ISB NEWS REPORT

COVERING AGRICULTURAL AND ENVIRONMENTAL BIOTECHNOLOGY DEVELOPMENTS

JANUARY 2003

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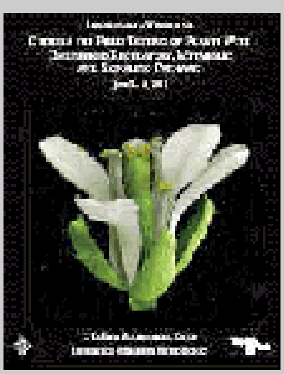

SPECIAL ISSUE

ISB sponsored a workshop on Criteria for Field Testing of Plants with Engineered Regulatory, Metabolic and Signaling Pathways in Washington, DC, on June 3 – 4, 2002. The workshop promoted a multi-disciplinary discussion about field testing and management of plants that contain the "newer," more complex genes emerging from plant genomics projects. The Executive Summary of the workshop is reprinted here. ISB is publishing a proceedings of the workshop that will be available at no charge. If you are interested in receiving a copy of the proceedings, you may sign up online at http://www.isb.vt.edu.

ISB WORKSHOP ON CRITERIA FOR FIELD TESTING OF PLANTS WITH ENGINEERED REGULATORY, METABOLIC, AND SIGNALING PATHWAYS

EXECUTIVE SUMMARY

L. LaReesa Wolfenbarger and Rebecca Grumet

Introduction and Purpose of Workshop

The rapidly growing number of field trials of transgenic plants reflects the rich diversity of types of genes and phenotypes becoming available for genetic engineering through plant molecular biology and genomics efforts. Increasingly, genes used in genetic engineering affect gene expression, metabolism, or signaling pathways and so may also have secondary effects on plant physiology due to pleiotropy or epistasis. These types of plant genes are used to engineer a variety of phenotypic changes, including altered growth and development (e.g., altered flowering, fruit ripening, growth rates, yield), modified metabolism, increased tolerance to environmental stresses (e.g., frost, drought, salt), or novel disease resistances (e.g., viral, bacterial or fungal). The use of these "newer genes" contrasts with the first wave of commercialized transgenic crops, which predominantly utilized genes whose direct gene product (e.g., specific protein) conferred the desired trait of interest and in which the potential for pleiotropic or epistatic effects was more likely to be a result of position effects rather than gene function.

As useful genes emerge with more complex effects, identifying secondary effects and evaluating their consequences become integral components of biosafety assessments. Field testing of these products is the first regulatory challenge as plants with engineered transcriptional control, metabolism, and signaling pathways are developed for commercial use.

THE ISB NEWS REPORT

The material in this News Report is compiled by Information Systems for Biotechnology, funded as the National Biological Impact Assessment Program by a grant from USDA/CSREES to Virginia Tech. Any opinions, findings, conclusions, or recommendations expressed in this publication are those of the author(s) and do not necessarily reflect the view of the US Department of Agriculture or of Virginia Tech. The News Report may be freely photocopied or otherwise distributed with attribution.

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ISB welcomes your comments and encourages article submissions. If you have a suitable article relevant to our coverage of the agricultural and environmental applications of genetic engineering, please email it to the Editor for consideration.

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This two-day workshop brought together regulators and industry and academic scientists from various disciplines to discuss and evaluate current knowledge and research on secondary effects of transgenes that function as transcription factors, in signal transduction, or to modify metabolic pathways. The workshop focused on examples and commercially-promising case studies to promote information exchange and discussion of data and experiments on secondary effects of these genes. We sought to evaluate the information that is available and to identify areas that would benefit from additional research. In particular, secondary effects that could alter confinement, including the propensity for gene flow to wild populations and adjacent, nontransgenic crops, were discussed. The collective knowledge and insight coming from this workshop should be valuable to those who develop these products for commercial purposes and to those who make regulatory decisions on field testing criteria of future transgenic plants.

Four formal objectives for the workshop were:

(1) to promote a multidisciplinary discussion about field testing releases and management of newer, more complex genes emerging from plant genomics projects among geneticists, plant breeders, biotechnologists, physiologists, and ecologists from government, industry, and academia;
(2) to evaluate current standards for gene characterization and identification of secondary effects with respect to newer, more complex genes emerging from plant molecular genetic and genomics projects;
(3) to discuss whether emerging genes and the phenotypes they affect present any new environmental issues relevant to field testing releases and management; and
(4) if data or research gaps appear to exist, to discuss what additional data and experiments would identify secondary effects that may impact field testing releases of transgenes that affect metabolic or signaling pathways.

