BIO
BIOTECHNOLOGY
INDUSTRY ORGANIZATION

February 24, 2009

FIFRA Advisory Panel
Environmental Protection Agency
1200 Pennsylvania Avenue, NW
Washington, DC 20460-0001

Re: Comments to the FIFRA Scientific Advisory Panel for its February 25-27, 2009 meeting

The Biotechnology Industry Organization (BIO) is pleased to submit these comments in response to the public notice regarding the February 25-27 meeting of a Scientific Advisory Panel (SAP) on **Scientific Issues Associated with the Data Required to Register Plant-Incorporated Protectants**. BIO appreciates the opportunity to provide input to the SAP as it discusses data requirements for the registration of PIPs.

BIO is the world's largest biotechnology organization, providing advocacy, business development, and communications services for more than 1,200 members worldwide. BIO members are involved in the research and development of innovative healthcare, agricultural, industrial, and environmental biotechnology technologies. We also represent state and regional biotechnology associations, service providers to the industry, and academic centers. BIO members provide technology and seed products for a significant part of the agricultural biotechnology industry, and in particular, BIO members have pioneered in the development of crops that can resist insect predation and disease, including those regulated by EPA as Plant Incorporated Protectants (PIPs).

Nature and traditional plant breeders have given us many varieties of plants that are able to protect themselves from insects, viruses and other enemies. Over the past twenty-five years, using the techniques of modern biotechnology, scientists have been able to modify or "genetically engineer" commodity crops such as corn, cotton, soybeans and canola to express a pesticidal substance in the plant itself in order to protect the plant from harmful insect pests. The pesticidal substance is typically a protein that originates in nature and is harmful only to a narrow range of target pests. With the active support of BIO and its food and agriculture member companies, these innovative new products are regulated by three separate federal agencies to ensure

that they are as safe to grow and as safe to eat as conventional crops. Plants with pest resistance traits are also being developed for non-food uses.

Plants expressing pesticidal substances have been safely tested in the field under EPA and USDA permits since 1986, and have been cleared numerous times for commercial use following review by EPA, USDA and FDA since 1995. Although subjected to intensive governmental, academic, and commercial monitoring and oversight, not a single instance of actual harm to health, safety, or the environment has ever been confirmed for any biotechnology-derived crop that has satisfactorily completed the U.S. regulatory process. In 2008, the total number of biotechnology-derived crops, including those with PIPs, increased to 125 million hectares, and these crops are now being grown safely in 25 countries worldwide.

BIO's members have always provided EPA with all required information pertaining to PIPs, at both the experimental field test stage and pursuant to product commercialization. Moreover, these companies intend to continue to provide such information as long as EPA deems it necessary. BIO simply asks that the EPA's data requirements are appropriate for PIPs and reflect the Agency's long experience with the safe field testing and commercialization of these products.

Risk Assessment

The charge of the SAP is to advise EPA in the creation of rules governing data requirements for PIPs. The purpose of the rules themselves is to improve the EPA's ability to perform appropriate human health and environmental risk assessments for PIPs and thereby make better regulatory decisions regarding these crops.

Traditionally, "risk" is quantified in the following equation:

RISK = HAZARD * EXPOSURE

Risk is therefore the function of two factors, an identified hazard and the extent and likelihood of exposure. In risk assessment, it is crucial that hazards be precisely and correctly identified and defined, and that exposure be quantified using the best science available.

The Agency must first identify harms over which it has a statutory mandate to prevent or mitigate. BIO reminds the agency that a mere impact is not a hazard. For example the discussion of gene flow in the guidelines implies that gene flow itself is a hazard.

Gene flow is, in fact, a natural process that has been taking place since the first organisms capable of sexual reproduction evolved. It is a neutral process with no inherent hazard. Even if gene flow resulted in a sexually compatible wild species' acquisition of a PIP trait, the Agency must still establish that such acquisition is actually harmful. To properly assess risk, the Agency must identify true hazards, that is, things causing actual harm. Then the Agency must determine how, if at all, crops with PIPs could cause such harm. If no link can be drawn between a regulable harm and a PIP, then there is no justifiable need for data collection regarding that harm.

