directly or indirectly.

<sup>6</sup> The issue of federal confidential business information laws and state public disclosure laws in agricultural biotechnology was recently addressed by the Pew Initiative on Food and Biotechnology (Agricultural Biotechnology Information Disclosure: Accommodating Conflicting Interests Within Public Access Norms, 2006); accessed on August 17, 2006 at <http://pewagbiotech.org/events/1214/>

- Establish a science-based and health protective public communications plan for biopharmaceuticals and related biotechnologies that is both general to the subject and specific for any applications received. The communications plan should address, among other issues, information on the benefits and risks of biopharmaceutical and genetic engineering technologies; the process for public notification if a permit application is under consideration; and the establishment of communication channels for scientific opinions, public comment, meetings and announcements for specific permits.