To accomplish these goals, the program consisted of a series of plenary talks followed by a day of discussion in small breakout groups.

Overview of Plenary Talks

The first set of plenary talks focused on presenting an overview of field testing of engineered plants from several perspectives to provide participants with the context of how field testing is regulated, the approach industry uses to conduct field testing, and the biological factors that may impact field testing.

Dr. Dave Heron (USDA-APHIS) provided information on how field testing is regulated by USDA. APHIS authorizes field testing through either a permit process or a notification process. Notifications use a simplified process for plants that are not noxious weeds, and six criteria must be met to be eligible for a notification procedure; whereas permits are used for any organism or trait but require more details, for example, on how biological containment is attained. The performance standards for field tests are intended to ensure biological containment so that the transgenic article will not persist in the environment. Notifications and permits occur with State concurrence and require field data reports within six months after the field test ends. Both may have site inspections. Any unusual occurrences (i.e., accidental release, plants destroyed by disease or other causes) must be reported to APHIS. Lack of regulatory compliance is subject to penalties of up to $500,000. Dr. Heron pointed out that more than 8,700 field tests have been authorized at approximately 30,000 sites since 1987, and no serious negative impacts on the environment have been reported. More than 36 species of crop plants, 10 species of grasses, 14 species of trees, and 9 species of ornamentals have been field tested since 1987.

Dr. Chuck Mihaliak (Dow AgroSciences) and Dr. James Astwood (Monsanto Co.) described the approach used by industry to prepare for and conduct field testing. Dr. Mihaliak focused on a general framework of how industry develops products. Broadly, the development stages progress from generating, selecting, and characterizing events to launching the product. Each successive step involves screening products for desirable and undesirable characters. The safety of biotech products is established through evaluating gene, protein, and crop safety criteria that include ecological and human/animal health assessments. Dr. Astwood focused on safety assessments of metabolically altered plants and used two case studies—high carotenoid *Brassica napus* and amino acid enhancement in corn—to demonstrate his points. He illustrated how industry applied the concept of relative safety to evaluate food/feed safety, and in particular he focused on the approach to evaluate intended and unintended alterations of metabolites. Pre-existing natural variability is a key component for safety assessments because it provides the context for examining any intended or unintended alterations. Analyzing the targeted metabolic pathway can generate hypotheses that can be tested. He posed questions that could lead to insights when manipulating pathways: What, if altered, would be a concern? What is likely to be altered, and would it be a concern? What is actually altered? As in the case of high carotenoid *Brassica*, other species can serve as points for comparison.

Two speakers, Drs. Steve Strauss (Oregon State University) and Allison Snow (Ohio State University), outlined biological issues of importance for field testing. Dr. Strauss offered five contentions on the biological impacts of transgenes that affect regulatory, metabolic, and signaling pathways. First, he contended that although, as a class, these are less well known, they are far safer than the first generation transgenes. Second, molecular biology would not provide general guidance on the potential for invasion, but rather phenotypes, fitness, and nutrition would be the most important criteria. Third, pleiotropic effects may alter development and are the rule in breeding, but these should not be equated with the potential for invasiveness. Fourth, the low frequency of transgenes present in small-scale field tests should minimize the spread of a transgene for most genes that alter existing regulatory, metabolic, or signaling pathways. And lastly, genes that affect pathways will rarely improve fitness in wild populations. Dr. Snow described the changes in plant development and morphology that could alter gene flow and plant fitness. In particular, she focused on how gene flow and plant persistence could be affected by changes in pollen (amount, longevity, dispersal distance, and degree of outcrossing); in seeds (number, longevity, dispersal distance through attractiveness to pollinators or through aerodynamics); and from the extent and dispersal of vegetative propagation. She noted that uncertainties remained about isolation distances needed for containment due to the fact that pollen dispersal is highly variable and that a small fraction of pollen or seeds may travel very long distances.

The second set of plenary talks examined examples of plant genetic engineering involving metabolic traits, signal transduction factors, and transcription-associated factors. In each case, the speakers also explored what is known about secondary effects associated with expression of the genes in question.