If a link can be made between a specific harm and a PIP, the Agency must then determine the exposure to that harm, including any means by which the registrant proposes to reduce exposure. As the Agency knows, USDA/APHIS regulates field tests of biotechnology-derived plants, including those with PIPs, and a key determining factor in the risk assessment performed by USDA is whether a permit applicant has demonstrated that sufficient confinement measures will be used to prevent the plant from escaping the field test and persisting in the environment. Demonstrated confinement therefore reduces the exposure component of the risk assessment equation to insignificance and concomitantly reduces any identified risks. It is therefore unnecessary for EPA to require registrants to develop and submit extensive data regarding the environment surrounding a proposed planting of a PIP crop if the registrant demonstrates adequate measures to prevent the surrounding environment's exposure to the crop.

In summary, the proposed rules must avoid needless data collection and submission by registrants. Because the stated object of the rule is to assist the agency in making regulatory decisions regarding PIPs, any extraneous information, that is, data not addressing significant risks identified by the agency, simply wastes registrants' and agency time and resources. The processing and analysis of such data prolongs and delays agency decisionmaking and increases the chances for error. Even worse, unreasonable and inappropriate data collection requirements stifle future efforts to develop what is already proven to be a safe and valuable technology and functionally denies access to the technology.

Scope of the guidance

Although current PIP crops are almost all agronomic row crops, such as corn and cotton, such will not always be the case. Already there are varieties of squash, papaya, and plum that have been genetically engineered to be virus resistant, and many more PIP crops are under development. The Agency should have a broad focus on a wide

variety of crops, including specialty crops, perennials, and woody species, such as trees. Considering the amount of effort that will be invested in the promulgation of these rules, the Agency should ensure that the rule development process solicits input from the broadest range of stakeholders possible, and any rules and additional guidance produced must be flexible enough to accommodate a wide variety of genetically engineered crops. Lack of flexibility in the rule will unduly hinder the development of valuable crops other than agronomic crops, and inevitably force the Agency to repeat this regulatory drafting process in the future to account for these crops.

Flexibility can be further built in to the regulations by focusing on specific risk assessment questions that must be answered by the registrant, rather than by creating an arbitrary list of studies to be completed or data to be submitted. This approach will reduce unnecessary work, time, and expense, and allow the registrant and the Agency to focus on information that most directly addresses the key questions and most efficiently assists Agency decisionmaking.

Specific data requirements

The Agency addresses information in regards to novel proteins produced by PIP crops, and several suggestions are made as to the use of bioinformatics to analyze protein sequences and determine similarities to known allergens and toxins. BIO strongly suggests that any requirements regarding bioinformatics data and its analysis be based on the most current, accepted science. Because bioinformatics is a rapidly developing field and bioinformatics databases are constantly expanding, researchers are continuously looking into new ways to use this data, and new studies are published every week. However, the fact that a new use is proposed in the scientific literature does not mean that such a use is accepted science. For example, although it is technologically possible to sequentially search short amino acid sequences in proteins to identify putative epitopes, the value of such searches for determining protein allergenicity is largely theoretical. Similarly, there are numerous databases containing protein sequence information, but the data in these databases is not of consistent quality or utility. Some databases are not updated on a regular basis or may contain duplications. Each database may have its own criteria for the amount of supporting scientific evidence needed for including a particular protein sequence in the database. Errors in the databases are difficult to detect and may not be quickly corrected once found. For these reasons, BIO supports the approach submitted to the Agency by the International Life Science Institute's Protein Allergenicity Technical Committee, for the analysis of protein amino acid sequences.

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BIO appreciates the opportunity to provide comments at this early stage in the rulemaking process and looks forward to working with EPA in the months ahead.
Sincerely,

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