



August 20, 2004

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Dr. Paul Gilman
Assistant Administrator
Office of Research and Development
U.S. Environmental Protection Agency
Washington, DC 20460

Dr. Larry Reiter
Director, NHEERL
U.S. Environmental Protection
Agency
Research Triangle Park, NC 27711

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Re: ORD Biotechnology Program Framework

Dear Drs. Gilman and Reiter:

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This is a letter report from the Board of Scientific Counselors (BOSC) reviewing the EPA ORD Biotechnology Research Program. An overview of the Program was presented by Dr. Reiter to the BOSC Executive Committee on May 13-14, 2004, at their meeting in Research Triangle Park, NC. The BOSC had been briefed previously on ORD biotechnology research during a BOSC Executive Committee meeting in Washington, DC, on September 23-24, 2002.

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The Framework document on the ORD Biotechnology Research Program was provided to members of the BOSC Ad Hoc Subcommittee on Biotechnology in the spring of 2004, and other Executive Committee members who requested it. The Subcommittee consisted of Jerry Schnoor, Chair, and members James H. Johnson, Jr., James Clark, George Daston, Rogene Henderson, and Gary Saylor. Dr. Daston succeeded as Subcommittee Chair upon Dr. Schnoor's retirement from the BOSC. Dr. Schnoor made notes of Executive Committee members' comments during the meeting on May 13, and wrote a draft letter report, which was circulated to members of the Subcommittee at the end of June. Subcommittee members made revisions to the initial draft, and these suggestions were incorporated into the final letter report by James Johnson, Chair of the BOSC. The letter report then was approved by the entire BOSC Executive Committee.

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The BOSC Subcommittee understands that EPA's role in the area of genetically modified crops is largely defined by statutory jurisdictional authority under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA). The Act requires that EPA ensures pesticides will not pose unreasonable risk to human health or the environment, so plant incorporated protectorants (PIPs), which serve in lieu of pesticide applications, are properly within EPA's regulatory control, and ORD seeks to provide research relevant to this mission of the Agency. The five areas

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of research that ORD has identified (risk to human health, risk to non-target organisms, the potential for gene flow, and insect resistance and management plans) are important and proper. The BOSC believes that the greatest emphasis in the ORD research portfolio at the present time should address genetically modified crops that contain genes for production of *Bacillus thuringiensis* toxin (Bt) because these could conceivably cause all four effects of concern: allergenicity, resistance in target populations, risks to non-target organisms, and conveyance of a selective advantage to cross-hybridized wild-type plants.

Human allergenicity has been addressed by ORD as a risk to human health, and the BOSC recommends that not all research in this area be related to digestibility. Respiratory allergenicity also should be included, and SAR-based approaches should be considered such as epitope mapping. However, developing an animal model (mouse model) for identifying mechanisms of allergenicity is believed to be important by the BOSC, as stated in the Framework document. In addition, ORD should consider how its approach on BT-products can be extrapolated to other GM crops that may be developed in the future, such as herbicide-resistant spring wheat and others. Collaboration that already has been established with NIAID and NIEHS, in matters of human allergenicity is encouraged, and use of the pharmaceutical models of FDA for safety testing (levels 1, 2, and 3) may prove helpful.

Risks to non-target organisms and the environment remain as one of the largest potential problems of GM crops in the minds of the public. The findings so far by EPA ORD, that Bt-proteins have narrow spectrum insecticidal activity and that no serious effects are anticipated on non-target organisms, seem justified, but ORD should be ever-vigilant to the possibility of subtle, long-term effects that are difficult to measure without an extensive monitoring program. The BOSC agrees that monitoring a few key indicator organisms and habitats over a long period of time is the proper approach to this problem. The BOSC further recommends that the ORD Biotechnology program include the recent ecological field studies of GM crops in the United Kingdom in their research database. These studies indicated that ecological diversity could either increase or decrease due to the use of GM crops, depending on the crops, non-target organisms, and cropping practices considered. It would be prudent to learn whatever can be gleaned from these studies and not to reproduce them. Also, the Agency should track closely the overall use of pesticides (both herbicides and insecticides) on GM-cropland in the United States, although the BOSC realizes that this responsibility is not a research activity.

The potential for gene flow between GM crops and wild-type plants is recognized by the BOSC as a consequence of all hybrid crops from conventional plant-breeding programs, as well as from genetically modified crops. As stated by ORD, the issue is whether cross-hybridization with wild-type plants (such as Bt-corn with wild maize in Mexico) is a serious consequence and whether it conveys

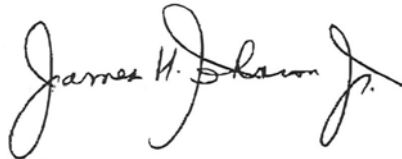
a selective advantage to crops in the wild. The Framework document outlines a good program to study gene flow from transgenic plants to non-crop hybrids using genomic techniques to confirm expression of transgenes and to evaluate the fitness and ecological effects on crops and non-crop hybrids. Canola and creeping bentgrass are model plants being utilized. Gene introgression (retention of the genetic characteristics in subsequent generations of the non-crop hybrids) and gene expression after 3-5 years in mesocosms is a good approach for studying these important ecological questions.

The insect resistance and management plan of ORD is an important component in the research portfolio of its biotechnology program. The idea to work with NASA on remote sensing of crops for risk management is excellent. The provision for creation of refuges is logical, but there should be some social/behavioral research considered that measures how and under what circumstances farmers actually perform the recommended practices. The rapid PCR screens and modeling strategy to assess resistance management is a good approach by ORD, but what are the markers being used to detect insect resistance? In the high dose, structured refuge resistance management research, the BOSC recommends that a population genetics study of resistance genes in root worm populations under Bt-crops be considered. However, because there are only two organisms that have ever been reported to become resistant to Bt-toxin in 30 years of use as a pure insecticide, the BOSC wonders whether proportionally there are too many resources overall being allocated to the resistance question.

During the briefings on the biotechnology program, the BOSC discussed other social justice issues of biotechnology including the potential for countries, especially in the developing world, to become dependent on a few companies for their food production system, rendering such countries vulnerable to price increases or even embargoes. These are important issues of food security, which are recognized by the United Nations Declaration of Human Rights and other international legal instruments. In addition, countries in sub-Saharan Africa have refused food-aid from the United States during times of famine because they perceived a problem with the safety of the crops and because they worried that farmers might be unable to trade with the European Union if grain bins became contaminated with GM-products. Another issue is the perception that organic farmers cannot assure that their produce is free from GM-pollen and GM-proteins because of the possibility of cross-hybridization with genetically modified crops. It was stated that it is not EPA's role to regulate intellectual property, global trade, or food security impacts. It is the role of the U.S. Department of Agriculture (USDA) to regulate organic food and the responsibility of the World Trade Organization to oversee trade. However, the BOSC asks that EPA and ORD be aware and sensitive to such concerns as they develop research products, interact with other Federal agencies, and communicate risks to the public, including the public beyond our Nation's borders.

In conclusion, members of the BOSC believe that EPA ORD is on the right track and making good progress with its Biotechnology Research Program. The BOSC is pleased to provide advice on this important initiative and is available to provide further information on this report as required.

Sincerely yours,

A handwritten signature in black ink that reads "James H. Johnson, Jr." The signature is written in a cursive style with a large, prominent initial "J" and a clear "jr." at the end.

James H. Johnson, Jr.
Chair, Board of Scientific Counselors