Dr. John Ohlrogge (Michigan State University) described two examples of metabolic engineering of fatty acids: high oleic soybean and high laurate canola. High oleic soybean oil, which could provide direct health benefits by reducing the levels of saturated and polyunsaturated fats in our diet, was achieved via suppression of the 18:0 fatty acid desaturase, while production of laurate, which is used for soaps and surfactants, was achieved in canola via expression of a 12:0 acyl-ACP thioesterase derived from the California Bay tree. Engineering for production of lauric acid showed that increasing levels of the 12:0 acyl-ACP thioesterase produced increasing laurate concentrations up to approximately 40% of the oil content, but had diminishing ability to increase laurate content above that point. Analysis of the inability to exceed the 40 – 60% plateau showed that, while making more thioesterase and laurate, the plants were not accumulating more laurate. High acyl-

ACP thioesterase activity was associated with induction of at least two enzymes involved in fatty acid degradation. Several enzymes involved in fatty acid synthesis also were increased. Thus, accelerated fatty acid synthesis occurred to compensate for losses due to breakdown, resulting in a futile cycle of production and oxidation of lauric acid. Microarray analysis showed changes in gene expression, including some encoding predicted fatty acid-associated enzymes, as well as other types of proteins, including putative transcription factors possibly involved in controlling expression of fatty acid synthesis enzymes. Overall, less than 1% of genes analyzed showed altered expression, indicating specific cellular response to altered fatty acid production rather than wholesale changes. The level of change can be contrasted with variations in gene expression as high as 30% at different stages of leaf development. The results indicated that it is possible to achieve metabolic changes, but such modification also can cause compensatory changes by the plant, including adjustments in both metabolic activity and gene expression.

Drs. Harry Klee (University of Florida) and Peter McCourt (University of Toronto) examined the manipulation of hormone and signal transduction pathways. Harry Klee discussed alterations in ethylene synthesis and perception. Controlled ability to induce ethylene production can be of value for increased post-harvest fruit quality in which ripening is ultimately desired, whereas inhibited perception of ethylene can be of value where indefinite delay of senescence (e.g., floral senescence) is desired. Induction of ethylene perception was associated with an array of undesirable secondary ethylene-related effects, including increased disease susceptibility to specific pathogens, reduced adventitious root formation, reduced ability of roots to penetrate soil, reduced ability to develop mature seeds, and reduced ability of stems to elongate in response to low light conditions. These phenotypes are consistent with the broad range of functions associated with ethylene action. Thus, although it is possible to make ethylene-insensitive plants, negative consequences may severely impair performance and competitiveness. Ethylene responses can show clear cell autonomy, indicating that tissue- or developmental-specific promoters may assist in targeting appropriate specificity for desirable ethylene insensitive phenotypes.

Peter McCourt examined the role of plant hormones on coordination of development and interactions among signaling pathways. A screen for mutants involved in water use efficiency was performed by identifying individuals with increased abscisic acid (ABA) sensitivity. These mutants were then used to identify second mutations affecting ABA response. The resultant genes were not only involved in ABA processes, but also were related to ethylene, gibberellins, and sugar sensing. These results indicate a complex interplay among different signaling pathways and may explain why many hormones have overlapping functions. Dr. McCourt emphasized that the analysis of the genome is only the first level of understanding. The resultant proteome is much more dynamic, as protein expression changes during development and in response to environmental stimuli. The expressed proteins, in turn, form complex interactions with other proteins and other cellular components, as has been demonstrated by profiles of networks of yeast-interacting proteins. Ultimately, it is the total network that is responsible for phenotype.

Two speakers discussed transcription-related factors: Drs. Xinnian Dong (Duke University) and Mike Thomashow (Michigan State University). Dr. Dong examined host-pathogen interactions, with emphasis on two types of genes involved in the systemic acquired resistance (SAR) pathways, *cpr* and *npr*. Selective forces operate on both the pathogen and the host to achieve a balance between virulence and resistance and the associated costs of each. Resistance mechanisms involve many genes and a diversion of resources, so that in many cases resistance responses, such as SAR, are inducible, rather than constitutive. Microarray analysis indicates that SAR induction results in induction of hundreds of genes. Mutant *Arabidopsis cpr* lines constitutively expressing SAR have increased disease resistance but reduced growth, indicating metabolic costs of constitutive SAR expression. Overexpression of the NPR gene, which encodes a master regulator of transcription of SAR-related genes, does not cause constitutive SAR expression. Thus, overexpression of NPR leads to enhanced resistance without negative effects on growth. Experiments measuring fitness in the growth chamber and field also showed negative effects with constitutive expression of *cpr*, but not *npr*. However, only *cpr* overexpressors, but not *npr* overexpressors, reduced disease severity rating. Neither *cpr* or *npr* overexpression gave increased seed yield relative to controls, even in the presence of the pathogen. It was concluded that constitutive activation of SAR has substantial fitness costs that outweigh benefits of enhanced resistance.

Fitness effects of constitutive expression of normally inducible responses were observed with freezing tolerance responses as described by Dr. Mike Thomashow. Environmental stresses severely limit crop productivity, both in terms of where crops can grow and the yield potential at those locations. Adaptations to these stresses involved complex physiological responses, including the action of multiple genes. Microarray analysis showed cold temperature induction of ca. 200 *Arabidopsis* genes and down-regulation of approximately 100 more. One approach to increase resistance is regulon engineering, allowing for coordinated induction of a suite of relevant genes by expression of appropriate transcription factors. A promising transcription factor is CBF, which is rapidly induced by cold, and, in turn, induces a subset of ca. 40 of the cold-induced genes, including the COR (cold-regulated) genes. Overexpression of CBF causes constitutive expression of COR genes, a higher level of COR gene expression following cold induction, and increased freezing tolerance for both pre-acclimated and non-acclimated plants. Other stress-related responses such as increased proline and sugar accumulation also are observed with overexpression of CBF. CBF-induced genes are also associated with other dehydration-related stresses such as drought and salt stress, indicating similar underlying mechanisms of resistance to the different stresses. In another cited example (Park *et al.*, 2001), stress and pathogen resistance was correlated, suggesting cross-talk among responses. Despite increased resistance, there were negative effects on growth, indicating that inducible rather than constitutive activation of complex systems may provide fitness benefits. Once again, targeted expression, e.g., via the use of stress-responsive promoters, may be of value in engineering desired phenotypes.

Collectively the speakers gave insight into the types of genes being used and the types of phenotypes being regulated, and touched on several recurring themes demonstrating the interconnectedness of genetic, signaling, and metabolic pathways. Plants, like all living organisms, have evolved a complex web of cellular activities that produce and receive feedback from the internal and external environment. Manipulation of one aspect often results in alteration of several others, including compensatory changes. While this can cause secondary effects, the majority of those effects have negative impacts on plant growth and fitness. This range of phenotypes and their effects on fitness provide a backdrop for evaluation of possible implications for field testing of these classes of genes.

An additional point made by several speakers was that many of the traits we might manipulate today have been (or can be) altered by conventional methods and often using similar types of genes. For example, Dr. McCourt related that, although the specific gene product was not identified at the time, the short stature wheat and rice varieties critical to the Green Revolution were achieved through the use of naturally occurring gibberellin-insensitive mutants. Dr. Klee also discussed the wide range of phenotypes available in natural populations (such as in the cultivated and wild tomato species) and emphasized the importance of examining effects of genetic engineering efforts within the context of the natural range of genetic variation available by crossing.

Synthesis of the Group Reports

The groups were asked to respond to a list of questions developed prior to the workshop by its organizers. The discussion had two phases. The first phase of questions was intended to have groups address general issues associated with field testing of plants with engineered regulatory, metabolic, and signaling pathways. The second phase asked the group to answer questions specific to a particular case study. The six case studies focused the questions on the use of transcription factors (cold tolerance, disease resistance), on alterations in signal transduction (altered ripening, altered flowering), and on modifications to metabolic pathways (lignin/wood modification, oil modification).

General issues discussed

The general questions posed to the groups included the following:

1. Given the regulatory criteria of field testing, what biochemical, physiological, or phenotypic changes may impact confinement of transgenic plants? How might these changes be detected prior to field testing?

2. Do existing standards and methods for gene characterization and identification of secondary effects encompass monitoring these changes?

3. What are the strengths of the industry approach to characterize genes from plant genomics projects? Are there areas where the approach should be improved?

4. Do any new environmental issues relevant to field testing releases and management arise when considering emerging genes and the phenotypes they affect?

Most groups highlighted gross morphological changes as most likely to impact confinement of transgenic plants. Although biochemical changes or changes in gene expression may have predictive value, their use will depend on how much we know about traits that could impact field testing confinement. Most groups pointed out that biochemical changes or changes in gene expression would be less critical to monitor at this stage of product development, primarily because correlations among biochemical changes or changes in gene expression and traits that would significantly impact field testing are not well established yet. The key issue for detecting and observing changes that could impact field testing became "what is a significant change?" Understanding how an alteration fits within or outside the range of natural variation was a recurring theme for answering the question "what changes would be important to detect?"

The groups agreed that standards and methods for gene characterization and identification of secondary effects were largely adequate but there may be cases for which more information is needed. The altered flowering group in particular suggested that APHIS include a question to trigger an investigator to think about possible secondary effects (i.e., are you working on a trait that could alter confinement?) so that investigators begin to think about how their manipulation might affect confinement.

Groups also agreed that, as field trials progress to larger scales, the need to test a much broader array of traits is created.

Groups noted the strengths of the large biotech organizations: strong bioinformatics and databases to draw upon; multidisciplinary research groups; a conservative approach due to costs, liability, and product stewardship; and an awareness of consumer safety issues. Within the groups, industry representatives stated that industry should have the responsibility to make their scientists aware of the potential for secondary effects and should help academics or smaller companies with procedures or experimental designs that would facilitate the identification of secondary effects. One concern noted was the need for more transparency, although it was also noted that the balance between transparency and protecting intellectual property is a challenge for industry. Data generated are not always of interest to journals (i.e., crop variety development trials) and the current corporate culture may make it logistically difficult to publish.

Each group stated that these newer genes do not change current criteria for field testing, but that specific protocols (e.g., isolation distances) could be affected. Again the key is the effect on changes in pollen, seeds, flowering, and plant persistence and how these changes may compare to the range of phenotypic variability and affect fitness. For small field releases, the spread of genes may be more likely to occur when fitness is increased; however, it was noted that decreased fitness also may have unintended effects, and these may be a concern at larger scales of release.

Brief Summaries of the Case Studies
Questions directed to the particular case study included the following:

1. Does the case study gene/trait differ from currently commercialized genes/traits in ways that are relevant to regulatory criteria for field testing?

2. Is there evidence to indicate that engineering the pathway under consideration may produce effects (either directly or secondarily) that impact confinement of field trials

Altered flowering
A complex genetic network regulates the transition to flowering and involves ca. 80 genes in multiple pathways. Interplay among pathways activates key genes. The flowering regulatory system includes features such as quantitative regulation of gene expression, redundancy, suppression and promotion of floral transition, having related genes with opposite effects, and operation of transcriptional, post-transcriptional, and epigenetic regulation mechanisms. Current knowledge of genes that regulate floral transition comes from work with *Arabidopsis*. Data from a limited number of genes cloned from other species suggest that the function of some of these genes is conserved among divergent species. However, the extent to which function is conserved remains unknown.

Based on work in *Arabidopsis*, the altered flowering group noted that engineering with regulatory genes that control flowering could potentially produce unintended changes, including dwarfism, increased branching, altered growth, sex-altered flowers, and changes in nectary formation. These alterations could impact the movement of pollen and affect confinement, but only if these changes were unnoticed and if protocols for confinement were not already adequate.

However, although these changes were possible, the current regulatory criteria for producing altered flowering is no different than for commercialized transgenic products. Protocols to meet these criteria may need to be altered.

Oil modification
The oil modification group focused on two case studies that have already been deregulated, high oleic acid soybeans and high laurate canola and also discussed in general future

oil modifications to plants for producing better food or animal feed or for industrial use.

Given that most modifications to plants will not increase total oil levels dramatically, this group emphasized that plants engineered with changes in oil metabolism were unlikely to have altered fitness characteristics of significance to the regulatory criteria for field testing. They also pointed out that the use of tissue specific promoters, such as seed specific promoters, for the case studies they considered helps to focus the risk evaluation on categories that involve that particular site.

Cold tolerance

Engineering cold tolerance has been accomplished through a wide variety of means, including overexpression of enzymes (sorbitol synthase, superoxide dismutase) or of genes that regulate stress response pathways (CBF1). The group indicated that the production of stress tolerance traits through engineering pathways or the use of transcription factors raised no new issues for field testing, but also noted that the range of possible phenotypes, and therefore unpredictability, might be increased. Similarly, the group pointed out that the cold tolerance phenotype may be more likely to affect life history traits than phenotypes engineered with Bt endotoxins or current herbicide tolerance phenotypes.

While recognizing the potential for increased unpredictability and effects on life history traits, the group saw no need to alter the regulatory criteria, but noted that the procedures used to comply with the criteria may need a change of emphasis, depending on the familiarity with the phenotype and the crop. The group recommended drawing upon knowledge from traditional breeding and information about common molecular processes to provide evidence on what correlated changes might be likely and in need of monitoring during field testing.

Disease resistance

For both current products with disease resistance genes and those under development with signal transduction modifiers, the potential for enhanced persistence in the environment due to release from pathogen pressures will be a concern if gene flow occurs between disease resistant transgenic plants and their wild relatives. Alterations to pathways that produce broad disease resistance may provide a selective advantage to wild relatives, but evaluating this effect will depend on the biology of host – pathogen interaction of wild relatives. The group indicated that pleiotropic or epistatic effects associated with manipulating disease resistance pathways would be more likely to be detrimental, although they noted that changes that could impact confinement were not without possibility.

Lignin modification

Overall, the group agreed that field testing criteria for low-lignin transgenic plants would be similar to criteria for currently commercialized transgenic plants. The lignin biosynthesis pathway is of great interest given the importance of lignin for digestibility of forage crops, for conversion of lignocellulose for use as bioenergy products, and for wood quality and paper-making. Some lignin group members felt that metabolic or phenotypic changes in low-lignin transgenic plants would fall within the range of natural variability for that species, and therefore, at the field testing stage, would not be of any greater concern than changes resulting from conventionally-bred low-lignin plants. However, other members noted that lignin is ubiquitous in the plant body and therefore, by modifying its content, unexpected metabolic or structural effects, which impact confinement or non-target species, could occur.

Altered ripening

The plant hormone ethylene plays a critical role in a number of processes, including fruit ripening, seed germination, abscission, senescence, root formation, and disease resistance. Given the interconnectedness of ethylene action, secondary effects as a consequence of modifications to ethylene synthesis or response would be expected. The group highlighted as an example transgenic petunias expressing a mutated version of the ethylene receptor gene *Etr1*, which clearly exhibited altered patterns of ripening as expected. In addition, these plants revealed a number of secondary effects that reduced plant fitness, including reduced rooting of cuttings, increased incidence of disease, brittle stems, and prostrate growth habit.

Research Needed

Groups were also asked to discuss whether areas exist that would benefit from additional research and, if so, to suggest what data or experiments would address these areas. Each group included lists within their reports, but several recurring themes emerged from these lists. Several groups stressed the continued, basic study of these genes, their control, and their interactions as necessary for understanding secondary effects and for minimizing negative, unintended effects. Multiple groups suggested that a database of information detailing natural variation of characteristics related to gene flow could provide background against which to evaluate any observed changes. Lastly, groups indicated that research on minimizing gene flow and on understanding the consequences of gene flow was also needed. Suggestions included studies to validate current isolation distances and to investigate the use of gene excision technologies and their effects on confining pollen, as well as others.

Overall Conclusions

A recurring theme from all breakout groups was that phenotypes and not specific genes are ultimately the relevant criteria for field testing considerations. Although alterations in metabolism, signaling, or transcription may in turn bring about additional changes in gene expression or metabolic profiles, specific information about those changes is less important than the translation of those changes into relevant phenotypes such as those influencing flowering, pollen biology, or persistence properties. Thus, the use of these new genes per se does not appear to provide novel concerns for confinement. However, their potential for more broad-reaching effects should stimulate researchers to look beyond the primary expected phenotype when establishing field trials and the regulatory system. It was noted that at larger, pre-commercial stages of field testing, monitoring is already required for these and other traits. Several groups also indicated the importance of phenotypic context (i.e., is the observed phenotype within the range of naturally occurring variability for that trait in the domesticated species and wild relatives?), and establishing phenotypic ranges may be an area where additional information/research is needed for some crops.

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UPCOMING MEETINGS

More meetings can be found at: http://www.isb.vt.edu

ISB WORKSHOP

FUTURE DIRECTIONS AND RESEARCH PRIORITIES FOR THE USDA BIOTECHNOLOGY RISK ASSESSMENT RESEARCH GRANTS PROGRAM

June 9 – 10, 2003
Westin Embassy Row Hotel
Washington, DC

A stakeholder workshop will be held June 9 – 10, 2003, at the Westin Embassy Row Hotel in Washington, DC. The goal of this workshop is to evaluate existing and future scientific research needs for the risk assessment and risk management of agricultural biotechnology as authorized by the U.S. Congress. The workshop is co-sponsored by Information Systems for Biotechnology at Virginia Tech University, and the Biotechnology and the Risk Assessment Research Grants Program (BRARGP) at the Cooperative State Research, Education and Extension Service of USDA, and supported by USDA-APHIS, USDA-ARS, EPA and FDA.

The meeting will bring together scientists from diverse disciplines and government agencies that regulate agricultural biotechnology to discuss the research needs of the regulatory community; review the current science available to assess and to manage risks; and identify gaps in current and future research and prioritize strategies to fill them. The workshop discussions will be useful to those whose research addresses ecological risk assessment or management of transgenic organisms and to those who set research priorities, make regulatory decisions, or address public concerns regarding the use of genetically engineered organisms.

Two keynote presentations by Drs. Martina Newell-McGloughlin (University of California, Davis) and Val Giddings (BIO) will address "The Five Year Forecast for Plant and Animal Biotechnology: Trends and Emerging Products." Following the keynote speakers, the workshop attendees will divide into six breakout groups, organized according to taxa and risk categories: Animals (mammals and birds); Fish and Insects; Microorganisms (bacteria, viruses, fungi, recombinant live viruses); Plants—Impact and Management of Transgene Flow; Plants—Pest Resistance Development and Management; and Plants—

Non-target Effects (Bt-tolerant/herbicide-tolerant/ PHARMA plants).

BRARGP recipients from fiscal years 1997 – 2001 will present their research in a Poster Session scheduled at the end of the first day. Reports and recommendations from the breakout groups will be presented on the second day of the workshop. In addition, a short Grant-Writing Workshop session will be offered by representatives of the federal regulatory agencies.

For further information and to register for this workshop, please go to www.isb.vt.edu. For questions, please contact Ruth Irwin at: rirwin@vt.edu, 540-231-3747; or LaReesa Wolfenbarger at lwolfenb@vt.edu, 402-238-2723.

INTROGRESSION FROM GENETICALLY MODIFIED PLANTS INTO WILD RELATIVES AND ITS CONSEQUENCES

January 21 – 24, 2003
Amsterdam - The Netherlands

This conference, a sequel to the Assessment of the Impact of Genetically Modified Plants series, aims to summarize the current scientific knowledge on the ecological and evolutionary effects of introduction of GM cultivars by integrating and discussing current research on crop-wild relatives hybridization, introgression, and measuring and predicting its consequences, including monitoring aims and tools by identifying areas that need further elaboration. All scientists, plant breeders, regulatory (governmental) specialists, and policymakers involved in this field are invited to join this meeting to achieve broad consensus.

For information contact:
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Website: http://www.science.uva.nl/research/ibed/intro-gression

ASSESSING THE RISK FROM TRANSGENIC PLANTS: THE NEXT STEP FORWARD

February 3 – 4, 2003
Høvik (Oslo), Norway

This International Conference in Norway, hosted by The Norwegian Biotechnology Advisory Board, Det Norske Veritas, and The Directorate for Nature Management, proposes to stimulate a discussion on the potential and limitations of methods for assessing risks from genetically modified plants. The Conference is targeting industry representatives, NGO representatives, policy decision-makers, regulators, and scientists involved in biotechnology and risk management.

- Session 1 - Risk Perception in Society
- Session 2 - Risk assessment and GMOs
- Session 3 - Risk Assessment of GM Plants
- Session 4 - Identifying parameters of use in the risk assessment of GM plants
- Session 5 - Design and execution of an appropriate post-release monitoring system
- Session 6 - Round table discussion on risk assessments in theory and in practice

For information contact:
http://www.bion.no/risiko/index.shtml

AGRICULTURAL SCIENCE AGRICULTURAL BIOTECHNOLOGY: 20 YEARS ON

February 16 – 21, 2003
Ventura Beach Marriott, Ventura, California

Sessions will be held on:

- Agricultural Biotechnology: 20 years on
- Engineering Traits
- Insect Resistance
- Progress and Prospects - Genomics
- Technological Challenges to Transformation
- Technologies and Alternatives
- Technologies vs. Societal/Market Needs
- Safety and Public Acceptanc
- Public Perception and Societal Needs

Keynote addresses will be given by:

Eugene Nester: 25 years of Agrobacterium: From plant pathology to genetic engineering;

Norman Borlaug: Global Needs for Agricultural Biotechnology; and

Roger Beachy: Major technologies that may effect the next 20 years

For information contact:
Gordon Research Conferences
Email: grc@grcmail.grc.uri.edu
Telephone: 401-783-4011
Fax: 401-783-7644
http://www.grc.org/programs/2003/agsci.htm

CONFERENCE ON PLANT-MADE PHARMACEUTICALS

March 16-19, 2003
Québec City, Canada

The Conference will address present challenges and future benefits of plant-made biopharmaceuticals through in-depth discussions of relevant science, business, regulatory and stewardship issues. Participants are expected from the biotechnology sector, pharma industry, universities, regulatory agencies, governments, consumer groups and the press. The conference is co-hosted by manufacturers of protein-based drugs in plants with the cooperation of BIO, BioteCanada, and DIA, and sponsored by Québec and Canadian governments.

The Conference is organized and funded by the organizations that use plants to produce biopharmaceuticals.

For information contact:
CPMP 2003 Conference Secretariat
Email: info@cpmp2003.org
Telephone: 418-658-6755
Fax: 418-658-8850
http://www.cpmp2003.org

2003 INTERNATIONAL CONFERENCE ON AGRICULTURAL SCIENCE AND TECHNOLOGY (ICAST) TOWARD A SUSTAINABLE GLOBAL FUTURE

April 13 – 16, 2003
George R. Brown Conv. Center, Houston, Texas

The 2003 ICAST will bring together scientists, academics, government policymakers, and business and industry leaders from around the world with the goal of sharing knowledge, building consensus, and developing leadership to effect change for a common sustainable global future. The purpose of the conference is to effect debate intended to ensure that the rapid progress of science and technology fosters a balanced and equitable development of economies, environments, resources, communities and cultures throughout the world.

Invited Keynote Speaker is President of the United States, George W. Bush. Featured presentations will be made by Norman E. Borlaug and The Honorable Xu Guanhua. The Conference is organized by Texas A&M University System Agriculture Program and the City of Houston.

For information contract:
Dr. Douglas K Loh
Email: secretariat@2003ICAST.org
Telephone: 979-845-1553
Fax: 979-845-9749
http://www.2003ICAST.org

1ST INTERNATIONAL CONFERENCE AND WORKSHOP ON CHALLENGES OF GENETICALLY MODIFIED FOOD: A TECHNOLOGY TRANSFER CONCEPT OF GMOS

May 27 - 30, 2003
Cairo, Egypt

IMPORTANT NOTE: THIS CONFERENCE HAS BEEN POSTPONED FROM JANUARY 21.

The conference will focus on the following topics:

- GM food of plant origin
- GM food obtained from genetically modified animals or animals fed on genetically modified feeds
- GM impacts on: public health, environment, economics, society, and ethical considerations
- Technology Transfer of the detection of the GM food
- Local and international legislation
- International corporation

For information contact:
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laway@hotmail.com
http://www.scienceinafrica.co.za/events.htm#gm

7th International Congress of Plant Molecular Biology

June 23-28, 2003
Barcelona, Spain

The scientific programme will cover current topics in Plant Molecular Biology. Specific topics include:

- Development
- Hormone action
- Biotic and abiotic stress
- Genomics and postgenomics
- Gene regulation and signal transduction
- Biodiversity and evolution
- Molecular breeding
- Plant biotechnology and its social impact

For information contact:
ISPMB 2003 Congress Secretariat
Email: congress@aopc.es
Telephone: +34 93 302 75 41
Fax: +34 93 301 12 55
http://www.ispmb2003.com/index.htm

News and Notes

BRARGP FY 2003
Request for Applications

CSREES solicits applications for an estimated $3.0 million in grants for the Biotechnology Risk Assessment Research Grants Program (BRARGP). **Applications must be received by close of business March 5, 2003 (5:00 p.m. Eastern Time).**

The purpose of the BRARGP is to assist Federal regulatory agencies in making science-based decisions about the effects of introducing into the environment genetically modified organisms, including plants, microorganisms (including fungi, bacteria, and viruses), arthropods, fish, birds, mammals, and other animals excluding humans. Investigations of effects on both managed and natural environments are relevant.

New for Fiscal Year (FY) 2003:
As a result of the passage of the Farm Security and Rural Investment Act of 2002 (FSRIA), CSREES anticipates having twice the FY 2002 funds available to make BRARGP grants in FY 2003.

In accordance with the legislative authority in section 7210 of the FSRIA, "research designed to identify and develop appropriate management practices to minimize physical and biological risks associated with genetically engineered animals, plants, and microorganisms" will also be solicited by the BRARGP.

Applications may be submitted by any United States public or private research or educational institution or organization. Award recipients may subcontract to organizations not eligible to apply, provided such organizations are necessary to conduct the project. Applications will be evaluated by a peer panel of scientists.

CSREES and the Agricultural Research Service (ARS) of the U.S. Department of Agriculture jointly administer the BRARGP.

For information and forms, visit the BRARGP Homepage:
http://www.reeusda.gov/crgam/biotechrisk/biotech.htm

For questions, please contact:
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Editor's Note

Dr. A. Blum, Curator at http://www.Plantstress.com, has refuted the results of a report titled "Enhanced Resistance to Water Deficit Stress in Transgenic Tomatoes," which is printed in the December, 2002, issue of the *ISB News Report* (http://www.isb.vt.edu/news/2002/news02.dec.html #dec0206). Dr. Blum invites *News Report* readers to review his comments. Please see: "Flawed evaluation of drought resistance is still hampering transgenic research," at http://www.plantstress.com/admin/Files/ Hsieh_PlantPhysiol_130.htm.

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